The Lifetime Prevention Schedule

Establishing Priorities among Effective Clinical Prevention Services in British Columbia

Summary and Technical Report
March 2020 Update

An update of clinically preventable burden and cost-effectiveness estimates for all services reviewed to date.

BRITISH COLUMBIA

Acknowledgments

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Executive Summary

Background

The report, *A Lifetime of Prevention*, was published by the Clinical Prevention Policy Review Committee (CPPRC) in December of 2009.[1] A key goal of the CPPRC was to determine which clinical prevention services are worth doing in British Columbia (BC), culminating in a proposed Lifetime Prevention Schedule (LPS). Clinical prevention services were included on the LPS if they were considered to be effective, had a significant positive impact on population health and were cost-effective.

Clinical prevention services (CPS) are defined as:

> *Manoeuvres pertaining to primary and early secondary prevention (i.e., immunization, screening, counselling and preventive medication/device) offered to the general population (asymptomatic) based on age, sex and risk factors for disease and delivered on a one-provider-to-one-client basis, with two qualifications:*
>
> > *(i) the provider could work as a member of a care team or as part of a system tasked with providing, for instance, a screening service; and*
> >
> > *(ii) the client could belong to a small group (e.g. a family, a group of smokers) that is jointly benefiting from the service.*

This definition does not refer to the type of provider or the type of funding. This allows for the evaluation of the appropriate implementation of the service as a separate program planning matter.

Since 2009, a total of 29 CPS have been reviewed by the Lifetime Prevention Schedule Expert Committee (LPSEC) for potential inclusion in the LPS. Two updated reviews were concluded in 2020; screening all children at least once between the ages of 3 and 5 years to detect the presence of amblyopia or its risk factors and screening for hepatitis C in people born between 1945 – 1964.

Note that this document has a companion document, the *Reference and Key Assumptions Document*, in which all key model assumptions are recorded in one location.

[1] Clinical Prevention Policy Review Committee. *A Lifetime of Prevention: A Report of the Clinical Prevention Policy Review Committee*. 2009. Available at http://www.health.gov.bc.ca/library/publications/year/2009/CPPR_Lifetime_of_Prevention_Report.pdf. Accessed July 2017.

CPS Intervention Rate

Table ES-1 provides a one-page summary of the 29 CPS reviewed by the LPSEC to date. Included on the table are the relevant cohort and the frequency with which the service is to be provided. In addition, an estimated rate of coverage for the service in British Columbia and the best rate in the world is provided.

For example, the best available evidence suggests that screening for colorectal cancer is effective in the general asymptomatic population ages 50 to 74 (the relevant cohort). Ideally, screening should take place every 2 years using a fecal occult blood test (FOBT) or every 10 years using sigmoidoscopy (frequency). An estimated 50% of the relevant cohort in BC are currently receiving screening at this frequency (rate of coverage in BC). International evidence suggests that this rate could be improved to 76% (best rate in the world).

Table ES1: Potential Clinical Prevention Services in B.C.
Summary of the Applicable Cohort, Service Frequency and Coverage

Clinical Prevention Services	Cohort / Timing	Frequency / Intensity	Estimated Coverage B.C.	Estimated Coverage 'BiW'(1)
Screening for Asymptomatic Disease or Risk Factors - Children/Youth (C/Y)				
Vision screening for amblyopia	Ages 3-5	At least once	93%	93%
Screening for depression	Ages 12 - 18	Annually	Unknown	7.4%
Behavioural Counseling Interventions - Children/Youth (C/Y)				
Interventions to support breastfeeding	During pregnancy and after birth	Multiple sessions	Unknown	46%
Screening for obesity and referral to comprehensive, intensive behavioral intervention to promote improvement in weight status	Ages 6 - 17	Screening - At all appropriate primary care visits	Unknown	13%
		Management - At least one-time of >25 hours of contact over a 6 month period	>3% for C/Y with obesity	>3% for C/Y with obesity
Preventing tobacco use (school-aged children & youth)	Ages 6 - 17	Annually	Unknown	53%
Preventive Medication / Devices - Children				
Fluoride varnish	On primary teeth at time of tooth eruption (ages 1 - 5)	Every six months	Unknown	62%
Dental sealants	On permanent teeth at time of tooth eruption (ages 6 - 12)	4 times (on 1st and 2nd bicuspids & molars)	Unknown	59%
Screening for Asymptomatic Disease or Risk Factors - Adults				
Screening for breast cancer	Ages 50 - 74	Every 2 -3 years	52%	88%
Screening (cytology-based) for cervical cancer	Ages 25 - 69	Every 3 years	69%	88%
Addition of HPV-based cervical cancer screening	Ages 30 - 65	Every 5 years	0%	88%
Screening for colorectal cancer	Ages 50 - 74	FOBT every 2 years or sigmoidoscopy every 10 years	50%	76%
Screening for lung cancer	Ages 55 - 74 with a 30 pack-year smoking history	Annually for 3 consecutive years	Unknown	6%/60%
Screening for hypertension	Ages 18 and older	Screening - At least once every 2 years	Unknown	79%
Screening for cardiovascular disease risk and treatment (with statins)	Ages 40 -74	Screening - Once every 5 years	Unknown	48%
		Management - Ongoing	Unknown	30%
Screening for type 2 diabetes mellitus (T2DM)	Ages 18 and older - risk assessment	Every 3-5 years	Unknown	58%
	High risk for T2DM - blood glucose	Every 3-5 years	Unknown	80%
	Very high risk for T2DM - blood glucose	Every year	Unknown	80%
Screening for depression	Nonpregnant adults ages 18+	At least once	Unknown	12%
Screening for depression	Pregnant and postpartum women	At least once per birth by 8 weeks postnatally	Unknown	39%
Screening for osteoporosis	Females age 65	One-time	Unknown	58%
Screening for abdominal aortic aneurysm	Males age 65 who have ever smoked	One-time	Unknown	86%
Screening for Sexually Transmitted Infections and Blood Borne Pathogens - Adults				
Screening for human immunodeficiency virus	Ages 15 - 65	Low risk - Once	20%	45%
		Increased risk - Every 3 - 5 years		63%
		Very high risk - Every year		83%
		During all pregnancies	96%	97%
Screening for chlamydia and gonorrhea	Sexually active females 24 years of age or younger	When sexual history reveals new or persistent risk factors since the last negative test	Unknown	55%
Screening for hepatitis C virus	Adults born between 1945 - 1965	One-time	31%	83%
Behavioural Counseling Interventions - Adults				
Prevention of sexually transmitted infections (STIs)	All sexually active adolescents and adults who are at increased risk for STIs	30 min to ≥2 hours of intensive behavioral counseling	Unknown	29%
Counselling and interventions to prevent tobacco use	Ages 18 and older	Up to 90 min of total counseling time, during multiple contacts	19%	51%
Alcohol misuse screening and brief counseling	Ages 18 and older	Screening - Annually to at least once (every 10 years)	Unknown	35%
		Counseling - Up to 120 min of total time, during multiple contacts	Unknown	30%
Screening for and management of obesity	Ages 18 and older	Screening - Ongoing	Unknown	73%
		Management - At least one-time of 12 - 26 sessions in a year	Unknown	33%
Preventing falls	Community–dwelling elderly ages 65+	Screening for risk - Every year	Unknown	18%
		Exercise or physical therapy - At least 150 minutes of moderate intensity / week	Unknown	Unknown
		Vitamin D supplementation - 800 IU / day for at least 12 months	Unknown	61%
Preventive Medication / Devices - Adults				
Routine aspirin use for the prevention of cardiovascular disease (CVD) and colorectal cancer	Age 50 - 69 with a 10% or greater 10-year CVD risk & at low risk of bleeding	Screening for CVD risk - At age 50 - 59	Unknown	33%
		Screening for bleeding risk - At age 50 - 59	Unknown	33%
		Management - Low-dose daily aspirin use for 10 years	Unknown	24%
Folic acid supplementation for the prevention of neural tube defects	Reproductive-age females	0.4 to 0.8 mg (400 - 800µg) of folic acid daily	Unknown	34%

(1) 'BiW' = best in world; (2) CPB = clinically preventable burden; (3) CE = cost-effectiveness

Summary of the Clinically Preventable Burden and Cost-Effectiveness

Table ES-2 also provides a one-page summary of the CPS reviewed by the LPSEC to date. Included on this table, however, is information on the clinically preventable burden (CPB) and cost-effectiveness (CE) associated with each of the maneuvers.

CPB is defined as the total quality-adjusted life years that could be gained if the clinical preventive service were delivered at recommended intervals to a BC birth cohort of 40,000 individuals over the years of life that a service is recommended. CE is defined as the average net cost per QALY gained in typical practice by offering the clinical preventive service at recommended intervals to a BC birth cohort over the recommended age range.

The *CPB* columns identify the clinically preventable burden (in terms of quality adjusted life years or QALYs) that is being achieved in BC based on current coverage, and the potential CPB if the best coverage rate in the world (BiW) is achieved. For example, if coverage for colorectal cancer screening were as high as the BiW (76%), we would expect a CPB of 1,189 QALYs. Since BC's coverage is at 50%, a CPB of 703 QALYs is being achieved. This is 486 QALYs short of the potential 1,189 QALYs achievable based on BiW coverage, as identified in the *Gap* column.

Note that coverage rates in BC are only known for 7 of the maneuvers reviewed by the LPSEC to date.

The *CE* columns identify the cost-effectiveness ratio associated with a service stated in terms of the cost per QALY. The ratio is given based on the use of a 1.5% and a 0% discount rate. For example, the cost/QALY associated with colorectal cancer screening in BC is estimated at $47,265, based on a discount rate of 1.5%. If a 0% discount rate is used, then the cost/QALY would be reduced to $44,213.

Table ES2: Potential Clinical Prevention Services in B.C.
Summary of the Clinically Preventable Burden and Cost-Effectiveness

Clinical Prevention Services	CPB(2) (0% Discount) B.C.	'BiW'(1)	Gap	CE(3) (% Discount) 1.5%	0%
Screening for Asymptomatic Disease or Risk Factors - Children/Youth (C/Y)					
Vision screening for amblyopia	2	2	0	$6,615,785	$541,075
Screening for depression (ages 12-18)	Unknown	222		$28,215	$27,331
Behavioural Counseling Interventions - Children/Youth (C/Y)					
Interventions to support breastfeeding	Unknown	5,002		($9,021)	($11,966)
Screening for obesity and referral to comprehensive, intensive behavioral intervention to promote improvement in weight status	Unknown	80		$77,441	$46,302
Preventing tobacco use (school-aged children & youth)	Unknown	4,123		($7,349)	($9,538)
Preventive Medication / Devices - Children					
Fluoride varnish	Unknown	150		$43,038	$43,038
Dental sealants	Unknown	157		($24,690)	($29,320)
Screening for Asymptomatic Disease or Risk Factors - Adults					
Screening for breast cancer	703	1,189	486	$19,720	$18,326
Screening (cytology-based) for cervical cancer	1,153	1,471	318	$25,542	$26,980
Addition of HPV-based cervical cancer screening	0	655	655	($21,556)	($19,264)
Screening for colorectal cancer	1,141	1,734	593	$47,265	$44,213
Screening for lung cancer	Unknown	1,745		$2,240	$2,080
Screening for hypertension	Unknown	11,587		$15,254	$10,760
Screening for cardiovascular disease risk and treatment (with statins)	Unknown	9,370		$3,223	$1,392
Screening for type 2 diabetes mellitus (T2DM)	Unknown	3,494		($3,121)	($3,453)
Screening for depression in general adult population	Unknown	-8		Dominated	Dominated
Screening for depression in pregnant and postpartum women	Unknown	109		$23,042	$10,140
Screening for osteoporosis	Unknown	91		($29,412)	($34,145)
Screening for abdominal aortic aneurysm	Unknown	340		$11,995	$9,973
Screening for Sexually Transmitted Infections and Blood Borne Pathogens - Adults					
Screening for human immunodeficiency virus	Unknown	360		$16,434	$16,434
Screening for chlamydia and gonorrhea	Unknown	143		$57,174	$53,410
Screening for hepatitis C virus	*	555		$3,170	$1,222
Behavioural Counseling Interventions - Adults					
Prevention of sexually transmitted infections (STIs)	Unknown	3,285		$10,267	$10,267
Counselling and interventions to prevent tobacco use	3,730	5,944	2,214	($1,863)	($3,344)
Alcohol misuse screening and brief counseling	Unknown	2,175		$23,607	$16,611
Screening for and management of obesity	Unknown	2,287		$12,160	$11,140
Preventing falls	Unknown	429		$35,213	$35,213
Preventive Medication / Devices - Adults					
Routine aspirin use for the prevention of cardiovascular disease (CVD) and colorectal cancer	Unknown	1,098		$2,302	$411
Folic acid supplementation for the prevention of neural tube defects	Unknown	95		$195,379	$113,155

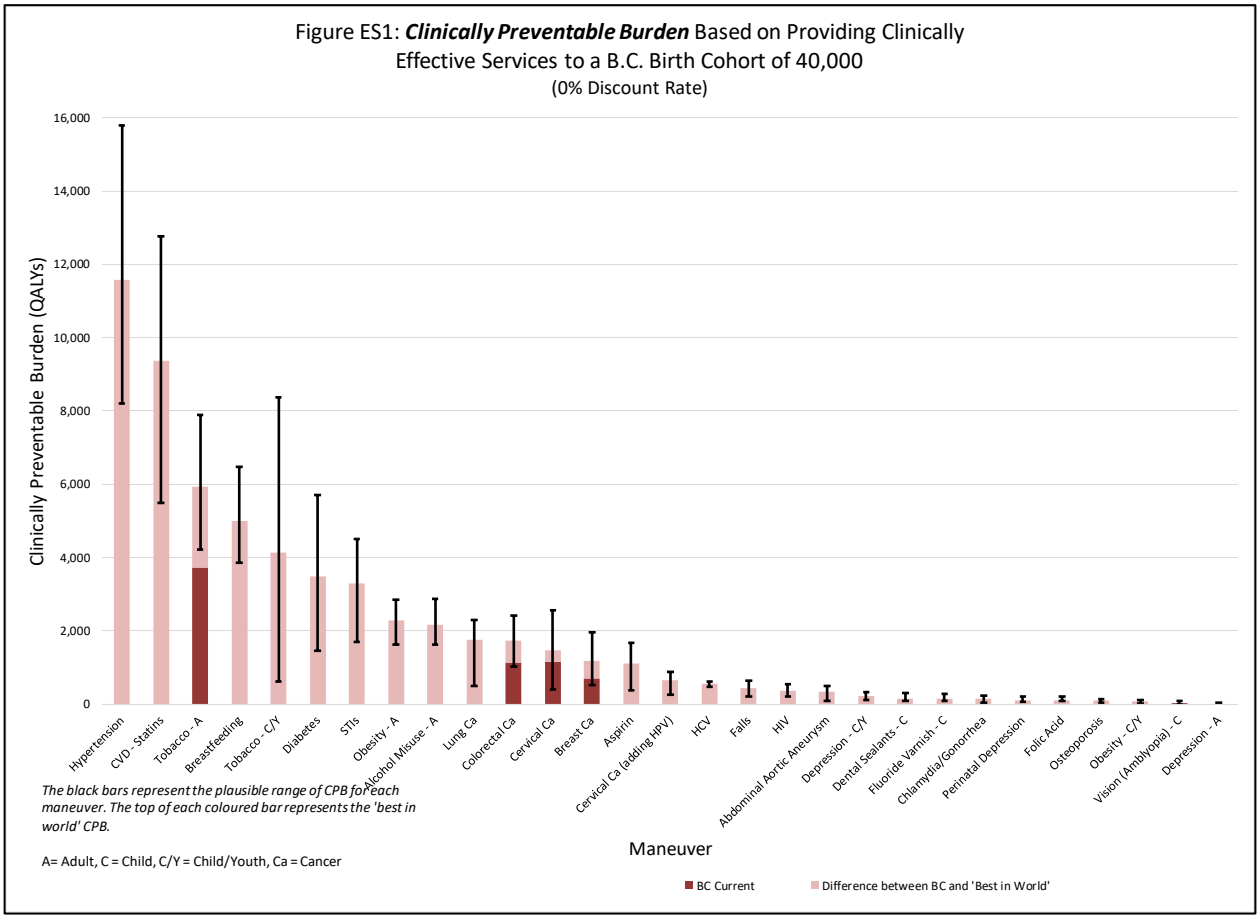
(1) 'BiW' = best in world; (2) CPB = clinically preventable burden; (3) CE = cost-effectiveness
** More than 31% of the 1945-1964 birth cohort in BC has been screened for hepatitis C. The CPB for this CPS is calculated based on the 1945 - 1964 birth cohort that has not yet been screened.*

Comparison by Clinically Preventable Burden

Figure ES-1 provides a summary of the CPB associated with each service. Results are displayed based on a 0% discount rate. Results based on a 1.5% discount rate are available in the body of the text. Using a 1.5% discount rate tends to reduce the CPB. The results are organized from left to right based on the services with the highest to lowest potential CPB. For example, full implementation of the service *hypertension screening and treatment* (Hypertension) (i.e., achieving levels that are comparable to the best in the world) would result in a CPB of 11,587 QALYs, the highest of any service reviewed.

For the six services for which BC coverage rates are known, we have indicated (by the darker bar insert) what proportion of the potential BiW rate is currently being achieved in BC.

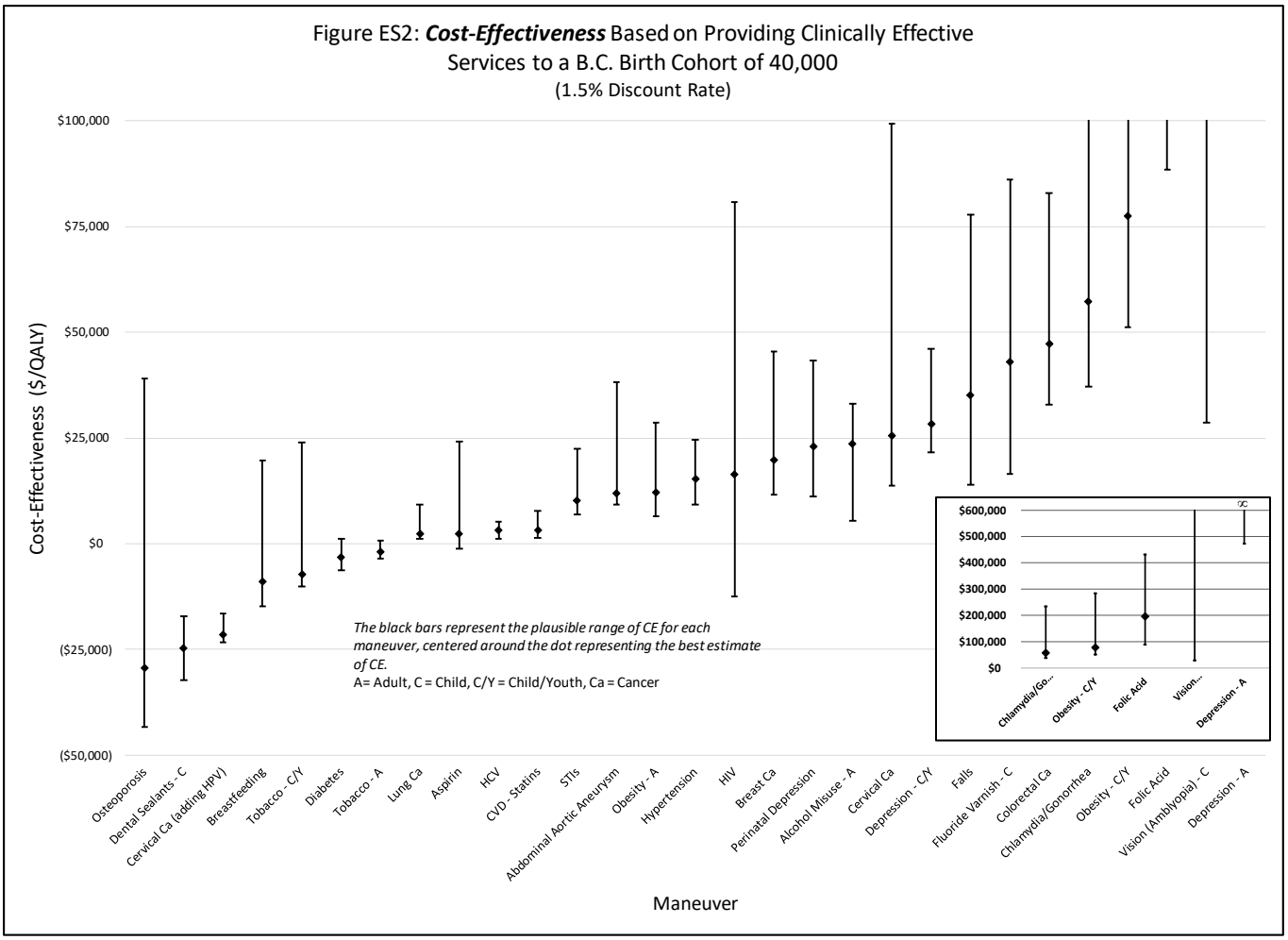
The black bars associated with each service represent a potential range in CPB based on one-way sensitivity analysis. That is, the range is based on varying (over a plausible range) the one assumption that has the largest effect on the results generated by the model. Simultaneously varying more than one assumption would increase the potential range. A larger range suggests a higher sensitivity to the assumptions used.



Note that the labels on the horizontal axis in Figures ES-1 and ES-2 refer to the CPS included in Table ES-1. The ‘A’ refers to adults, the ‘C’ to children, the ‘C/Y’ to children/youth and the ‘Ca’ to cancer.

Comparison by Cost-Effectiveness

Figure ES-2 provides a summary of the CE associated with each service. Results are displayed based on a 1.5% discount rate. Results based on a 0% discount rate are available in the body of the text. Using a 0% discount rate tends to improve the CE. Furthermore, the results are organized from left to right based on the services with the best to worst potential CE, including a plausible range for each service based on sensitivity analysis. *Screening for osteoporosis in women 65+* has the best CE result of any service reviewed. That is, this service is considered to be cost-saving, with a cost per QALY of -$29,412 (with a potential range from -$43,257 to $38,997). The chart inset shows the results for interventions with plausible ranges extending over $100,000 / QALY.



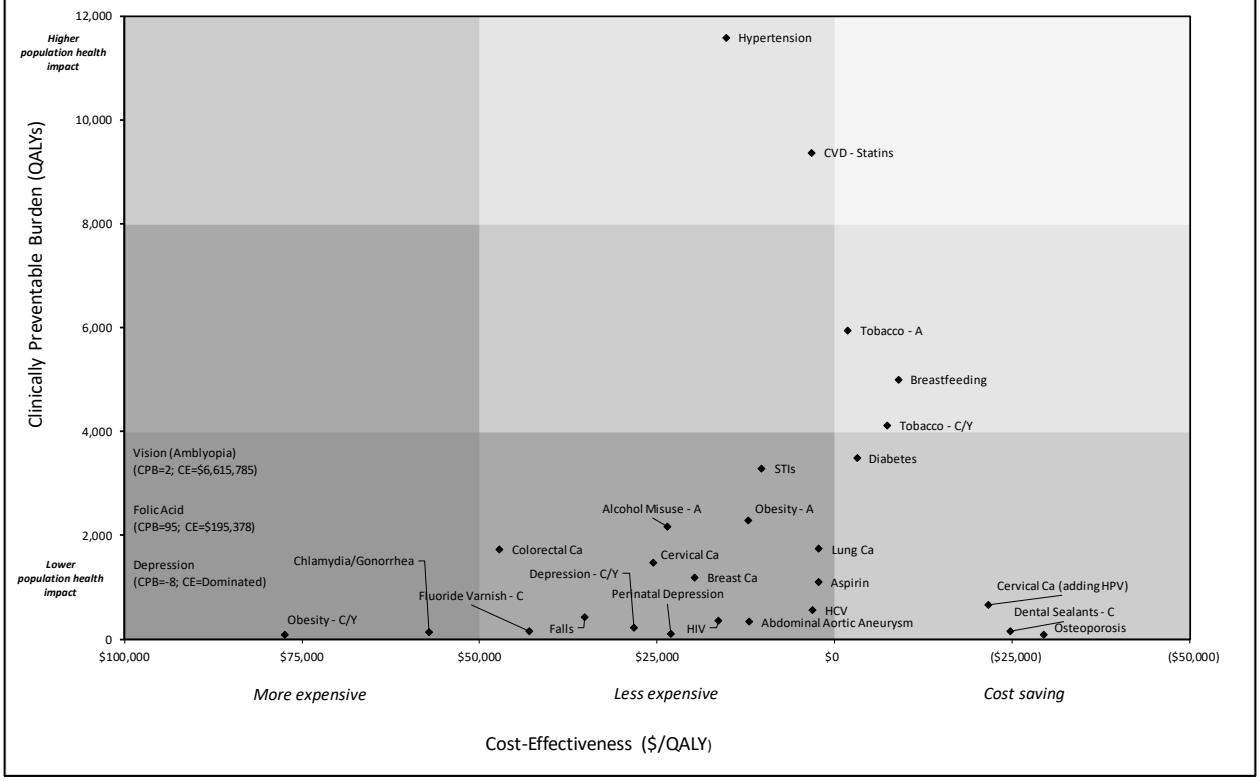
The base models include an estimate of costs associated with a person's time used in accessing the preventive service. The most significant effect of these inclusions/exclusions is seen in services that require frequent contact with health care providers, such as behavioural counselling to prevent alcohol misuse. For this service, the cost/QALY is reduced from $23,607 to $4,572 if patient time costs are excluded.

Combined Comparison Using CPB and CE

The results for CPB and CE are combined in Figure ES-3. CPB is on the vertical axis, ranging from 0 to 12,000 QALYs. CE is on the horizontal axis, ranging from $100,000/QALY at the intersection of the x- and y-axis to -$50,000 at the far right of the x-axis. By arranging CPB and CE in this manner, the most positive results are on the upper right of the chart and the least positive results are in the lower left of the chart. We also divided CPB into three equal segments as follows; 0 to 4,000 QALYs, 4,001 to 8,000 QALYs and 8,001 to 12,000 QALYs. CE was also divided into three equal segments as follows: $100,000 to $50,000 per QALY, $50,000 to $0 per QALY and $0 to -$50,000 per QALY.

The resulting nine equivalent segments are shown in Figure ES-3. Services in the upper right segment have the most favourable combination of CPB and CE while services in the lower left segment have the least favourable combination of CPB and CE.

Figure ES3: **Establishing Priorities Among Effective Clinical Prevention Services in BC**
Combining Clinically Preventable Burden and Cost-Effectiveness
Summary Results



In Figures ES-4 to ES-7, we have incorporated visual information on plausible ranges (based on one-way sensitivity analysis) with the point estimates for each service. To avoid overcrowding the above figure (ES-3), we have separated the services into four figures. Figure ES-4 includes services specific to children and youth, Figures ES-5 and ES-6 includes screening services for non-cancer and cancer conditions respectively, and Figure ES-7 includes the remainder of the services reviewed.

Figure ES4: **Establishing Priorites Among Effective Clinical Prevention Services in BC**

Combining Clinically Preventable Burden and Cost-Effectiveness
Summary Results for Children and Youth

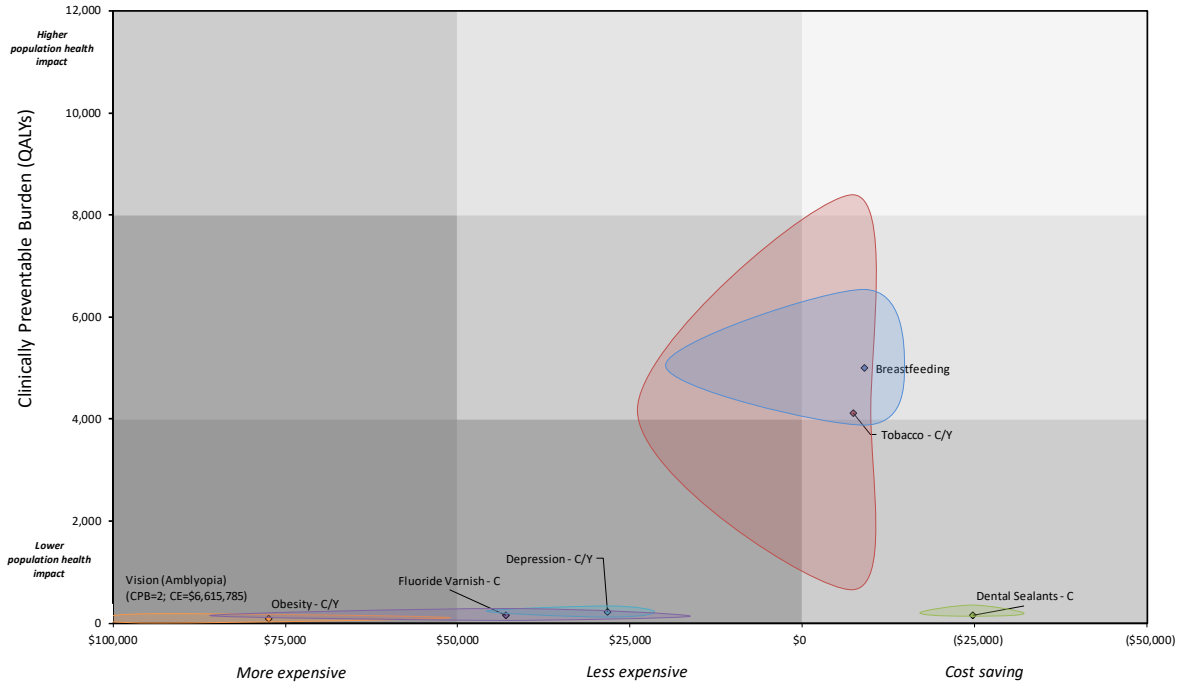


Figure ES5: **Establishing Priorites Among Effective Clinical Prevention Services in BC**

Combining Clinically Preventable Burden and Cost-Effectiveness
Summary Results for Non-Cancer Screening Maneuvers

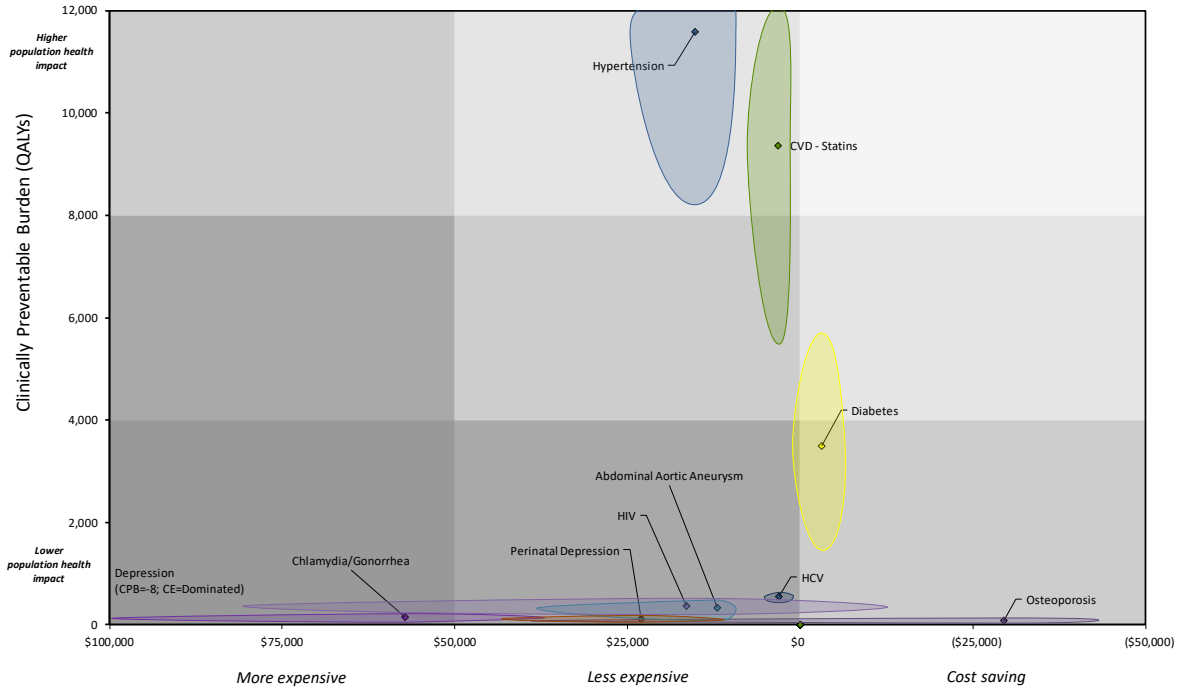


Figure ES6: **Establishing Priorites Among Effective Clinical Prevention Services in BC**

Combining Clinically Preventable Burden and Cost-Effectiveness
Summary Results for Cancer Screening

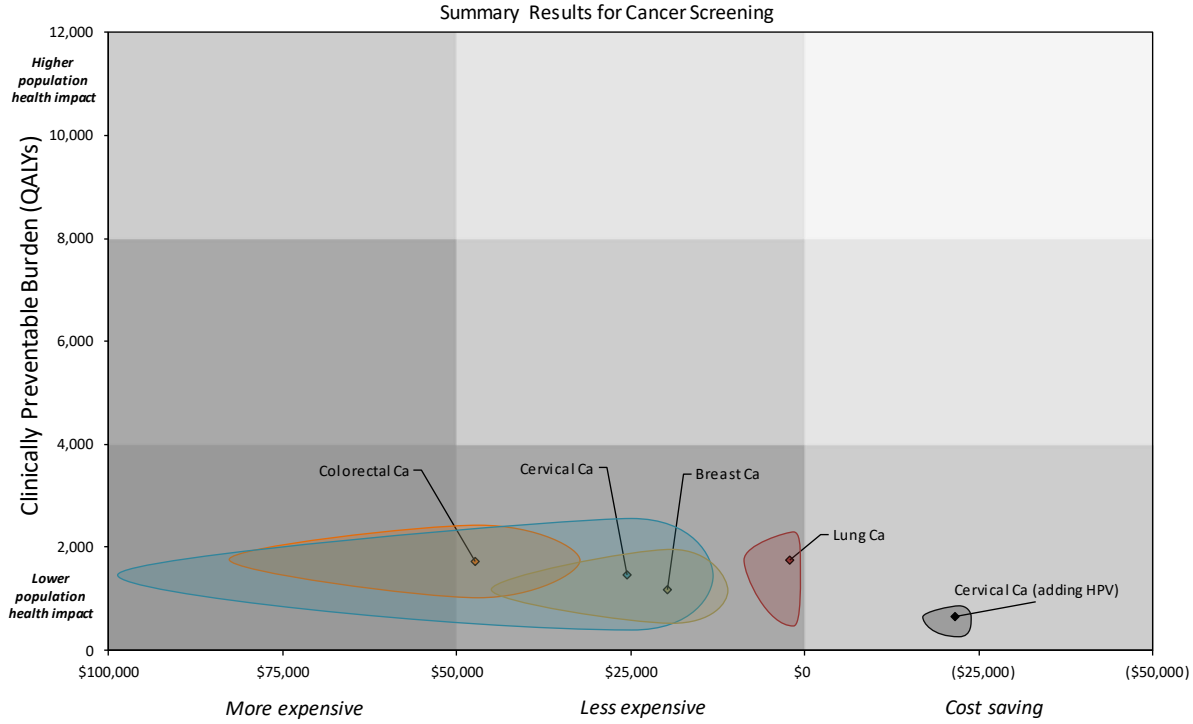
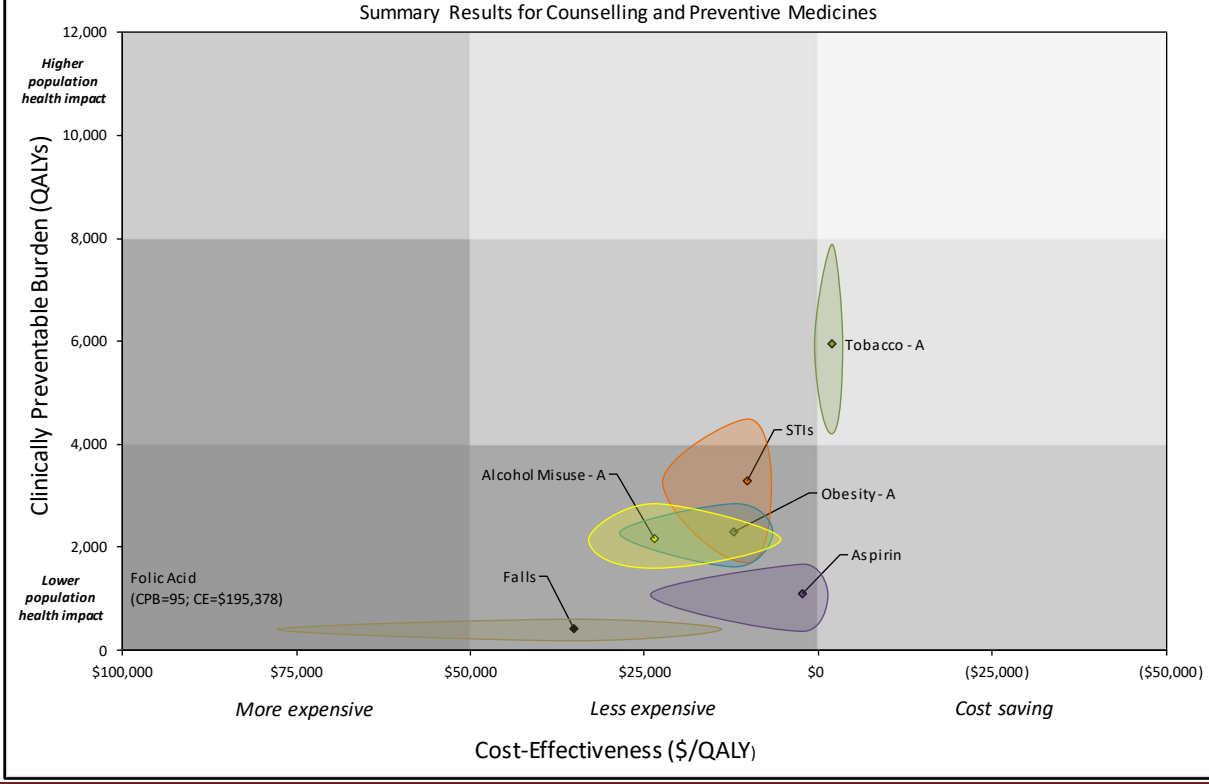


Figure ES7: **Establishing Priorites Among Effective Clinical Prevention Services in BC**

Combining Clinically Preventable Burden and Cost-Effectiveness
Summary Results for Counselling and Preventive Medicines



List of Abbreviations

AAA – Abdominal Aortic Aneurysm

AABR – Automated Auditory Brainstem Response

ABR – Auditory Brainstem Response

ACC – American College of Cardiology

AD – Anti-Depressant(s)

AD – Atopic Dermatitis

ADAM – Aneurysm Detection and Management

AHA – American Heart Association

apoB – Apolipoprotein B

ASA – Acetylsalicylic Acid

ASCVD – Atherosclerotic Cardiovascular Disease

AOAE – Automated Otoacoustic Emissions

AUD – Australian Dollars

AUDIT - Alcohol Use Disorders Identification Test

AUGIB – Acute Upper Gastrointestinal Bleeding

BC – British Columbia

BCEHP – British Columbia Early Hearing Program

BC-HTC – BC Hepatitis Testers Cohort

BDI – Beck Depression Inventory

BiW – Best in the World

BFHI – Baby Friendly Hospital Initiative

BMD – Bone Mineral Density

BMI – Body Mass Index

BMT – Bone Marrow Transplant

CAD – Canadian Dollars

CAGE – Cut Down, Annoyed, Guilty, Eye-Opener

CBT – Cognitive Behavioural Therapy

CCHD – Critical Coronary Heart Disease – also used for Critical Congenital Heart Defects

CCHS – Canadian Community Health Survey

CCS – Canadian Cardiovascular Society

CDC – Centers for Disease Control and Prevention

CE – Cost-Effectiveness

CHD – Coronary Heart Disease

CI – Confidence Interval

CIN – Cervical Intraepithelial Neoplasia

CLEM – Cardiovascular Life Expectancy Model

CMG – Case Mix Group

CPB – Clinically Preventable Burden

CPS – Clinical Prevention Service

CRC – Colorectal Cancer

CSS – Canadian Cardiovascular Society

CSVS – Canadian Society for Vascular Surgery

CTFPHC – Canadian Task Force on Preventive Health Care

CV - Cardiovascular

CVD – Cardiovascular Disease

DAA – Direct-acting antivirals

dB – Decibels

DSM - Diagnostic and Statistical Manual of Mental Disorders

DXA - Dual-Energy X-ray Absorptiometry

ES – Executive Summary

ETS – Environmental Tobacco Smoke

EVAR – Endovascular Aneurysm Repair

FASD – Fetal Alcohol Spectrum Disorder

FDA – Food and Drug Administration (US)

FIT – Fecal Immunochemical Test

FOBT – Fecal Occult Blood Test

FRS – Framingham Heart Study Risk Score

FTE – Full Time Equivalent

gFOBT – Guaiac Fecal Occult Blood Test

GBD study – Global Burden of Disease study

GI – Gastrointestinal

GP – General Practitioner

HBV - Hepatitis B virus

HCC - Hepatocellular Carcinoma

HCV - Hepatitis C Virus

HDL-C – High-Density Lipoprotein Cholesterol

HMO – Health Maintenance Organization

HPV – Human Papillomavirus

HR – Hazard Ratio

ICD – International Classification of Diseases

IR – Intermediate Risk

IQ – Intelligence Quotient

ISH – Intentional Self-Harm

LEEP – Loop Electrosurgical Excision Procedure

LDL – Low-Density Lipoprotein

LDL-C – Low-Density Lipoprotein Cholesterol

LHA – Local Health Areas

LRTI – Lower Respiratory Tract Infection

LPS – Lifetime Prevention Schedule

LPSEC – Lifetime Prevention Schedule Expert Committee

MASS – Multicentre Aneurysm Screening Study

MAST - Michigan Alcoholism Screening Test

MDD – Major Depressive Disorder

MEA – Middle Ear Analysis

MSP – Medical Service Plan

NHANES – National Health and Nutrition Examination Survey

NICE – National Institute for Health and Clinical Excellence

NSAID – Nonsteroidal Anti-Inflammatory Drug

NSDUH – National Survey on Drug Use and Health

NTD – Neural Tube Defect

NAT - Nucleic Acid Testing

OM – Otitis Media

OME – Otitis Media with Effusion

OR – Odds Ratio

OAE – Otoacoustic Emissions

PCHI – Permanent Childhood Hearing Impairment

PCI – Percutaneous Coronary Intervention

PCP – Primary Care Provider

PDC – Proportion of Days Covered

PHQ-A – Patient Health Questionnaire for Adolescents

PHSA – Provincial Health Services Authority

POS – Pulse Oximetry Screening

PSBC – Perinatal Services British Columbia

PWID - Persons Who Inject Drugs

QALY – Quality-Adjusted Life-Year

QoL – Quality of life

RCT – Randomized Controlled Trial

RNA - Ribonucleic Acid

RR – Relative Risk

SCID – Severe Combined Immune Deficiency

SF-36 – Short Form (Health Survey) with 36 items

SIDS – Sudden Infant Death Syndrome

SVR - Sustained Virologic Response

TC – Total Cholesterol

TEOAE –Transient Evoked Otoacoustic Emissions

TG – Triglycerides

TREC – T-cell Receptor Excision Circles

UK – United Kingdom

UKSAT – United Kingdom Small Aneurysm Trial

UNHS – Universal Newborn Hearing Screening

US – United States

USD – United States Dollars

USPSTF – United States Preventive Services Task Force

WHO – World Health Organization

Screening for Asymptomatic Disease or Risk Factors

Vision Screening for Amblyopia

United States Preventive Service Task Force Recommendations (2017)

> *Among children younger than 6 years, 1% to 6% have amblyopia or its risk factors (strabismus, anisometropia, or both). Early identification of vision abnormalities could prevent the development of amblyopia.*
>
> *The USPSTF recommends vision screening at least once in all children aged 3 to 5 years to detect amblyopia or its risk factors (B recommendation).*
>
> *The USPSTF concludes that the current evidence is insufficient to assess the balance of benefits and harms of vision screening in children younger than 3 years (I statement).*[2]

Canadian Task Force on Preventive Health Care Recommendations (1990)

In the 1990 publication on well-baby care in the first 2 years of life, the CTFPHC recommended that there was good evidence to include repeated examination of the eyes and hearing during the first year of life in the periodic health examination. This was given an 'A' recommendation.[3] Based on this information, vision screening was included in the BC Lifetime Prevention Schedule.[4]

Canadian Task Force on Preventive Health Care Recommendations (1994)

> *Once detected, simple refractive errors affecting visual acuity are readily treatable with eye glasses. However, evidence for the treatment of amblyopia is more controversial and inconclusive. It is widely held that for any potential benefit to be realized, amblyopia must be detected during the "sensitive" period, i.e. between birth and about the seventh year.*
>
> *Systematic screening for visual deficits has been found to decrease prevalence later.*
>
> *Fair evidence for inclusion in periodic health examination (B Recommendation).*[5]

The Canadian Task Force website does state: "Guidelines and other material from the Canadian Task Force on the Periodic Health Examination (1979-2006) are presented for informational purposes only. The material has not been reviewed or approved by the

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[2] Grossman DC, Curry SJ, Owens DK et al. Vision Screening in Children Aged 6 Months to 5 Years: US Preventive Services Task Force Recommendation Statement. *Journal of the American Medical Association.* 2017; 318(9): 836-44.

[3] Canadian Task Force on the Periodic Health Examination. Periodic health examination, 1990 update: 4. Well-baby care in the first 2 years of life. *Canadian Medical Association Journal*. 1990; 143(9): 867-72.

[4] Clinical Prevention Policy Review Committee. *A Lifetime of Prevention: A Report of the Clinical Prevention Policy Review Committee*. 2009. Available at http://www.health.gov.bc.ca/library/publications/year/2009/CPPR_Lifetime_of_Prevention_Report.pdf. Accessed August 2013.

[5] Feightner JW. *Canadian Guide to Clinical Preventive Health Care: Chapter 27: Routine Preschool Screening for Visual and Hearing Problems*. 1994. Available at http://canadiantaskforce.ca/wp-content/uploads/2013/03/Chapter27_preschool_visualhear94.pdf?0136ff. Accessed November 2013.

current Canadian Task Force on Preventive Health Care. It may not reflect current evidence or current standards of practice."[6]

In short, the Canadian Task Force on Preventive Health Care does not have a current recommendation on vision screening for children.

BC Early Childhood Vision Screening Program

In 2005, the BC Ministry of Health (MoH) announced its intention to screen all children in the province for vision disorders before they reached six years of age. This universal vision screening program was established with the goal of not only detecting amblyopia or its risk factors but also major refractive errors (e.g. myopia or nearsightedness, hyperopia or farsightedness and astigmatism).[7] The current model, based on evidence of effectiveness from the 2017 USPSTF review, only includes screening for amblyopia and its risk factors.

The Human Early Learning Partnership at UBC was asked to conduct an evaluation of the Vision Screening Program to track the program's effectiveness in achieving the provincial goal established by the Ministry of Health. The results of the evaluation were published in 2012, and form the basis for much of our modeling.[8]

What is Amblyopia

Amblyopia is a "functional reduction in visual acuity characterized by abnormal processing of visual images by the brain".[9] More simply, it is a condition in which the brain ceases to process normal visual inputs from (usually) one or (rarely) both eyes. It can result from several underlying conditions, such as misalignment of the eyes (strabismus) or unequal refractive power (anisometropia) that if untreated early in life (i.e. by 7 or 8 years old) eventually result in the visual processing center of the brain ignoring information (in whole or part) from the eye providing less useful visual information.

A primary reason behind early childhood screening for amblyopia is the assumption that there is a developmental 'critical period' during which the neural circuitry can potentially be reshaped by experience, with this critical period closing by about age seven. Current evidence suggests that neuroplasticity continues through later childhood and into adulthood and that the adult brain retains the capacity to re-wire, although perhaps in ways distinct from the brain prior to age seven. This suggests the possibility that treatment for amblyopia in adults as well as children may be effective.[10]

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[6] Canadian Task Force on Preventive Health Care. *The Red Brick: The Canadian Guide to Clinical Preventive Health Care (1994)*. 1994. Available at https://canadiantaskforce.ca/the-red-brick-the-canadian-guide-to-clinical-preventive-health-care-1994/. Accessed May 2019.

[7] Human Early Learning Partnership. Screening Research and Evaluation Unit. *BC Early Childhood Vision Screening Program. Final Evaluation Report.* 2012. Available at https://www2.gov.bc.ca/assets/gov/health/managing-your-health/women-children-maternal-health/bc-early-childhood-vision-screening-program.pdf. Accessed May 2019.

[8] Human Early Learning Partnership. Screening Research and Evaluation Unit. *BC Early Childhood Vision Screening Program. Final Evaluation Report.* 2012. Available at https://www2.gov.bc.ca/assets/gov/health/managing-your-health/women-children-maternal-health/bc-early-childhood-vision-screening-program.pdf. Accessed May 2019.

[9] Grossman DC, Curry SJ, Owens DK et al. Vision Screening in Children Aged 6 Months to 5 Years: US Preventive Services Task Force Recommendation Statement. *Journal of the American Medical Association.* 2017; 318(9): 836-44.

[10] The Lasker/IRRF Initiative for Innovation in Vision Science. *Amblyopia: Challenges and Opportunities*. 2017. Available online at http://www.laskerfoundation.org/new-noteworthy/articles/amblyopia-challenges/. Accessed January 2020.

Modelling the Clinically Preventable Burden

In this section, we will calculate the CPB associated with screening of all children at least once between the ages of 3 and 5 years to detect the presence of amblyopia or its risk factors. We base our calculations on BC data reported in the evaluation of the BC Early Childhood Vision Screening Program.

In modelling CPB, we made the following assumptions:

- 99.56% of individuals in a birth cohort of 40,000 (or 39,824, Table 2, row *a*) would survive to age 5, based on data from the BC life tables for 2010 to 2012.
- Solebo et al. conducted a systematic review and found the prevalence of amblyopia in children under the age of 6 ranged from 1.0% to 3.8% depending on the criteria for amblyopia.[11]
- The USPSTF estimates the prevalence of strabismus, anisometropia (both risk factors for amblyopia) and amblyopia combined range from 1% to 6% among US children younger than 6 years.[12]
- For our model, we use the mid-point of the range for the USPSTF reported combined prevalence of amblyopia and its risk factors (3.50%) for the base case (Table 2, row *b*) and the range in sensitivity analysis.
- In the eight consecutive school years starting in 2007/08, 93.1% of BC kindergarten students completed vision screens (Table 2, row *d*). Completed screens ranged from a low of 79.2% of students in the Northern Health Authority in 2007/08 school year to a high of 96.6% in the Vancouver Island Health Authority the 2007/08 school year.[13,14] We use the range of completed screens in our sensitivity analysis.
- The BC Early Childhood Vision Screening Program (BCECVSP) uses two of three tests to screen kindergarten children, combining the Randot Preschool Stereotest (for stereopsis) with either the SureSight Vision Screener or the HOTV vision chart for detection of refractive errors.
- The Vision in Preschoolers study compared vision screening tests administered by professionals. At a specificity (rate of true negatives) of 90% the SureSight Vision Screener had a sensitivity (rate of true positives) of 89% to detect amblyopia. The HOTV vision chart had a sensitivity of 73% at a specificity of 89%. The Random Dot E stereotest had a sensitivity of 63% to detect amblyopia at a specificity of 90%.[15]
- Nishimura and colleagues tested vision screening tests / devices on children ages 4 and 5 in a Canadian school. The results of the vision screening tests / devices were compared with the results of an eye exam by a licensed optometrist. The sensitivity

[11] Solebo AL, Cumberland PM and Rahi JS. Whole-population vision screening in children aged 4–5 years to detect amblyopia. *The Lancet*. 2015; 385(9984): 2308-19.
[12] Jonas DE, Amick HR, Wallace IF et al. Vision screening in children aged 6 months to 5 years: evidence report and systematic review for the US Preventive Services Task Force. *Journal of the American Medical Association.* 2017; 318(9): 845-58.
[13] Human Early Learning Partnership. Screening Research and Evaluation Unit. *BC Early Childhood Vision Screening Program. Final Evaluation Report.* 2012. Available at https://www2.gov.bc.ca/assets/gov/health/managing-your-health/women-children-maternal-health/bc-early-childhood-vision-screening-program.pdf. Accessed May 2019.
[14] Keren Massey, Manager, Early Childhood Health, Public Health Services Branch, BC Ministry of Health. September 25, 2019. Personal communication.
[15] Vision in Preschoolers Study Group. Comparison of preschool vision screening tests as administered by licensed eye care professionals in the Vision in Preschoolers Study. *Ophthalmology*. 2004; 111(4): 637-50.

of each test / device individually was calculated along with all possible combination of devices. The results of the two photoscreeners (Plusoptix S12 and Spot) and an acuity test (Cambridge Crowded Acuity cards) in addition to the Randot Preschool Stereotest are shown in Table 1 below.[16]

Table 1: Sensitivity and Specificity of Screening Tool Combinations

Tools	Sensitivity	Specificity
Acuity and Randot	0.67 (0.60 - 0.72)	0.69 (0.64 - 0.72)
Plusoptix and Randot	0.72 (0.65 - 0.78)	0.80 (0.77 - 0.84)
Spot and Randot	0.68 (0.61 - 0.74)	0.85 (0.82 -0.88)

- Notwithstanding slight differences between individual photo screeners and between acuity tests, the sensitivity results for the tests combined with the Randot test appear to converge to a relatively narrow range.
- We model a sensitivity for testing in BC of 0.695 (midpoint of 0.67 and 0.72) using a combination of either the SureSight photo screener or the HOTV acuity test along with the Randot Preschool Stereotest. (Table 2, row *e*). We range this from 0.60 to 0.78 in our sensitivity analysis.
- In a study including 86 children diagnosed with amblyopia by age 5, Campbell and Charney found that 28 (32.6%) were diagnosed during routine eye exams by a primary care physician while the others were identified by a school screener, an ophthalmologist or an optometrist.[17] We assumed, therefore, that amblyopia would be diagnosed in 32.6% in the absence of an organized, universal screening program (Table 2, row *f*).
- Across the 2007/08 – 2009/10 school years, 54.2% of children who were referred from the Vision Screening Program in BC saw an eye doctor within one year of referral, with most of those visits within four months of referral (Table 2, row *h*).[18]
- A review of childhood amblyopia by Tailor et al. suggests that treatment adherence ranges from less than 50% for occlusion without educational intervention, to 80% for occlusion with educational intervention, to between 80.6 – 93% for binocular treatments, especially those involving computer games or videos.[19]

- We model a treatment adherence of 50% given that there does not appear to be any standard educational intervention in BC, and vary this between 50% and 80% in our sensitivity analysis (Table 2, row *j*).

[16] Nishimura M, Wong A, Cohen A et al. Choosing appropriate tools and referral criteria for vision screening of children aged 4–5 years in Canada: a quantitative analysis. *BMJ Open.* 2019; 9(9): e032138.
[17] Campbell LR and Charney E. Factors associated with delay in diagnosis of childhood amblyopia. *Pediatrics*. 1991; 87(2): 178-85.
[18] Human Early Learning Partnership. Screening Research and Evaluation Unit. *BC Early Childhood Vision Screening Program. Final Evaluation Report.* 2012. Available at https://www2.gov.bc.ca/assets/gov/health/managing-your-health/women-children-maternal-health/bc-early-childhood-vision-screening-program.pdf. Accessed May 2019.
[19] Tailor V, Bossi M, Greenwood JA et al. Childhood amblyopia: current management and new trends. *British Medical Bulletin.* 2016; 119(1): 75-86.

- The reported incidence of recurrence in successfully treated cases of amblyopia varies substantially.[20,21] McConachie and Gottlieb suggest a range in recurrence rates of between 13 – 24% for two or more logMAR lines at one year.[22]

- In keeping with considering two or more logMAR lines to be clinically significant, we model using a recurrence rate of 18.5% (midpoint of 13% and 24%, Table 2, row *l*), and use the upper and lower bounds in our sensitivity analysis.

- We assumed an average life expectancy for a 5 year-old of 77.6 years (Table 2, row *q*), based on data from the BC life tables for 2010 to 2012.

- Individuals with amblyopia rely on their non-amblyopic eye for visual information. Since the amblyopic eye does not contribute to vision, the loss of vision for any reason in the non-amblyopic eye is a significant event.

- The annual incidence of permanent visual impairment or blindness attributable to loss of vision in the non-amblyopic eye (for any reason) has been estimated at .00004 (.00001 to 0.00006) during the ages of 5 to 15 years, 0.00005 (0.00004 to 0.00007) for ages 16 to 64 and 0.00046 (0.00039 to 0.00052) for ages 65+[23] (Table 2, rows *r*, *s* and *t*).

- In screening a cohort of 40,000, we would expect to find and treat 165 five-year olds with amblyopia (Table 2, row *k*). Of these, approximately 134 (Table 2, row *m*) would retain the benefits of treatment. Without treatment, 1.6 would be expected to have permanent visual impairment or blindness attributable to loss of vision in the non-amblyopic eye. Most of this visual impairment / blindness (75%) would occur after age 65.

- In assessing the disability associated with vision impairment, the Global Burden of Disease (GBD) study found the following:[24]
    - mild vision impairment ("has some difficulty with distance vision, for example reading signs, but no other problems with eyesight") is associated with a disability weight of 0.003 (95% CI of 0.001 to 0.007)
    - monocular distance vision loss ("is blind in one eye and has difficulty judging distances") is associated with a disability weight of 0.017 (95% CI of 0.009 to 0.029)
    - moderate vision impairment ("has vision problems that make it difficult to recognize faces or objects across a room") is associated with a disability weight of 0.031 (95% CI of 0.019 to 0.049)
    - severe vision impairment ("has severe vision loss, which causes difficulty in daily activities, some emotional impact [for example worry], and some difficulty going outside the home without assistance") is associated with a disability weight of 0.184 (95% CI of 0.125 to 0.258)

[20] Saxena R, Puranik S, Singh D et al. Factors predicting recurrence in successfully treated cases of anisometropic amblyopia. *Indian Journal of Ophthalmology.* 2013; 61(11): 630.
[21] Gunton KB. Advances in amblyopia: what have we learned from PEDIG trials? *Pediatrics*. 2013; 131(3): 540-7.
[22] Maconachie GD and Gottlob I. The challenges of amblyopia treatment. *Biomedical Journal.* 2015; 38(6): 510-6.
[23] Carlton J, Karnon J, Czoski-Murray C et al. The clinical effectiveness and cost-effectiveness of screening programmes for amblyopia and strabismus in children up to the age of 4-5 years: a systematic review and economic evaluation. *Health Technology Assessment*. 2008; 12(25): xi-194.
[24] Institute for Health Metrics and Evaluation. *GBD 2016 sequelae, health states, health state lay descriptions, and disability weights*. Available online at http://ghdx.healthdata.org/record/global-burden-disease-study-2016-gbd-2016-disability-weights. Accessed December 2019.

- blindness is associated with a disability weight of 0.187 (95% CI of 0.124 to 0.260).

- We model a disability weight of 0.187 (Table 2, row *u*) if the non-amblyopic eye becomes blind.

- While blindness is associated with a reduced QoL, considerable debate exists about whether or not **living with amblyopia** reduces QoL.
- In a 2002 study assessing the cost-effectiveness of *treatment* for amblyopia, Membrano and colleagues assumed a reduction in QoL of 3.5% associated with living with amblyopia, based on their own assessment of 75 patients.[25]
- In 2004, Konig and Barry published the results of the long-term cost-effectiveness of a hypothetical screening program for untreated amblyopia in 3-year-old children in German kindergartens.[26] They assumed a reduction in QoL of 4.0% associated with living with amblyopia (yielding a cost per QALY of $14,323[27]) and then used a range of 0% to 8.0% in their univariate sensitivity analysis (yielding a cost per QALY of $3.67 million and $7,176, respectively).
- In 2008, Carlton and colleagues published an extensive systematic review and economic evaluation of the clinical effectiveness and cost-effectiveness of screening programmes for amblyopia and strabismus in children up to the age of 4-5 years.[28] Based on their review, they then developed their own model in which the base case included the assumption of no change in QoL associated with living with amblyopia due to the lack of "direct evidence of a utility effect". The resulting costs per QALY for screening at ages 3 or 4 ranged from $1.07 to $1.62 million. In their sensitivity analysis they included a 2.0% reduction in QoL associated with living with amblyopia, resulting in the costs per QALY for screening at ages 3 or 4 being reduced to between $12,980 and $20,891.
- In 2011, Carlton and Kaltenthaler published a systematic review to identify the health-related quality of life (HRQoL) implications of amblyopia and/or its treatment.[29] Based on a review of 35 publications, they conclude that the HRQoL implications of amblyopia are "related specifically to amblyopia treatment, rather than to the condition itself. These included impact on family life, social interactions, difficulties in undertaking daily activities, as well as feelings and behaviour." They recommend that "further research is required to assess the immediate and long-term effects of amblyopia and/or its treatment on HRQoL".

[25] Membreno JH, Brown MM, Brown GC et al. A cost-utility analysis of therapy for amblyopia. *Ophthalmology*. 2002; 109(12): 2265-71.
[26] König H-H and Barry J-C. Cost-utility analysis of orthoptic screening in kindergarten: a Markov model based on data from Germany. *Pediatrics*. 2004; 113(2): e95-e108.
[27] All costs in the following sections have been converted to 2017 Canadian dollars.
[28] Carlton J, Karnon J, Czoski-Murray C et al. The clinical effectiveness and cost-effectiveness of screening programmes for amblyopia and strabismus in children up to the age of 4-5 years: a systematic review and economic evaluation. *Health Technology Assessment*. 2008; 12(25): xi-194.
[29] Carlton J and Kaltenthaler E. Amblyopia and quality of life: a systematic review. *Eye*. 2011; 25(4): 403.

- Research on the QoL implications of amblyopia and/or its treatment continues, with the focus seemingly remaining on the QoL implications associated with treatment rather than living with amblyopia.[30,31 ,32]

- Sufficient evidence exists to suggest a *disutility* associated with **treatment for amblyopia.** We model a 3.6% disutility (based on the midpoint of the reduction in QoL observed by Membrano et al[33] (3.5%) and van de Graaf et al[34] (3.7%)) for a period of six months for children receiving treatment (Table 2, rows *n* & *o*).

- We have found no convincing evidence of significant QoL reductions associated with **living with amblyopia** and therefore do not include these impacts in the base model. In our sensitivity analysis, we include a QoL reduction of 0.003 (ranging from 0.001 to 0.007), based on disability weights calculated by the Global Burden of Disease study for mild vision impairment.[35] In addition, we calculate what the threshold QoL reductions associated with living with amblyopia would be to achieve a cost per QALY of $50,000 and $25,000.

- Beyond correcting refractive errors, experts differ as to whether amblyopia should be treated at all (especially with occlusion therapy).[36]

- The effectiveness of interventions in improving amblyopia is fairly contentious. The USPSTF noted an average improvement of approximately one line on the logMAR chart among children treated with patching plus eyeglasses (without any pretreatment).[37] The other treatment methods reviewed resulted in an average of less than one line on the Snellen eye chart. A change of one line in the Snellen eye chart is not considered to be clinically significant.[38,39,40] Indeed, the most recent evidence review for the USPSTF concluded that "studies directly evaluating the effectiveness

[30] Chen Y, Chen X, Chen J et al. Longitudinal impact on quality of life for school-aged children with amblyopia treatment: perspective from children. *Current Eye Research.* 2016; 41(2): 208-14.
[31] Bokhary K. Impact of amblyopia treatment on vision-related quality of life. *Optometry: Open Access*. 2016; 1(2):
[32] Buckley CY, Whittle JC, Verity L et al. The effect of childhood eye disorders on social relationships during school years and psychological functioning as young adults. *British and Irish Orthoptic Journal*. 2018; 14(1): 35-44.
[33] Membreno JH, Brown MM, Brown GC et al. A cost-utility analysis of therapy for amblyopia. *Ophthalmology*. 2002; 109(12): 2265-71.
[34] van de Graaf ES, van Kempen-du Saar H, Looman CW et al. Utility analysis of disability caused by amblyopia and/or strabismus in a population-based, historic cohort. *Graefe's Archive for Clinical and Experimental Ophthalmology.* 2010; 248(12): 1803-7.
[35] Institute for Health Metrics and Evaluation. *GBD 2016 sequelae, health states, health state lay descriptions, and disability weights*. Available online at http://ghdx.healthdata.org/record/global-burden-disease-study-2016-gbd-2016-disability-weights. Accessed December 2019.
[36] Kulp MT, Cotter SA, Connor AJ et al. Should amblyopia be treated? *Ophthalmic and Physiological Optics*. 2014; 34(2): 226-32.
[37] Grossman DC, Curry SJ, Owens DK et al. Vision Screening in Children Aged 6 Months to 5 Years: US Preventive Services Task Force Recommendation Statement. *Journal of the American Medical Association.* 2017; 318(9): 836-44.
[38] Gibson R and Sanderson H. Observer variation in ophthalmology. *British Journal of Ophthalmology*. 1980; 64(6): 457-60.
[39] Laidlaw D, Abbott A and Rosser D. Development of a clinically feasible logMAR alternative to the Snellen chart: performance of the "compact reduced logMAR" visual acuity chart in amblyopic children. *British Journal of Ophthalmology.* 2003; 87(10): 1232-4.
[40] Beck RW, Moke PS, Turpin AH et al. A computerized method of visual acuity testing: adaptation of the early treatment of diabetic retinopathy study testing protocol. *American Journal of Ophthalmology.* 2003; 135(2): 194-205.

of screening were limited and do not establish whether vision screening in preschool children is better than no screening."[41]

- Other assumptions used in assessing the clinically preventable burden are detailed in the Reference Document.

Based on these assumptions, the CPB associated with screening for amblyopia in children ages 3 to 5 is 2.3 QALYs (Table 2, row *w*).

Table 2: CPB of Screening for Amblyopia in 5 Year-Olds in a Birth Cohort of 40,000 (B.C.)

Row Label	Variable	Base Case	Data Source
a	5 Year olds in cohort	39,824	BC Life Tables
b	Prevalence of amblyopia	3.50%	√
c	5 year-olds with amblyopia in birth cohort	1,394	= a * b
d	Rate of screening for kindergarten children	93.1%	√
e	Average sensitivity of refractive and stereo tests combined	69.5%	√
f	% of amblyopia that are undetected (asymptomatic)	67.4%	√
g	5 year-olds with amblyopia or risk factors detected through screening and referred to eye doctor	608	= c * d * e * f
h	Proportion of referrals that see eye doctor	54.2%	√
i	5 year-olds with amblyopia or risk factors detected through screening seeing physician for followup	329	= g * h
j	Treatment compliance	50.0%	√
k	Individuals with amblyopia who are treatment compliant	165	= i * j
l	Recurrence in those treated for amblyopia	18.5%	√
m	Individuals with lasting change due to screening and treatment	134	= k * (1- l)
n	Quality of Life reduction due to treatment	0.036	√
o	Length of Treatment, months	6	√
p	Estimated QALYs lost due to treatment	3.0	= k * n * (o / 12)
q	Average life expectancy of a 5 year old	77.6	BC Life Table
r	Incidence of permanent visual impairment or blindness - 5-15 yrs	0.00004	√
s	Incidence of permanent visual impairment or blindness - 16-64 yrs	0.00005	√
t	Incidence of permanent visual impairment or blindness - 65+ yrs	0.00046	√
u	Change in QoL associated with permanent visual impairment or blindness	0.187	√
v	Estimated QALYs gained due to avoided vision loss	5.3	Calculated
w	**Net QALYs gained through intervention, CPB**	**2.3**	= v - p

√ = Estimates from the literature

We also modified several major assumptions and recalculated the CPB as follows:

- Assume the disutility associated with living with amblyopia is changed from 0.0 to 0.001: CPB = 12.9
- Assume the disutility associated with living with amblyopia is changed from 0.0 to 0.003: CPB = 34.1

[41] Jonas DE, Amick HR, Wallace IF et al. Vision screening in children aged 6 months to 5 years: evidence report and systematic review for the US Preventive Services Task Force. *Journal of the American Medical Association.* 2017; 318(9): 845-58.

- Assume the disutility associated with living with amblyopia is changed from 0.0 to 0.007: CPB = 76.4

As expected, assumptions about the disutility associated with living with amblyopia dominate the sensitivity analysis. Moving from an assumption of no disutility to just 0.7% disutility changes the CPB from 3.2 (the base case) to 76.4. No other variable even comes close to influencing the results in such an important manner (see below).

- Assume the prevalence of amblyopia is reduced from 3.5% to 1.0% (Table 2, row b): CPB = 0.7
- Assume the prevalence of amblyopia is increased from 3.5% to 6.0% (Table 2, row b): CPB = 4.0
- Assume the screening rate decreases from 93.1% to 79.2% (Table 2, row d): CPB = 2.0
- Assume the screening rate increases from 93.1% to 96.6% (Table 2, row d): CPB = 2.4
- Assume joint testing sensitivity decreases from 69.5% to 60%. (Table 2, row e): CPB = 2.0
- Assume joint testing sensitivity increases from 69.5% to 78%. (Table 2, row e): CPB = 2.6
- Assume treatment compliance increases from 50% to 80% (Table 2, row j): CPB = 3.7
- Assume the recurrence of amblyopia decreases from 18.5% to 13.0% (Table 2, row l): CPB = 2.7
- Assume the recurrence of amblyopia increases from 18.5% to 24.0% (Table 2, row l): CPB = 2.0
- Assume the incidence of permanent visual impairment or blindness is at the low end of the range (Table 2, rows r, s, t): CPB = 0.9
- Assume the incidence of permanent visual impairment or blindness is at the high end of the range (Table 2, rows r, s, t): CPB = 4.0
- Assume the disutility associated with permanent visual impairment or blindness is reduced from -0.187 to -0.124 (Table 2, row u): CPB = 0.5
- Assume the disutility associated with permanent visual impairment or blindness is increased from -0.187 to -0.260 (Table 2, row u): CPB = 4.4

Modelling Cost-Effectiveness

In this section, we will calculate the CE associated with screening all children at least once between the ages of 3 and 5 years, to detect the presence of amblyopia or its risk factors.

In modelling CE, we made the following assumptions:

- The BC government provides approximately $4.5 million in funding annually to the provincial Health Authorities to carry out the early childhood vision screening program.[42] Most of this screening takes place while the child is in kindergarten. Between 2007/08 and 2009/10, an average of 36,397 children were screened per year,[43] suggesting an average screening cost of $123.64. There is significant uncertainty associated with whether the $4.5 million is utilized for just vision screening or if it is utilized for other programs as well.
- In their 2008 analysis, Carlton and colleagues estimated a cost per screen of between £9.26 and £12.90, equivalent to between $19.63 and $27.35 in 2017 CAD.[44] They included screening invitation, orthoptists time, equipment costs, room rental and data entry costs in their estimate. We use the midpoint of the range ($23.49) for an average cost per screen (Table 3, row *d*).
- Visits to the optometrist cost $47.08 for a full eye exam (Table 3, row i).[45]
- For patient time and travel costs, we estimated two hours of patient time required per physician visit.
- The estimated cost of interventions (Table 3, row *l*) are based on information in the economic evaluation by Carlton et al.[46] The cost of an intervention is estimated at 1,015 (95% CI of 907 to 1,122) in 2006 British Pounds Sterling (£) or $2,168 (95% CI of $1,938 to $2,397) in 2017 CAD.
- Other costs and assumptions used in assessing cost-effectiveness are detailed in the Reference Document.
- Discount rate of 1.5%, varied from 0% to 3% in the sensitivity analysis.

Based on these assumptions, the CE associated with screening for amblyopia in children ages 3 to 5 is $6,615,785 per QALY (Table 3, row *r*).

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[42] Keren Massey, Manager, Early Childhood Health, Public Health Services Branch, BC Ministry of Health. July 25, 2019. Personal communication.

[43] Human Early Learning Partnership. Screening Research and Evaluation Unit. *BC Early Childhood Vision Screening Program. Final Evaluation Report.* 2012. Available at https://www2.gov.bc.ca/assets/gov/health/managing-your-health/women-children-maternal-health/bc-early-childhood-vision-screening-program.pdf. Accessed May 2019.

[44] Carlton J, Karnon J, Czoski-Murray C et al. The clinical effectiveness and cost-effectiveness of screening programmes for amblyopia and strabismus in children up to the age of 4-5 years: a systematic review and economic evaluation. *Health Technology Assessment*. 2008; 12(25): xi-194.

[45] BC Doctors of Optometry. *MSP and Your Eye Health.* 2019. Available at https://bc.doctorsofoptometry.ca/patients/msp/. Accessed August 2019.

[46] Carlton J, Karnon J, Czoski-Murray C et al. The clinical effectiveness and cost-effectiveness of screening programmes for amblyopia and strabismus in children up to the age of 4-5 years: a systematic review and economic evaluation. *Health Technology Assessment*. 2008; 12(25): xi-194.

Table 3: CE of Screening for Amblyopia in 3-5 Year-Olds in a Birth Cohort of 40,000 (B.C.)			
Row Label	**Variable**	**Base Case**	**Data Source**
a	5 Year olds in cohort	39,824	Table 1 row b
b	Screening rate	93%	Table 1, row d
c	# of screens	37,076	= a * b
	Costs of screening		
d	Screening cost per child in BC	$23.49	√
e	Cost of screening over lifetime of birth cohort	$870,919	= c * d
	Costs of follow-up visits to Optometrist		
f	Cases of amblyopia detected through screening and referred to optometrist	608	Table 1, row i
g	Proportion of referrals that see optometrist	54.2%	Table 1, row j
h	Number seeing optometrist	329	= f * g
i	Cost of full eye exam	$47.08	√
j	Value of patient time and travel for office visit	$59.38	Ref Doc
k	Costs of follow-up visits to Optometrist	$35,073	= h * (i + j)
	Costs of interventions		
l	Estimated intervention cost	$2,168	√
m	# of interventions	165	Table 1, row m
n	Total cost over lifetime of birth cohort	$357,187	= l * m
	CE calculation		
o	Lifetime cost of screening and interventions	$1,263,178	= e + k + n
p	QALYs saved (0% discount rate)	2.3	Table 1, row y
q	QALYs saved (1.5% discount rate)	0.2	Calculated
r	**CE ($/QALY saved)**	**$6,615,785**	= o / q

√ = Estimates from the literature

We also modified several major assumptions and recalculated the cost per QALY as follows:

- Assume the disutility associated with treating amblyopia is reduced from 0.036 to 0.0 (Table 2, row n): CE = $400,255
- Assume the disutility associated with living with amblyopia is changed from 0.0 to 0.001: CE = $195,519
- Assume the disutility associated with living with amblyopia is changed from 0.0 to 0.003: CE = $66,483
- Assume the disutility associated with living with amblyopia is changed from 0.0 to 0.007: CE = $28,647
- Threshold disutility for living with amblyopia required to produce a CE of $50,000 / QALY: 0.004
- Threshold disutility for living with amblyopia required to produce a CE of $25,000 / QALY: 0.008
- Assume the disutility associated with treating amblyopia is reduced from 0.036 to 0.0 (Table 2, *row p*) ***and*** assume the disutility associated with living with amblyopia is changed from 0.0 to 0.007: CE = $26,851

Any assumption about the disutility associated with **living with amblyopia** dramatically reduces the cost / QALY. Adding just a 0.1% disutility changes the cost / QALY from $6.6 million to $0.2 million. If the disutility is changed to 0.8%, the cost / QALY would be $25,000.

- Assume the prevalence of amblyopia is reduced from 3.5% to 1.0% (Table 2, row b): CE = $18,019,186
- Assume the prevalence of amblyopia is increased from 3.5% to 6.0% (Table 2, row b): CE = $4,715,218
- Assume joint testing sensitivity decreases from 69.5% to 60%. (Table 2, row e): CE = $7,338,001
- Assume joint testing sensitivity increases from 69.5% to 78%. (Table 2, row e): CE = $6,118,714
- Assume treatment compliance increases from 50% to 80% (Table 2, row j): CE = $4,836,391
- Assume the recurrence of amblyopia decreases from 18.5% to 13.0% (Table 2, row l): CE = $3,127,367
- Assume the recurrence of amblyopia increases from 18.5% to 24.0% (Table 2, row l): CE = n/a (intervention is harmful [1.5% discount])
- Assume the incidence of permanent visual impairment or blindness is at the low end of the range (Table 2, rows r, s, t): CE = n/a (intervention is harmful [1.5% discount])
- Assume the incidence of permanent visual impairment or blindness is at the high end of the range (Table 2, rows r, s, t): CE = $947,057
- Assume the disutility associated with permanent visual impairment or blindness is reduced from -0.187 to -0.124 (Table 2, row u): CE = n/a (intervention is harmful [1.5% discount])
- Assume the disutility associated with permanent visual impairment or blindness is increased from -0.187 to -0.260 (Table 2, row u): CE = $887,731
- Assume the cost per intervention is reduced from $2,168 to $1,938 (Table 3, row l): CE = $6,416,734
- Assume the cost per intervention is increased from $2,168 to $2,397 (Table 3, row l): CE = $6,812,992

Summary

The clinically preventable burden (CPB) associated with screening all children at least once between the ages of 3 and 5 years, to detect the presence of amblyopia or its risk factors, is 2.3 quality-adjusted life years (QALYs) while the cost-effectiveness (CE) is estimated at $6,615,785 per QALY (see Table 4).

Table 4: Screening for Amblyopia in 3-5 Year-Olds in a Birth Cohort of 40,000

Summary

	Base Case	Range	
CPB (Potential QALYs Gained)			
Assume No Current Service			
1.5% Discount Rate	**0.2**	-0.9	44
3% Discount Rate	-0.8	-1.6	28
0% Discount Rate	2.3	0.5	76
CE ($/QALY) **including** patient time costs			
1.5% Discount Rate	**$6,615,785**	$28,657	$18,019,186
3% Discount Rate	-*	$44,706	-*
0% Discount Rate	$541,075	$16,540	$1,473,707
CE ($/QALY) **excluding** patient time costs			
1.5% Discount Rate	$6,513,329	$28,213	$17,916,730
3% Discount Rate	-*	$44,014	-*
0% Discount Rate	$532,695	$16,284	$1,465,327

* Intervention resulted in a loss of QALYs. Therefore CE was dominated.

Whether or not the screening of all children at least once between the ages of 3 and 5 years to detect the presence of amblyopia or its risk factors is cost-effective depends largely on assumptions made regarding QoL reductions associated with **living with amblyopia**. The uncertainty associated with this single parameter is so large that reasonable assumptions could result in a range of values indicating that screening is clearly **not cost-effective** to it being **highly cost-effective**. As noted by Karnon et al, the "existing evidence is so weak that it is difficult to even assign a probability of disutility, let alone an expected disutility value."[47] Nevertheless, the lack of research evidence does not necessarily mean the lack of an effect. Models such as the one above can help clarify "the decision-making process by explicitly identifying the key factors underlying the uncertainty in the cost-effectiveness estimates. Decision makers can then consider the likely value of these specific parameters…or they may choose to focus on other decision factors" [48] when choosing to implement, enhance or disinvest / de-adopt a specific program.

In summary, the cost-effectiveness of screening all children in BC at least once between the ages of 3 and 5 years to detect the presence of amblyopia or its risk factors is highly sensitive to assumptions about the disutility associated with living with amblyopia. If we assume no disutility (the base case), then the cost per QALY is $6.6 million. However, adding just a 0.1% disutility changes the cost / QALY from $6.6 million to $0.2 million. If the disutility is changed to 0.7%, the cost / QALY would be $28,647.

[47] Karnon J, Carlton J, Czoski-Murray C et al. Informing disinvestment through cost-effectiveness modelling. *Applied Health Economics and Health Policy.* 2009; 7(1): 1-9.

[48] Karnon J, Carlton J, Czoski-Murray C et al. Informing disinvestment through cost-effectiveness modelling. *Applied Health Economics and Health Policy.* 2009; 7(1): 1-9.

Screening for Major Depressive Disorder in Youth

United States Preventive Services Task Force Recommendations[49]

> *This recommendation applies to children and adolescents aged 18 years or younger who do not have a diagnosis of MDD [major depressive disorder].*
>
> *The USPSTF recommends screening for MDD in adolescents aged 12 to 18 years. Screening should be implemented with adequate systems in place to ensure accurate diagnosis, effective treatment, and appropriate follow-up. (B recommendation)*
>
> *The USPSTF concludes that the current evidence is insufficient to assess the balance of benefits and harms of screening for MDD in children aged 11 years or younger. (I statement)*

Canadian Task Force on Preventive Health Care Recommendations

The CTFPHC does not have a specific recommendation on depression screening for children or adolescents.[50]

Modelling the Clinically Preventable Burden

In this section, we will calculate the CPB associated with screening for MDD in adolescents ages 12 to 18.

In modelling CPB, we made the following assumptions:

- The USPSTF "found no evidence on appropriate or recommended screening intervals, and the optimal interval is unknown…opportunistic screening may be appropriate for adolescents, who may have infrequent health care visits."[51] For adolescents with risk factors for MDD, "repeated screening may be most productive."[52]
- Rand and colleagues evaluated primary care visits by US adolescents and found that many did not have any primary care visits during a 12-month period.[53] Averaging the data presented for the relevant 12 – 18 year old group, 56.9% had a primary care visit during the last 12-month period.
- Skehar and colleagues found that adolescents 12 – 14 years old who were continuously enrolled in private insurance in the US made an average of 0.58 well-care visits per year.[54]

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[49] Siu AL. Screening for depression in children and adolescents: US Preventive Services Task Force recommendation statement. *Annals of Internal Medicine.* 2016; 164(5): 360-6.
[50] Joffres M, Jaramillo A, Dickinson J et al. Recommendations on screening for depression in adults. *Canadian Medical Association Journal*. 2013; 185(9): 775-82.
[51] Siu AL. Screening for depression in children and adolescents: US Preventive Services Task Force recommendation statement. *Annals of Internal Medicine.* 2016; 164(5): 360-6.
[52] Siu AL. Screening for depression in children and adolescents: US Preventive Services Task Force recommendation statement. *Annals of Internal Medicine.* 2016; 164(5): 360-6.
[53] Rand CM and Goldstein NP. Patterns of primary care physician visits for US adolescents in 2014: implications for vaccination. *Academic Pediatrics.* 2018; 18(2): S72-S8.
[54] Sekhar DL, Ba DM, Liu G et al. Major depressive disorder screening remains low even among privately insured adolescents. *Journal of Pediatrics*. 2018: Available at https://www-sciencedirect-com.ezproxy.library.ubc.ca/science/article/pii/S0022347618310850. Accessed December 2018.

- Using data provided by the BC Ministry of Health, Health Sector Information, Analysis and Reporting Division[55] we were able to generate BC-specific rates of primary care visits and average visits per year for the fiscal years ending in 2012/13 to 2016/17, in total and by sex, as shown in Table 1 below.
- For the five years considered, the average proportion of adolescents ages 10-19 visiting a GP is 70%, and the average number of GP visits per adolescent is 2.07 per year. The proportion of males visiting a GP was 65.4% and for females it was 75.0%. The average number of visits per male in the population was 1.75 and for females was 2.42.

Table 1: General Practitioner Visits by Adolescents
British Columbia, 2012/13 to 2016/17

Age Group	2012/13	2013/14	2014/15	2015/16	2016/17	Total
	Population in Each Age Group					
10 - 14	234,780	231,544	230,178	230,177	232,010	1,158,689
15 - 19	284,482	282,214	279,997	276,909	272,677	1,396,279
Total	519,262	513,758	510,175	507,086	504,687	2,554,968
	Number of Unique Individuals with GP Visit					
10 - 14	163,332	160,912	158,653	160,260	159,826	802,983
15 - 19	205,821	200,410	196,629	192,566	189,547	984,973
Total	369,153	361,322	355,282	352,826	349,373	1,787,956
	Proportion of Individuals with a GP Visit					
10 - 14	69.6%	69.5%	68.9%	69.6%	68.9%	69.3%
15 - 19	72.3%	71.0%	70.2%	69.5%	69.5%	70.5%
Total	71.1%	70.3%	69.6%	69.6%	69.2%	70.0%
	Number of GP Visits					
10 - 14	429,881	422,188	412,182	413,411	407,442	2,085,104
15 - 19	681,806	659,038	641,316	619,790	601,925	3,203,875
Total	1,111,687	1,081,226	1,053,498	1,033,201	1,009,367	5,288,979
	GP Visits per Individual in Total Population					
10 - 14	1.83	1.82	1.79	1.80	1.76	1.80
15 - 19	2.40	2.34	2.29	2.24	2.21	2.29
Total	2.14	2.10	2.06	2.04	2.00	2.07

[55] Aciemme (Sam) Ospan, Senior Manager, Lifetime Prevention Schedule, Healthy Living and Health Promotion Branch, BC Ministry of Health. January 30, 2019. Personal communication.

Table 1: General Practitioner Visits by Adolescents

British Columbia, 2012/13 to 2016/17

Males

Age Group	2012/13	2013/14	2014/15	2015/16	2016/17	Total
	Population in Each Age Group					
10 - 14	121,031	119,378	118,720	118,572	119,586	597,287
15 - 19	149,279	147,563	145,417	143,117	140,451	725,827
Total	270,310	266,941	264,137	261,689	260,037	1,323,114
	Number of Unique Males with GP Visit					
10 - 14	82,970	81,960	80,756	81,067	80,862	407,615
15 - 19	95,992	93,224	91,170	89,118	87,596	457,100
Total	178,962	175,184	171,926	170,185	168,458	864,715
	Proportion of Males with a GP Visit					
10 - 14	68.6%	68.7%	68.0%	68.4%	67.6%	68.2%
15 - 19	64.3%	63.2%	62.7%	62.3%	62.4%	63.0%
Total	66.2%	65.6%	65.1%	65.0%	64.8%	65.4%
	Number of GP Visits					
10 - 14	215,841	211,444	206,909	206,013	202,386	1,042,593
15 - 19	270,303	259,637	253,874	244,381	238,257	1,266,452
Total	486,144	471,081	460,783	450,394	440,643	2,309,045
	GP Visits per Male in Total Population					
10 - 14	1.78	1.77	1.74	1.74	1.69	1.75
15 - 19	1.81	1.76	1.75	1.71	1.70	1.74
Total	1.80	1.76	1.74	1.72	1.69	1.75

Table 1: General Practitioner Visits by Adolescents

British Columbia, 2012/13 to 2016/17

Females

Age Group	2012/13	2013/14	2014/15	2015/16	2016/17	Total
	Population in Each Age Group					
10 - 14	113,749	112,166	111,458	111,605	112,424	561,402
15 - 19	135,203	134,651	134,580	133,792	132,226	670,452
Total	248,952	246,817	246,038	245,397	244,650	1,231,854
	Number of Unique Females with GP Visit					
10 - 14	80,381	78,955	77,909	79,202	78,985	395,432
15 - 19	109,865	107,210	105,496	103,488	101,995	528,054
Total	190,246	186,165	183,405	182,690	180,980	923,486
	Proportion of Females with a GP Visit					
10 - 14	70.7%	70.4%	69.9%	71.0%	70.3%	70.4%
15 - 19	81.3%	79.6%	78.4%	77.3%	77.1%	78.8%
Total	76.4%	75.4%	74.5%	74.4%	74.0%	75.0%
	Number of GP Visits					
10 - 14	214,033	210,738	205,270	207,393	205,052	1,042,486
15 - 19	411,487	399,386	387,411	375,393	363,660	1,937,337
Total	625,520	610,124	592,681	582,786	568,712	2,979,823
	GP Visits per Female in Total Population					
10 - 14	1.88	1.88	1.84	1.86	1.82	1.86
15 - 19	3.04	2.97	2.88	2.81	2.75	2.89
Total	2.51	2.47	2.41	2.37	2.32	2.42

Source: BC Ministry of Health, Health Sector Information, Analysis and Reporting Division

Calculations by H. Krueger & Associates, Inc.

- In our model, we assume a maximum (best in the world) adolescent depression screening rate of 7.4% (10.6%[56] times 70.0%) and that screening for this 7.4% of adolescents (Table 6, row *ah*) is completed at each well-care visit, or 2.07 times per year (Table 6, row *ag)*,[57] during the seven years of an adolescent's life between 12 and 18 years of age.
- In our model for **males**, we assume a maximum (best in the world) depression screening rate of 6.9% (10.6%[58] times 65.4%) and that screening for this 6.9% of male adolescents (Table 6a, row *ah*) is completed at each well-care visit, or 1.75 times per year (Table 6a, row *ag)*,[59] during the seven years of an adolescent's life between 12 and 18 years of age.
- In our model for **females**, we assume a maximum (best in the world) depression screening rate of 8.0% (10.6%[60] times 75.0%) and that screening for this 8.0% of female adolescents (Table 6b, row *ah*) is completed at each well-care visit, or 2.42 times per year (Table 6b, row *ag)*,[61] during the seven years of an adolescent's life between 12 and 18 years of age.

- Patten et al. estimate that for the Canadian population aged 15-25 the annual prevalence of MDD was 5.0% (95% CI 4.2% - 5.7%) and the lifetime prevalence was 8.8% (95% CI 7.9% - 9.7%).[62]
- Avenevoli et al. report that the annual and lifetime prevalence of MDD in 13-18 year olds in the US is 7.5% and 11.0% respectively.[63]
- Using data from the US National Survey on Drug Use and Health (NSDUH) Mojtabai and colleagues found that the annual prevalence of MDD in the US has increased from 5.6% in 2005 to 7.2% in 2014 for 12-13year olds, 9.1% to 11.8% in 14-15 year olds and 11.2% to 14.7% in 16-17 year olds.[64]
- Vasiliadis and colleagues found that there was no significant difference between Canadian and US rates of depression and subsequent use of mental health services.[65]
- Using the detailed data tables publicly available from the US NSDUH, we calculated the aggregate rates of 12-month major depressive episodes for the years 2014 (the

[56] Lewandowski RE, O'Connor B, Bertagnolli A et al. Screening for and diagnosis of depression among adolescents in a large health maintenance organization. *Psychiatric Services*. 2016; 67(6): 636-41.
[57] Sekhar DL, Ba DM, Liu G et al. Major depressive disorder screening remains low even among privately insured adolescents. *Journal of Pediatrics*. 2018: Available at https://www-sciencedirect-com.ezproxy.library.ubc.ca/science/article/pii/S0022347618310850. Accessed December 2018.
[58] Lewandowski RE, O'Connor B, Bertagnolli A et al. Screening for and diagnosis of depression among adolescents in a large health maintenance organization. *Psychiatric Services*. 2016; 67(6): 636-41.
[59] Sekhar DL, Ba DM, Liu G et al. Major depressive disorder screening remains low even among privately insured adolescents. *Journal of Pediatrics*. 2018: Available at https://www-sciencedirect-com.ezproxy.library.ubc.ca/science/article/pii/S0022347618310850. Accessed December 2018.
[60] Lewandowski RE, O'Connor B, Bertagnolli A et al. Screening for and diagnosis of depression among adolescents in a large health maintenance organization. *Psychiatric Services*. 2016; 67(6): 636-41.
[61] Sekhar DL, Ba DM, Liu G et al. Major depressive disorder screening remains low even among privately insured adolescents. *Journal of Pediatrics*. 2018: Available at https://www-sciencedirect-com.ezproxy.library.ubc.ca/science/article/pii/S0022347618310850. Accessed December 2018.
[62] Patten SB, Wang JL, Williams JV et al. Descriptive epidemiology of major depression in Canada. *The Canadian Journal of Psychiatry*. 2006; 51(2): 84-90.
[63] Avenevoli S, Swendsen J, He J-P et al. Major depression in the National Comorbidity Survey–Adolescent Supplement: prevalence, correlates, and treatment. *Journal of the American Academy of Child & Adolescent Psychiatry*. 2015; 54(1): 37-44.
[64] Mojtabai R, Olfson M and Han B. National trends in the prevalence and treatment of depression in adolescents and young adults. *Pediatrics*. 2016; 138(6): e20161878.
[65] Vasiliadis H-M, Lesage A, Adair C et al. Do Canada and the United States differ in prevalence of depression and utilization of services? *Psychiatric Services*. 2007; 58(1): 63-71.

end of Mojtabai and colleague's data) through 2017, using the tables from 2015[66] (containing data for 2014 and 2015) and 2017[67] (containing data for 2016 and 2017), splitting the results by age and sex. The results, shown in Table 2, indicate a substantial difference in major depressive episodes between the sexes, with the annual prevalence of MDE being consistently lower in males than females.

- Similar overall data to the US NSDUH has been reported in the McCreary Centre's *Balance and Connection in BC* report summarizing the results of the 2018 BC adolescent Health Survey. Adolescents in grades 7 through 12 were surveyed and 10% of males reported "mental health conditions", while 20% of females reported the same.[68]

[66] Substance Abuse and Mental Health Services Administration. *Reports and Detailed Tables from the 2015 National Survey on Drug Use and Health (NSDUH)*. 2015. Available at https://www.samhsa.gov/data/nsduh/reports-detailed-tables-2015-NSDUH. Accessed February 2019.
[67] Substance Abuse and Mental Health Services Administration. *Reports and Detailed Tables from the 2017 National Survey on Drug Use and Health (NSDUH)*. 2017. Available at https://www.samhsa.gov/data/nsduh/reports-detailed-tables-2017-NSDUH. Accessed February 2019.
[68] McCreary Centre Society. *Balance and Connection in BC: The Health and Well-Being of our Youth. Results of the 2018 BC Adolescent Health Survey.* 2019. Available at https://www.mcs.bc.ca/pdf/balance_and_connection.pdf. Accessed May 2019.

Table 2: (US) National Survey on Drug Use and Health

12-Month MDE Events, By Age and Sex

2014 - 2017 Results

12 Year Olds

	Male			Female			Calculated Total		
Year	Sample Size	MDE %	MDE (n)	Sample Size	MDE %	MDE (n)	Sample Size	MDE %	MDE (n)
2014	1,347	2.8%	38	1,293	8.9%	115	2,640	5.8%	153
2015	1,346	2.2%	30	1,307	8.7%	114	2,653	5.4%	143
2016	1,323	3.1%	41	1,291	6.9%	89	2,614	5.0%	130
2017	1,329	2.7%	36	1,269	7.0%	89	2,598	4.8%	125
Total	**5,345**	**2.7%**	**144**	**5,160**	**7.9%**	**407**	**10,505**	**5.2%**	**551**

13 Year Olds

	Male			Female			Calculated Total		
	Sample Size	MDE %	MDE (n)	Sample Size	MDE %	MDE (n)	Sample Size	MDE %	MDE (n)
2014	1,433	3.9%	56	1,388	13.8%	192	2,821	8.8%	247
2015	1,428	3.9%	56	1,394	16.8%	234	2,822	10.3%	290
2016	1,479	3.8%	56	1,414	15.3%	216	2,893	9.4%	273
2017	1,507	3.6%	54	1,423	14.5%	206	2,930	8.9%	261
Total	**5,847**	**3.8%**	**222**	**5,619**	**15.1%**	**848**	**11,466**	**9.3%**	**1,070**

14 Year Olds

	Male			Female			Calculated Total		
	Sample Size	MDE %	MDE (n)	Sample Size	MDE %	MDE (n)	Sample Size	MDE %	MDE (n)
2014	1,491	4.6%	69	1,443	17.1%	247	2,934	10.7%	315
2015	1,491	4.1%	61	1,411	19.0%	268	2,902	11.3%	329
2016	1,484	5.2%	77	1,432	20.5%	294	2,916	12.7%	371
2017	1,492	5.2%	78	1,385	19.0%	263	2,877	11.8%	341
Total	**5,958**	**4.8%**	**284**	**5,671**	**18.9%**	**1,072**	**11,629**	**11.7%**	**1,356**

15 Year Olds

	Male			Female			Calculated Total		
Year	Sample Size	MDE %	MDE (n)	Sample Size	MDE %	MDE (n)	Sample Size	MDE %	MDE (n)
2014	1,483	5.5%	82	1,451	20.7%	300	2,934	13.0%	382
2015	1,438	5.3%	76	1,486	26.7%	397	2,924	16.2%	473
2016	1,512	6.5%	98	1,498	21.0%	315	3,010	13.7%	413
2017	1,460	7.4%	108	1,427	27.2%	388	2,887	17.2%	496
Total	**5,893**	**6.2%**	**364**	**5,862**	**23.9%**	**1,400**	**11,755**	**15.0%**	**1,764**

16 Year Olds

	Male			Female			Calculated Total		
	Sample Size	MDE %	MDE (n)	Sample Size	MDE %	MDE (n)	Sample Size	MDE %	MDE (n)
2014	1,467	7.5%	110	1,469	20.7%	304	2,936	14.1%	414
2015	1,459	9.9%	144	1,384	22.3%	309	2,843	15.9%	453
2016	1,487	9.4%	140	1,409	25.8%	364	2,896	17.4%	503
2017	1,508	9.8%	148	1,389	24.1%	335	2,897	16.7%	483
Total	**5,921**	**9.2%**	**542**	**5,651**	**23.2%**	**1,311**	**11,572**	**16.0%**	**1,853**

17 Year Olds

	Male			Female			Calculated Total		
	Sample Size	MDE %	MDE (n)	Sample Size	MDE %	MDE (n)	Sample Size	MDE %	MDE (n)
2014	1,392	9.7%	135	1,350	21.0%	284	2,742	15.3%	419
2015	1,434	9.1%	130	1,333	21.5%	287	2,767	15.1%	417
2016	1,415	9.7%	137	1,337	24.7%	330	2,752	17.0%	467
2017	1,419	11.6%	165	1,418	25.5%	362	2,837	18.5%	526
Total	**5,660**	**10.0%**	**567**	**5,438**	**23.2%**	**1,262**	**11,098**	**16.5%**	**1,829**

Source for Sample Size and MDE %: National Survey on Drug Use and Health, 2014 - 2017

Calculations by H. Krueger & Associates, Inc.

- Based on the data in Table 2, we assume an annual prevalence of MDD of 5.2% in 12 year olds (Table 6, row *b*), 7.9% in 12 year old females (Table 6b, row *b*) and 2.7% in 12 year old males (Table 6a, row *b*).
- We assume an annual prevalence of MDD of 9.3% in 13 year olds (Table 6, row *f*), 15.1% in 13 year old females (Table 6b, row *f*) and 3.8% in 13 year old males (Table 6a, row *f*).
- We assume an annual prevalence of MDD of 11.7% in 14 year olds (Table 6, row *j*), 18.9% in 14 year old females (Table 6b, row *j*) and 4.8% in 14 year old males (Table 6a, row *j*).
- We assume an annual prevalence of MDD of 15.0% in 15 year olds (Table 6, row *n*), 23.9% in 15 year old females (Table 6b row *n*) and 6.2% in 15 year old males (Table 6a, row *n*).
- We assume an annual prevalence of MDD of 16.0% in 16 year olds (Table 6, row *r*), 23.2% in 16 year old females (Table 6b row *r*) and 9.2% in 16 year old males (Table 6a, row *r*).
- We assume an annual prevalence of MDD of 16.5% in 17 and 18 year olds (Table 6, row *v*), 23.2% in 17 and 18 year old females (Table 6b row *v*) and 10.0% in 17 and 18 year old males (Table 6a, row *v*).

- In 2017, 17.2% of US high school students had seriously considered attempting suicide during the previous 12 months, 13.6% had made a plan about how they would attempt suicide, 7.4% had actually attempted suicide and 2.4% had made a suicide attempt resulting in an injury, poisoning or overdose that had to be treated by a doctor or nurse.[69]
- In BC in 2013, 12.2% of students in grades 7 - 12 had seriously considered attempting suicide during the previous 12 months and 6.2% had actually attempted suicide.[70]
- Suicide mortality among youth ages 15 – 19 in BC between 2011 and 2013 is 4.7 / 100,000 population.[71]
- The ratio of attempted suicides to completed suicides among adolescents is estimated to be 50:1 to 100:1.[72]
- Rohde and colleagues report that 19% (95% CI of 14.4% - 22.9%) of adolescents with MDD had at least one suicide attempt by age 30, compared with 3% (95% CI of 1.6% and 5.1%) of adolescents without MDD.[73]

[69] Kann L, McManus T, Harris WA et al. Youth risk behavior surveillance—United States, 2017. *MMWR Surveillance Summaries*. 2018; 67(8): 1.
[70] BC Office of the Provincial Health Officer. *Is "Good", Good Enough? A Report on the Health & Well-Being of Children & Youth in BC*. Available online at http://www.childhealthindicatorsbc.ca/findings/mental-emotional-health-well-being/suicidality. Accessed December 2018.
[71] BC Office of the Provincial Health Officer. *Is "Good", Good Enough? A Report on the Health & Well-Being of Children & Youth in BC*. Available online athttp://www.childhealthindicatorsbc.ca/findings/mental-emotional-health-well-being/suicidality. Accessed December 2018.
[72] Shain BN. Suicide and suicide attempts in adolescents. *Pediatrics*. 2007; 120(3): 669-76.
[73] Rohde P, Lewinsohn PM, Klein DN et al. Key characteristics of major depressive disorder occurring in childhood, adolescence, emerging adulthood, and adulthood. *Clinical Psychological Science*. 2013; 1(1): 41-53.

- A 2018 systematic review by Johnson et al found that adolescent depression increased the risk of adult depression by 2.78 times (OR of 2.78; 95% CI of 1.97 – 3.93).[74]

- Based on the evidence from Rohde et al [75] and Johnson et al[76] noted above, we have assumed that the effect of adolescent depression on suicide would continue until age 34.

- Based on data from the 2013[77], 2014[78] and 2015[79] BC Vital Statistics annual reports, 24.3% of deaths in males and 15.5% of deaths in females ages 15-19 are due to intentional self-harm (see Table 3).

Table 3: Total Deaths and Deaths Attributable to Intentional Self-Harm (ISH)
British Columbia, 2013 to 2015

Males

Age Group	2013 All Deaths	2013 Deaths Attributable to ISH	2013 % of Deaths Attributable to ISH	2014 All Deaths	2014 Deaths Attributable to ISH	2014 % of Deaths Attributable to ISH	2015 All Deaths	2015 Deaths Attributable to ISH	2015 % of Deaths Attributable to ISH	2013 - 2015 Combined All Deaths	2013 - 2015 Combined Deaths Attributable to ISH	2013 - 2015 Combined % of Deaths Attributable to ISH
10-14	10	1	10.0%	12	2	16.7%	12	1	8.3%	34	4	11.8%
15-19	58	5	8.6%	64	24	37.5%	59	15	25.4%	181	44	24.3%
20-24	119	16	13.4%	99	22	22.2%	110	22	20.0%	328	60	18.3%
25-44	650	107	16.5%	669	119	17.8%	757	89	11.8%	2,076	315	15.2%
	837	**129**	**15.4%**	**844**	**167**	**19.8%**	**938**	**127**	**13.5%**	**2,619**	**423**	**16.2%**

Females

Age Group	2013 All Deaths	2013 Deaths Attributable to ISH	2013 % of Deaths Attributable to ISH	2014 All Deaths	2014 Deaths Attributable to ISH	2014 % of Deaths Attributable to ISH	2015 All Deaths	2015 Deaths Attributable to ISH	2015 % of Deaths Attributable to ISH	2013 - 2015 Combined All Deaths	2013 - 2015 Combined Deaths Attributable to ISH	2013 - 2015 Combined % of Deaths Attributable to ISH
10-14	11	0	0.0%	3	0	0.0%	5	0	0.0%	19	0	0.0%
15-19	29	6	20.7%	26	3	11.5%	29	4	13.8%	84	13	15.5%
20-24	55	15	27.3%	37	9	24.3%	43	9	20.9%	135	33	24.4%
25-44	368	42	11.4%	392	44	11.2%	337	25	7.4%	1,097	111	10.1%
	463	**63**	**13.6%**	**458**	**56**	**12.2%**	**414**	**38**	**9.2%**	**1,335**	**157**	**11.8%**

- Tables 4 and 5 provide data on the expected number of deaths in a BC birth cohort of 20,000 males (see Table 4) and 20,000 females (see Table 5) and how many of those deaths would be attributable to intentional self-harm (see Table 3). Total deaths and deaths attributable to intentional self-harm (ISH) from age 12 to 34 are considered.

[74] Johnson D, Dupuis G, Piche J et al. Adult mental health outcomes of adolescent depression: a systematic review. *Depression and Anxiety.* 2018; 35: 700-16.
[75] Rohde P, Lewinsohn PM, Klein DN et al. Key characteristics of major depressive disorder occurring in childhood, adolescence, emerging adulthood, and adulthood. *Clinical Psychological Science*. 2013; 1(1): 41-53.
[76] Johnson D, Dupuis G, Piche J et al. Adult mental health outcomes of adolescent depression: a systematic review. *Depression and Anxiety.* 2018; 35: 700-16.
[77] BC Vital Statistics Agency. *Annual Report 2013. Selected Vital Statistics and Health Status Indicators.* 2015. Available at https://www2.gov.bc.ca/assets/gov/birth-adoption-death-marriage-and-divorce/statistics-reports/annual-reports/2013/pdf/annual-report-2013.pdf. Accessed December 2018.
[78] BC Vital Statistics Agency. *Annual Report 2014. Selected Vital Statistics and Health Status Indicators.* 2015. Available at https://www2.gov.bc.ca/assets/gov/birth-adoption-death-marriage-and-divorce/statistics-reports/annual-reports/2014/pdf/annual-report-2014.pdf. Accessed December 2018.
[79] BC Vital Statistics Agency. *Annual Report 2015. Selected Vital Statistics and Health Status Indicators.* 2015. Available at https://www2.gov.bc.ca/assets/gov/birth-adoption-death-marriage-and-divorce/statistics-reports/annual-reports/2015/pdf/annual-report-2015.pdf. Accessed December 2018.

- In the birth cohort of 20,000 males, 45 of the 267 (17.0%) deaths between the ages of 12 and 34 are due to ISH, resulting in 2,159 life-years lost due to ISH (see Table 4). In the birth cohort of 20,000 females, 17 of 131 (13.2%) deaths between the ages of 12 and 34 are due to ISH, resulting in 1,030 life-years lost due to ISH (see Table 5).

Table 4: Deaths and Life Years Lost Attributable to Intentional Self-Harm (ISH)
in a British Columbia Male Birth Cohort of 20,000

Age Group	Individuals in Birth Cohort	Deaths	% of Deaths due to ISH	# of Deaths due to ISH	Average Life Years Lived	Life Years Lost due to ISH
11	19,898					
12	19,896	2	11.8%	0.2	68.6	13
13	19,894	2	11.8%	0.3	67.6	17
14	19,892	3	11.8%	0.3	66.6	20
15	19,888	3	24.3%	0.8	65.7	54
16	19,884	4	24.3%	1.0	64.7	66
17	19,878	6	24.3%	1.4	63.7	87
18	19,871	7	24.3%	1.8	62.7	110
19	19,862	9	24.3%	2.2	61.7	138
20	19,850	12	18.3%	2.1	60.8	129
21	19,837	14	18.3%	2.5	59.8	149
22	19,821	16	18.3%	2.9	58.9	168
23	19,805	17	18.3%	3.0	57.9	176
24	19,788	17	18.3%	3.1	57.0	175
25	19,772	16	15.2%	2.5	56.0	138
26	19,756	15	15.2%	2.3	55.1	127
27	19,742	15	15.2%	2.2	54.1	120
28	19,727	15	15.2%	2.2	53.1	118
29	19,713	14	15.2%	2.2	52.2	114
30	19,698	15	15.2%	2.2	51.2	115
31	19,683	15	15.2%	2.3	50.2	117
32	19,666	16	15.2%	2.5	49.3	121
33	19,649	17	15.2%	2.6	48.3	125
34	19,631	18	15.2%	2.7	47.4	129
Total		**267**	**17.0%**	**45**		**2,159**

Table 5: Deaths and Life Years Lost Attributable to Intentional Self-Harm (ISH)
in a British Columbia Female Birth Cohort of 20,000

Age Group	Individuals in Birth Cohort	Deaths	% of Deaths due to ISH	# of Deaths due to ISH	Average Life Years Lived	Life Years Lost due to ISH
11	19,912					
12	19,911	1	0.0%	0.0	72.6	0
13	19,910	1	0.0%	0.0	71.6	0
14	19,909	1	0.0%	0.0	70.6	0
15	19,907	2	15.5%	0.3	69.6	22
16	19,904	3	15.5%	0.4	68.6	30
17	19,900	4	15.5%	0.7	67.6	46
18	19,894	6	15.5%	0.9	66.6	62
19	19,887	6	15.5%	1.0	65.7	65
20	19,881	6	24.4%	1.6	64.7	101
21	19,874	7	24.4%	1.6	63.7	103
22	19,868	7	24.4%	1.6	62.7	101
23	19,861	6	24.4%	1.6	61.7	97
24	19,855	7	24.4%	1.6	60.8	98
25	19,848	6	24.4%	1.6	59.8	94
26	19,842	6	10.1%	0.6	58.8	37
27	19,836	6	10.1%	0.6	57.8	37
28	19,829	7	10.1%	0.7	56.8	38
29	19,822	7	10.1%	0.7	55.9	38
30	19,815	7	10.1%	0.7	54.9	39
31	19,808	8	10.1%	0.8	53.9	41
32	19,799	8	10.1%	0.8	52.9	45
33	19,791	9	10.1%	0.9	51.9	46
34	19,781	10	10.1%	1.0	51.0	50
Total		**131**	**15.0%**	**20**		**1,030**

- Depression has an important influence on a person's QoL. Studies have also shown that individuals with current or treated depression report lower preference scores for depression health states than the general population.[80,81] Pyne and colleagues suggest that "public stigma may result in the general population being less sympathetic to the suffering of individuals with depression and less willing to validate the impact of depression symptoms."[82] Revicki and Wood, based on input from patients with depression who had completed at least eight weeks of anti-depressant (AD) medication, identified the following health state utilities: severe depression = 0.30, moderate depression = 0.55 to 0.63, mild depression = 0.64 to 0.73 and

[80] Pyne JM, Fortney JC, Tripathi S et al. How bad is depression? Preference score estimates from depressed patients and the general population. *Health Services Research*. 2009; 44(4): 1406-23.
[81] Gerhards SA, Evers SM, Sabel PW et al. Discrepancy in rating health-related quality of life of depression between patient and general population. *Quality of Life Research*. 2011; 20(2): 273-9.
[82] Pyne JM, Fortney JC, Tripathi S et al. How bad is depression? Preference score estimates from depressed patients and the general population. *Health Services Research*. 2009; 44(4): 1406-23.

antidepressant maintenance therapy = 0.72 to 0.83.[83] Whiteford and colleagues[84] suggest the following health utilities:

- Severe depression 0.35 (95% CI of 0.18-0.53)
- Moderate depression 0.59 (95% CI of 0.45-0.72)
- Mild depression 0.84 (95% CI of 0.78-0.89)

- For modelling purposes we assumed an equal proportion of individuals with mild, moderate and severe depression and used the average quality of life provided by Whiteford and colleagues of 0.59 (95% CI of 0.47 to 0.72). Based on a general population QoL of 0.85 (see Reference Document), depression results in a reduction in QoL of 31% (0.85-0.59 / 0.85) (95% CI of 15% to 45%) (see Table 6, row *z*).

- When a longitudinal perspective is taken, 30% of adult patients with depression remain undetected at 1 year and only 14% at the end of 3 years, or approximately one out of seven patients with treatable depression.[85,86,87]
- Applying the adult rate of undiagnosed treatable depression to adolescents may result in understating the number of adolescents with undetected depression in BC as adolescents are more likely than adults to seek advice from peers rather than seek professional help.[88]

- For modelling purposes, we assumed that 25% of adolescent major depressive disorder is undiagnosed treatable depression and varied this between 15% and 35% in the sensitivity analysis (Table 6, row *ae*).

- The USPSTF only found two screening methods that it deemed adequate for use with adolescents, the Patient Health Questionnaire for Adolescents (PHQ-A) and the Beck Depression Inventory (BDI). The sensitivity of a screening instrument refers to the number of people with the illness, in this case, depression correctly identified by the test. The specificity of the test is the number of people without the illness that are correctly identified by the test.
- For the PHQ-A, Johnson et al. found a sensitivity of 73% and a specificity of 94%.[89] They report a positive predictive value (probability that the disease is present when the test is positive) of 56% for MDD and a negative predictive value of 97%. The PHQ-A has been validated compared to a structured clinical interview.

[83] Revicki DA and Wood M. Patient-assigned health state utilities for depression-related outcomes: differences by depression severity and antidepressant medications. *Journal of Affective Disorders*. 1998; 48(1): 25-36.
[84] Whiteford HA, Degenhardt L, Rehm J et al. Global burden of disease attributable to mental and substance use disorders: findings from the Global Burden of Disease Study 2010. *The Lancet*. 2013; 382(9904): 1575-86.
[85] Kessler D, Heath I, Lloyd K et al. Cross sectional study of symptom attribution and recognition of depression and anxiety in primary care. *BMJ*. 1999; 318(7181): 436-40.
[86] Kessler D, Bennewith O, Lewis G et al. Detection of depression and anxiety in primary care: follow up study. *BMJ*. 2002; 325(7371): 1016-7.
[87] Tylee A and Walters P. Underrecognition of anxiety and mood disorders in primary care: why does the problem exist and what can be done? *The Journal of Clinical Psychiatry*. 2006; 68(2): 27-30.
[88] Dr. Jana Davidson, Psychiatrist-in-Chief, Children's & Women's Mental Health Programs, Children's and Women's Health Centre of BC. May 6, 2019. Personal communication.
[89] Johnson JG, Harris ES, Spitzer RL et al. The patient health questionnaire for adolescents: validation of an instrument for the assessment of mental disorders among adolescent primary care patients. *Journal of Adolescent Health*. 2002; 30(3): 196-204.

- In their analysis of the BDI, Canals et al. found for a cut-off score of 11 (i.e. 11 and higher = depressed) the sensitivity of BDI was 90%, the specificity was 86% and the positive predictive value was 20%.[90]
- Roberts et al. found sensitivity of BDI at 83.7%, specificity at 80.9% and positive predictive value at 10.2% when referenced against DSM III clinical diagnosis.[91]

- The USPSTF considers the PHQ-A to be the best test to use in assessing adolescent depression. We will therefore assume use of the PHQ-A in our base model (with a sensitivity of 73% and a specificity of 94%) (Table 6, rows *ai & aj*). We will assume use of the BDI in our sensitivity analysis, taking the average of the Canals and Roberts studies for sensitivity (86.9%) and specificity (83.5%) of the BDI. Because of the potential harms of misdiagnosis, it is useful to apply a second test if individuals test positive with the PHQ-A. When this is modelled we begin with the PHQ-A and then apply the BDI. In the base model, the second test sensitivity is set to 100% and the specificity to 0% in order to correctly carry through the all first tests results to the rest of the model (Table 6, rows *am & an*).

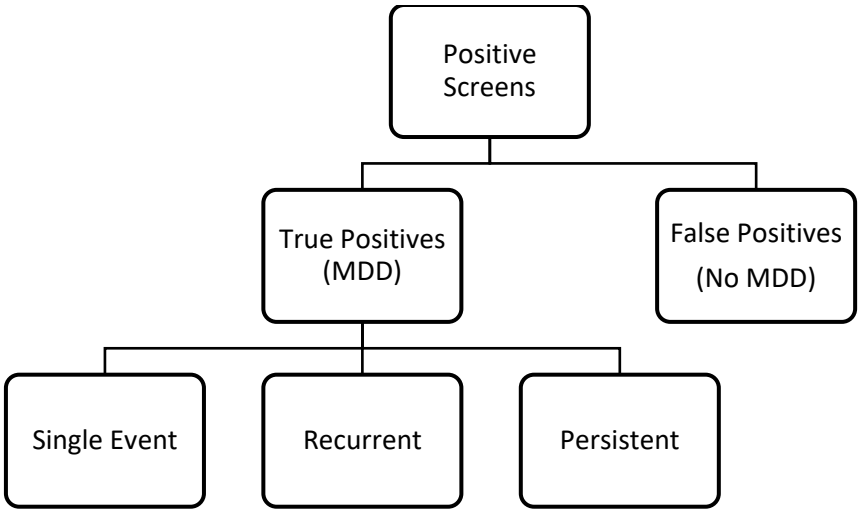
- Merikangas and colleagues found that 40.9% of female and 36.5% of male adolescents in the US aged 13-17 years with major depressive disorder received mental health services for their illness.[92]
- Mojtabai and colleagues found a similar overall rate in 2005, reporting that 36.4% of adolescents 12 -17 sought treatment. This rate increased modestly to 42.0% in 2014 in US adolescents aged 12-17.[93]
- On the other hand, research by Ghandour et al based on 2016 survey results in the US found that 79.0% (95% CI of 74.4% to 83.0%) of adolescents aged 12-17 with diagnosed depression received mental health treatment or counselling.[94] In females 3 – 17 years old (the only sex breakdown available), the number was 80.7% (95% CI of 76.2 to 84.5%) and in males 3 – 17 years old it was 75.2% (95% CI of 67.9 to 81.3%). Unfortunately, the study by Ghandour et al does not provide information on the extent of that treatment or the type of treatment.
- Updating Mojtabai and colleague's numbers using the 2016 and 2017 data from the NSDUH shows that a total of 40.3% of individuals with a 12-month major depressive episode either saw or talked to a health professional or used prescription medication. Averaging the rates for the two years, the number is 31.8% for males and 43.3% for females.[95]
- Mojtabai and colleagues found that of those US adolescents aged 12-17 seeking treatment for their MDD, 20.0% reported use of prescription medication while 50.7%

[90] Canals J, Blade J, Carbajo G et al. The Beck Depression Inventory: Psychometric characteristics and usefulness in nonclinical adolescents. *European Journal of Psychological Assessment*. 2001; 17(1): 63.
[91] Roberts RE, Lewinsohn PM and Seeley JR. Screening for adolescent depression: A comparison of depression scales. *Journal of the American Academy of Child & Adolescent Psychiatry*. 1991; 30(1): 58-66.
[92] Merikangas KR, He J-p, Burstein M et al. Service utilization for lifetime mental disorders in US adolescents: results of the National Comorbidity Survey–Adolescent Supplement (NCS-A). *Journal of the American Academy of Child & Adolescent Psychiatry*. 2011; 50(1): 32-45.
[93] Mojtabai R, Olfson M and Han B. National trends in the prevalence and treatment of depression in adolescents and young adults. *Pediatrics*. 2016; 138(6): e20161878.
[94] Ghandour RM, Sherman LJ, Vladutiu CJ et al. Prevalence and treatment of depression, anxiety, and conduct problems in US children. *The Journal of Pediatrics.* 2018:
[95] Substance Abuse and Mental Health Services Administration. *Reports and Detailed Tables from the 2017 National Survey on Drug Use and Health (NSDUH)*. 2017. Available at https://www.samhsa.gov/data/nsduh/reports-detailed-tables-2017-NSDUH. Accessed February 2019.

reported receiving counselling or therapy.[96] No sex breakdown of counselling or therapy rates was available. NSDUH data for 2016 and 2017 show medication rates of 17.3% for males and 21.7% for females.[97]

- The Mental Health Parity and Addiction Equity Act in the US "generally prevents group health plans and health insurance issuers that provide mental health or substance use disorder (MH/SUD) benefits from imposing less favorable benefit limitations on those benefits than on medical/surgical benefits."[98] The lack of similar legislation in BC may result in treatment seeking rates being lower in BC than are reflected in the US data, especially for non-pharmacological interventions (e.g. counselling).[99]
- In our model, we reduce the US treatment rate(s) by an absolute value of 10% to account for possibly lower treatment rates in BC.
- Data provided by the BC Ministry of Health indicate that for fiscal years 2011/12 through 2015/16 (5 years), 15.7% of BC adolescents (12 -18) diagnosed with major depression had a prescription for fluoxetine filled within one month of diagnosis, 19.7% within three months of diagnosis (i.e. an additional 4%) and 22.2% within six months of diagnosis (i.e. an additional 2.5% since the three-month point). These rates are 14.1%, 17.5% and 19.5%, respectively, for males and 16.6%, 20.9% and 23.6%, respectively, for females.[100]
- It is not uncommon to see wait times of 2 – 6 months for non-pharmacological depression interventions (e.g. cognitive behavioural therapy or individual counselling) in BC.[101]
- We consider four distinct groups in our model, that branch from the group of individuals who received a positive screen for major depressive disorder as follows:

[96] Mojtabai R, Olfson M and Han B. National trends in the prevalence and treatment of depression in adolescents and young adults. *Pediatrics*. 2016; 138(6): e20161878.
[97] Substance Abuse and Mental Health Services Administration. *Reports and Detailed Tables from the 2017 National Survey on Drug Use and Health (NSDUH)*. 2017. Available at https://www.samhsa.gov/data/nsduh/reports-detailed-tables-2017-NSDUH. Accessed February 2019.
[98] Centers for Medicare & Medicaid Services. *The Mental Health Parity and Addiction Equity Act (MHPAEA).* 2019. Available at https://www.cms.gov/cciio/programs-and-initiatives/other-insurance-protections/mhpaea_factsheet.html. Accessed May 2019.
[99] Dr. Jana Davidson, Psychiatrist-in-Chief, Children's & Women's Mental Health Programs, Children's and Women's Health Centre of BC. May 6, 2019. Personal communication.
[100] Aciemme (Sam) Ospan, Senior Manager, Lifetime Prevention Schedule, Healthy Living and Health Promotion Branch, BC Ministry of Health. April 18, 2019. Personal communication.
[101] Dr. Jana Davidson, Psychiatrist-in-Chief, Children's & Women's Mental Health Programs, Children's and Women's Health Centre of BC. May 6, 2019. Personal communication.



- We model each group over different time horizons:
    - False Positives (no MDD) are modelled as being treated for six months after which time we assume that it becomes clear that this group has been incorrectly screened positive and treatments cease for this group.
    - The group with correctly diagnosed MDD that ends up being single event MDD, is also modelled as receiving treatment for six months after which time we assume that no further treatments are undertaken or necessary.
    - The group with correctly diagnosed MDD that ends up being recurrent is modelled as receiving treatment for one year after the index event. We model that this group receives treatment for seven subsequent events during their lifetime, each lasting one year.
    - The group with correctly diagnosed MDD that ends up being persistent is modelled as receiving treatment for twenty years after the index event. We model that this group continues to use anti-depressants throughout this time.

- For modelling purposes, we assume that 50.5% (60.5% - 10%) of adolescents with MDD seek treatment (60.5% is the mid-point of 42%[102] and 79%[103]) and vary this from 32% to 69% in our sensitivity analysis (Table 6, rows *be, bu & co*).
- Of those seeking treatment, 50.7% receive counselling or therapy (Table 6, rows *bf, bv & cp*).
- In modelling for males, we assume that 43.5% (53.5% - 10%) of male adolescents with MDD seek treatment (53.5% is the mid-point of 31.8%[104] and 75.2%[105]) and vary this from 21.8% to 65.2% in our sensitivity analysis (Table 6a, rows *be, bu & co*).

[102] Mojtabai R, Olfson M and Han B. National trends in the prevalence and treatment of depression in adolescents and young adults. *Pediatrics*. 2016; 138(6): e20161878.
[103] Ghandour RM, Sherman LJ, Vladutiu CJ et al. Prevalence and treatment of depression, anxiety, and conduct problems in US children. *The Journal of Pediatrics.* 2018:
[104] Substance Abuse and Mental Health Services Administration. *Reports and Detailed Tables from the 2017 National Survey on Drug Use and Health (NSDUH)*. 2017. Available at https://www.samhsa.gov/data/nsduh/reports-detailed-tables-2017-NSDUH. Accessed February 2019.
[105] Ghandour RM, Sherman LJ, Vladutiu CJ et al. Prevalence and treatment of depression, anxiety, and conduct problems in US children. *The Journal of Pediatrics.* 2018:

- In modelling for females, we assume that 52.0% (62.0% - 10%) of female adolescents with MDD seek treatment (62.0% is the mid-point of 43.3%[106] and 80.7%[107]) and vary this from 33.3% to 70.7% in our sensitivity analysis (Table 6b, rows *be, bu & co*).
- In our model, we assume that 19.7% (Table 6, row *ap*) of ***all individuals*** screened positive for depression will fill anti-depressant prescriptions during the first three months of treatment and that this increases to 22.2% during months 4 – 6 after a positive screen (Table 6, row *ar*).
- In our model for males, we assume that 17.5% (Table 6a, row *ap*) of ***all males*** screened positive for depression will fill anti-depressant prescriptions during the first three months of treatment and that this increases to 19.5% during months 4 – 6 after a positive screen (Table 6a, row *ar*).
- In our model for females, we assume that 20.9% (Table 6b, row *ap*) of ***all females*** screened positive for depression will fill anti-depressant prescriptions during the first three months of treatment and that this increases to 23.6% during months 4 – 6 after a positive screen (Table 6b, row *ar*).
- We model anti-depressant use among recurrent MDD cases and the first year of persistent MDD at 22.2% (Table 6, row *bo*) and assume that after the first year, ***all*** of the persistent MDD cases are taking anti-depressant medication (Table 6, row *cj*)
- In males, we model anti-depressant use among recurrent MDD cases and the first year of persistent MDD at 19.5% (Table 6a, row *bo*) and assume that after the first year, ***all*** of the persistent MDD cases are taking anti-depressant medication (Table 6, row *cj*)
- In females, we model anti-depressant use among recurrent MDD cases and the first year of persistent MDD at 23.6% (Table 6b, row *bo*) and assume that after the first year, ***all*** of the persistent MDD cases are taking anti-depressant medication (Table 6, row *cj*)

- Cognitive behavioural therapy (CBT) is considered to be a "well-established intervention" for depression in adolescents.[108]
- The systematic review prepared by Forman-Hoffman and colleagues for the USPSTF estimated that CBT leads to a clinical improvement in MDD for 12.1% (Table 6, row *au*) of adolescents receiving this therapy compared to a placebo.[109]

[106] Substance Abuse and Mental Health Services Administration. *Reports and Detailed Tables from the 2017 National Survey on Drug Use and Health (NSDUH)*. 2017. Available at https://www.samhsa.gov/data/nsduh/reports-detailed-tables-2017-NSDUH. Accessed February 2019.
[107] Ghandour RM, Sherman LJ, Vladutiu CJ et al. Prevalence and treatment of depression, anxiety, and conduct problems in US children. *The Journal of Pediatrics.* 2018:
[108] Weersing VR, Jeffreys M, Do M-CT et al. Evidence base update of psychosocial treatments for child and adolescent depression. *Journal of Clinical Child & Adolescent Psychology*. 2017; 46(1): 11-43.
[109] Forman-Hoffman V, McClure E, McKeeman J et al. Screening for Major Depressive Disorder in children and adolescents: a systematic review for the US Preventive Services Task Force. *Annals of Internal Medicine.* 2016; 164(5): 342-9.

- Cipriani and colleagues conducted a meta-analysis on efficacy and tolerability of antidepressants in adolescents with major depressive disorder and concluded that "only fluoxetine was statistically significantly more effective than placebo."[110]
- In the clinical guideline for the USPSTF, Siu only identifies one type of selective serotonin reuptake inhibitor (SSRI) with a "good" quality study supporting its use in treating MDD in adolescents: fluoxetine.[111]
- The systematic review prepared by Forman-Hoffman and colleagues for the USPSTF estimated that fluoxetine alone leads to a clinical improvement in MDD for 25.7% (95% CI of 16.2% to 35.2%) of adolescents taking it.
- The systematic review prepared by Forman-Hoffman and colleagues for the USPSTF estimated that when fluoxetine is combined with CBT, the clinical improvement in MDD increases to 36.2% (95% CI of 27.2% to 45.2%) (Table 6, row *av*).
- The Canadian Network for Mood and Anxiety Treatments (CANMAT) 2016 Clinical Guidelines recommend two treatment phases for depression:[112]
    - an acute phase, lasting 8 to 12 weeks, targeting symptom remission and restoration of functioning
    - a maintenance phase, lasting 6 to 24 months, targeting prevention of recurrence and return to full functioning and quality of life
- Depression is a highly recurrent disorder.[113] On average, half of individuals experiencing at least one MDE during their lifetime will experience between 5-9 recurrent episodes during their lifetime.[114,115,116]
- In a follow-up of individuals using anti-depressants, Colman and colleagues reported that 24% of patients were still using anti-depressants 10-years later.[117]

- In our model, we assume that 50% of the MDD cases are single events and the remainder will be recurrent or persistent MDD (Table 6, row *ax*).
- We model that 5.3% of the MDD cases are persistent (22.2% 6-month anti-depressant use in BC adolescents x 24% still using anti-depressants 10 years later = 5.3% of MDD) (Table 6, row *cc*), which leaves 44.7% of the initial MDD cases that recur multiple times in an individual's lifetime (100% - 50% - 5.3% = 44.7%) (Table 6, row *bm*).

[110] Cipriani A, Zhou X, Del Giovane C et al. Comparative efficacy and tolerability of antidepressants for major depressive disorder in children and adolescents: a network meta-analysis. *The Lancet*. 2016; 388(10047): 881-90.
[111] Siu AL. Screening for depression in children and adolescents: US Preventive Services Task Force recommendation statement. *Annals of Internal Medicine.* 2016; 164(5): 360-6.
[112] Lam RW, McIntosh D, Wang J et al. Canadian Network for Mood and Anxiety Treatments (CANMAT) 2016 clinical guidelines for the management of adults with major depressive disorder: section 1. Disease burden and principles of care. *The Canadian Journal of Psychiatry*. 2016; 61(9): 510-23.
[113] Burcusa SL and Iacono WG. Risk for recurrence in depression. *Clinical Psychology Review*. 2007; 27(8): 959-85.
[114] Kessler RC, Zhao S, Blazer DG et al. Prevalence, correlates, and course of minor depression and major depression in the National Comorbidity Survey. *Journal of Affective Disorders*. 1997; 45(1): 19-30.
[115] Kessler RC and Walters EE. Epidemiology of DSM-III-R major depression and minor depression among adolescents and young adults in the national comorbidity survey. *Depression and Anxiety*. 1998; 7(1): 3-14.
[116] Colman I, Naicker K, Zeng Y et al. Predictors of long-term prognosis of depression. *Canadian Medical Association Journal*. 2011; 183(17): 1969-76.
[117] Colman I, Croudace TJ, Wadsworth ME et al. Psychiatric outcomes 10 years after treatment with antidepressants or anxiolytics. *The British Journal of Psychiatry*. 2008; 193(4): 327-31.

- For males, we model that 4.7% of the MDD cases are persistent (19.5% 6-month anti-depressant use in BC adolescents x 24% still using anti-depressants 10 years later = 4.7% of MDD) (Table 6, row *cc*), which leaves 45.3% of the initial MDD cases that recur multiple times in an individual's lifetime (100% - 50% - 4.7% = 45.3%) (Table 6, row *bm*).
- For females, we model that 5.7% of the MDD cases are persistent (23.6% 6-month anti-depressant use in BC adolescents x 24% still using anti-depressants 10 years later = 5.7% of MDD) (Table 6, row *cc*), which leaves 44.3% of the initial MDD cases that recur multiple times in an individual's lifetime (100% - 50% - 5.7% = 44.3%) (Table 6, row *bm*).
- We have modelled an additional 7 episodes after the index MDD episode for a total of eight (8) MDD events for recurrent MDD (Table 6, row *bs*). For discounting purposes, we model these as occurring eight years apart throughout the lifetime of the affected individuals.

- Approximately 60% of patients stay on anti-depressant medication for at least 3 months and 45% for at least 6 months.[118,119] For those diagnosed with depression and taking medication, an average of 71% of days in a 180-day period had anti-depressant use and 62% of days in a 365-day period had anti-depressant use. [120] On average, anti-depressants are taken on 226 days each year.[121]
- The average length of an adolescent depressive episode has been reported to range between 24.4 and 27 weeks.[122,123]
- Van der Voort and colleagues report that single episodes of MDD recover within six months of onset and that individuals with syndromal (recurrent) MDD take up to twelve months to recover fully.[124]

- Following van der Voort and colleagues, we model single episodes of MDD as recovering within 6 months (Table 6, row *bc*) and recurrent episodes as recovering within one year (Table 6, row *br*). We model persistent MDD as requiring treatment throughout the lifetime (Table 6, row *ct*). We model persistent treatment for the 20 years from 15 years old (mid-point of the 12 -18 year old cohort) to 34 years of age, consistent with Tables 4 & 5.

[118] Solberg LI, Trangle MA and Wineman AP. Follow-up and follow-through of depressed patients in primary care: the critical missing components of quality care. *The Journal of the American Board of Family Practice*. 2005; 18(6): 520-7.
[119] Cantrell CR, Eaddy MT, Shah MB et al. Methods for evaluating patient adherence to antidepressant therapy: a real-world comparison of adherence and economic outcomes. *Medical Care*. 2006; 44(4): 300-3.
[120] Puyat JH, Kazanjian A, Wong H et al. Comorbid chronic general health conditions and depression care: a population-based analysis. *Psychiatric Services.* 2017; 68(9): 907-15.
[121] Puyat JH, Kazanjian A, Wong H et al. Comorbid chronic general health conditions and depression care: a population-based analysis. *Psychiatric Services.* 2017; 68(9): 907-15.
[122] Rohde P, Lewinsohn PM, Klein DN et al. Key characteristics of major depressive disorder occurring in childhood, adolescence, emerging adulthood, and adulthood. *Clinical Psychological Science*. 2013; 1(1): 41-53.
[123] Avenevoli S, Swendsen J, He J-P et al. Major depression in the National Comorbidity Survey–Adolescent Supplement: prevalence, correlates, and treatment. *Journal of the American Academy of Child & Adolescent Psychiatry*. 2015; 54(1): 37-44.
[124] van der Voort T, Seldenrijk A, van Meijel B et al. Functional versus syndromal recovery in patients with major depressive disorder and bipolar disorder. *Journal of Clinical Psychiatry*. 2015; 76: e809-e14.

- Several recent meta-analyses suggest that internet-based cognitive behavioural therapy may be effective in treating general depression in adults.[125,126] The evidence that is currently available is insufficient to justify modelling this approach for adolescents with MDD.
- We model treatment for those with a positive MDD screen by time period as follows:
    - 0 – 3 months after screening: 19.7% of positive screened adolescents (17.5% males, 20.9% females) are taking anti-depressants.
    - 4 – 6 months after screening: 22.2% of positive screen adolescents are taking anti-depressants and 25.6% are in counselling or therapy (Table 6 rows *bg, bw & cq*), with half of the therapy group in individual sessions and half in group sessions. The 25.6% is based on 50.5% seeking treatment multiplied by 50.7% of those seeking treatment attending therapy / counselling.
        - For males the counselling rate is 22.1% (43.5% treatment seeking x 50.7% counselling rate among treatment seekers) (Table 6a rows *bg, bw & cq*).
        - For females the counselling rate is 26.4% (52.0% treatment seeking x 50.7% counselling rate among treatment seekers) (Table 6a rows *bg, bw & cq*).
    - 7 – 12 months after screening: 22.2% of **correctly diagnosed** adolescents with **recurrent or persistent MDD** are on anti-depressants and 25.6% are in counselling or therapy, with half of the therapy group in individual sessions and half in group sessions.
    - 13+ months after screening: all of the **correctly diagnosed** adolescents with **persistent MDD** are on anti-depressants. We assume that the 25.6% in counselling or therapy receive four (4) individual sessions annually.
    - Recurrent MDD: for each year of recurrent MDD, 22.2% of individuals with recurrent MDD take anti-depressants and 25.6% receive therapy (5 sessions).

[125] Karyotaki E, Riper H, Twisk J et al. Efficacy of self-guided internet-based cognitive behavioral therapy in the treatment of depressive symptoms: a meta-analysis of individual participant data. *JAMA Psychiatry.* 2017; 74(4): 351-9.

[126] Twomey C and O'Reilly G. Effectiveness of a freely available computerised cognitive behavioural therapy programme (MoodGYM) for depression: meta-analysis. *Australian & New Zealand Journal of Psychiatry*. 2017; 51(3): 260-9.

<table>
<tr><th colspan="6">Treatment Modeling for Positive MDD Screens</th></tr>
<tr><th colspan="2" rowspan="2"></th><th colspan="3">True Positive Screens</th><th rowspan="2">False Positive Screens</th></tr>
<tr><th>Single Event</th><th>Recurrent</th><th>Persistent</th></tr>
<tr><td rowspan="2">0 - 3 Months</td><td>Pharmacological</td><td colspan="4">19.7% anti-depressant rate</td></tr>
<tr><td>Therapeutic</td><td colspan="4">None</td></tr>
<tr><td rowspan="2">4 - 6 Months</td><td>Pharmacological</td><td colspan="4">22.2% anti-depressant rate</td></tr>
<tr><td>Therapeutic</td><td colspan="4">25.6% receiving therapy</td></tr>
<tr><td rowspan="2">7 -12 Months</td><td>Pharmacological</td><td rowspan="4">No treatment</td><td colspan="2">22.2% anti-depressant rate</td><td rowspan="4">No treatment</td></tr>
<tr><td>Therapeutic</td><td colspan="2">25.6% receiving therapy</td></tr>
<tr><td rowspan="2">13+ Months</td><td>Pharmacological</td><td rowspan="2">No Treatment</td><td>100% anti-depressant rate</td></tr>
<tr><td>Therapeutic</td><td>25.6% receiving therapy</td></tr>
</table>

- Revicki and Wood found that antidepressant maintenance therapy resulted in a weighted average QoL of 0.78 (95% CI of 0.63 to 0.93).[127] Based on a general population QoL of 0.85 (see Reference Document), antidepressant maintenance therapy results in a reduction in QoL of 8% (0.85-0.78 / 0.85) (95% CI of 26% to no reduction) (Table 6, row *bg*).

[127] Revicki DA and Wood M. Patient-assigned health state utilities for depression-related outcomes: differences by depression severity and antidepressant medications. *Journal of Affective Disorders*. 1998; 48(1): 25-36.

CPB for Both Sexes

Based on these assumptions, the CPB associated with screening for major depressive disorder in adolescents (both sexes) ages 12 to 18 is 222 QALYs (see Table 6, row *da*).

Table 6: CPB of Screening for MDD in Adolescents Ages 12 - 18
In a BC Birth Cohort of 40,000

Row Label	Variable	Base case	Data Source
a	Number of life years, 12 year olds	39,804	BC Life Table
b	Annual rate of MDD, 12 year olds	5.2%	√
c	Life years with MDD, 12 year olds	2,070	= a * b
d	Life years without MDD, 12 year olds	37,735	= a - c
e	Number of life years, 13 year olds	39,801	BC Life Table
f	Annual rate of MDD, 13 year olds	9.3%	√
g	Life years with MDD, 13 year olds	3,702	= e * f
h	Life years without MDD, 13 year olds	36,100	= e - g
i	Number of life years, 14 year olds	39,797	BC Life Table
j	Annual rate of MDD, 14 year olds	11.7%	√
k	Life years with MDD, 14 year olds	4,656	= i * j
l	Life years without MDD, 14 year olds	35,141	= i - k
m	Number of life years, 15 year olds	39,792	BC Life Table
n	Annual rate of MDD, 15 year olds	15.0%	√
o	Life years with MDD, 15 year olds	5,969	= m * n
p	Life years without MDD, 15 year olds	33,823	= m - o
q	Number of life years, 16 year olds	39,784	BC Life Table
r	Annual rate of MDD, 16 year olds	16.0%	√
s	Life years with MDD, 16 year olds	6,365	= q * r
t	Life years without MDD, 16 year olds	33,419	= q - s
u	Number of life years, 17 and 18 year olds	79,534	BC Life Table
v	Annual rate of MDD, 17 and 18 year olds	16.5%	√
w	Life years with MDD, 17 and 18 year olds	13,123	= u * v
x	Life years without MDD, 17 and 18 year olds	66,411	= u - w
y	**Life years with MDD between 12 and 18**	**35,885**	= c + g + k + o + s + w
z	QoL decrement due to depression	0.31	√
aa	QALYs lost during adolescence due to depression	11,124	= y * z
ab	Deaths attributable to ISH between the ages of 12 and 34	65	Tables 4 & 5
ac	QALYS lost due to deaths attributable to ISH between the ages of 12 and 34	3,189	Tables 4 & 5
ad	**Total QALYs lost due to depression in adolescence**	**14,313**	= aa + ac
ae	% MDD undetected in lifetime	25.0%	√
af	Life years with undetected MDD in cohort between 12 - 18 years of age	8,971	= y * ae
ag	Number of well care visits per year	2.07	√
ah	Depression screening rate	7.4%	√
ai	Sensitivity (rate of true positives), initial test	73.0%	√
aj	Specificity (rate of true negatives), initial test	94.0%	√
ak	Number of MDD cases correctly identified, initial test	1,003	= af * ag * ah * ai
al	Number of MDD cases diagnosed incorrectly, initial test	2,230	= (d + h + l + p + t + x) * ag * ah * (1 - aj)
am	Sensitivity (rate of true positives), 2nd test	100.0%	No second test in base model
an	Specificity (rate of true negatives), 2nd test	0.0%	No second test in base model
	Incorrectly Diagnosed MDD Cases		
ao	Number of MDD cases diagnosed incorrectly, overall	2,230	= al * (1 - an)
ap	Rate of anti-depressants, months 0 - 3	19.7%	√
aq	Number taking anti-depressants months 0 - 3	439	= ao * ap
ar	Rate of anti-depressants, months 4 - 6	22.2%	√
as	Number taking anti-depressants months 4 - 6	495	= ao * ar
at	Life years on anti-depressants	234	= (aq * 0.25) + (as * 0.25)
au	QoL decrement due to anti-depressant therapy	0.08	√
av	**QALYs Gained (or Lost), Incorrectly Diagnosed MDD**	**-18.7**	= - (at * au)

Table 6: CPB of Screening for MDD in Adolescents Ages 12 - 18 In a BC Birth Cohort of 40,000			
	Correctly Diagnosed MDD Cases		
	Single Event MDD		
aw	Number of MDD cases correctly identified, overall	1,003	= ak * am
ax	Rate of single event MDD in correct diagnoses	50.0%	√
ay	Number of single event MDD cases	502	= aw * ax
az	Rate of 6-month anti-depressant use	22.2%	√
ba	Number on anti-depressants	111	= ay * az
bb	Clinical improvement rate due to anti-depressants	25.7%	√
bc	Length of single event MDD, years	0.5	√
bd	**Depression-free life years gained due to anti-depressants**	**14.3**	= ab * bb * bc
be	Treatment seeking rate	50.5%	√
bf	Rate counselling among treatment seekers	50.7%	√
bg	Overall counselling rate	25.6%	= be * bf
bh	Number in counselling	128	= ay * bg
bi	Clinical improvement rate due to counselling	12.1%	√
bj	Length of single event MDD counselling, years	0.25	√
bk	**Depression-free life years gained due to counselling**	**3.9**	= bh * bi * bj
	Recurrent MDD		
bl	Number of MDD cases correctly identified, overall	1,003	= ak * am
bm	Rate of recurrent MDD in correct diagnoses	44.7%	√
bn	Number of recurrent MDD cases	448	= bl * bm
bo	Rate of 12-month anti-depressant use	22.2%	√
bp	Number on anti-depressants	99	= bn * bo
bq	Clinical improvement rate due to anti-depressants	25.7%	√
br	Length of recurrent MDD event, years	1.0	√
bs	Number of recurrent episodes, lifetime	8.0	√
bt	**Depression-free life years gained due to anti-depressants**	**205**	= bp * bq * br * bs
bu	Treatment seeking rate	50.5%	√
bv	Rate counselling among treatment seekers	50.7%	√
bw	Overall counselling rate	25.6%	= bu * bv
bx	Number in counselling	115	= bn * bw
by	Clinical improvement rate due to counselling	12.1%	√
bz	Length of recurrent MDD counselling, years	0.75	√
ca	**Depression-free life years gained due to counselling**	**83**	= bx * by * bz *bs
	Persistent MDD		
cb	Number of MDD cases correctly identified, overall	1,003	= ak * am
cc	Rate of persistent MDD in correct diagnoses	5.3%	√
cd	Number of persistent MDD cases	53	= cb * cc
ce	Rate of first year anti-depressant use	22.2%	√
cf	Number on anti-depressants	12	= cd * ce
cg	Clinical improvement rate due to anti-depressants	25.7%	√
ch	Length of treatment	1.0	√
ci	**Depression-free life years gained due to anti-depressants, year 1**	**3.0**	= cf * cg * ch
cj	Rate of anti-depressant use years 2 - 20	100.0%	√
ck	Number on anti-depressants	53	= cd * cj
cl	Clinical improvement rate due to anti-depressants	25.7%	√
cm	Length of treatment	19.0	√
cn	**Depression-free life years gained due to anti-depressants, years 2 - 20**	**261**	= ck * cl * cm
co	Treatment seeking rate	50.5%	√
cp	Rate counselling among treatment seekers	50.7%	√
cq	Overall counselling rate	25.6%	= co * cp
cr	Number in counselling	14	= cd * cq
cs	Clinical improvement rate due to counselling	12.1%	√
ct	Length of effect persistent event MDD counselling, years	20.0	√
cu	**Depression-free life years gained due to counselling**	**33**	= cr * cs * ct
	Summary of QALYs Gained with Screening		
cv	Individuals with MDD helped by treatment	88	= aw * ((az * bb) + (bg * bi))
cw	Depression free life years due to screening, correctly diagnosed MDD	603	= (bd + bk) + (bt + ca) + (ci + cn + cu)
cx	Reduction in % of total life years with MDD due to screening	1.68%	= cw / y
cy	QALYs gained due to screening, correctly diagnosed MDD	241	= cx * ad
cz	QALYs due to treating incorrectly diagnosed MDD	-19	= av
da	**Net QALYs as a result of screening (CPB)**	**222**	= cy + cz

√ = Estimates from the literature

For the sensitivity analysis of the base model (both sexes), we modified a number of major assumptions and recalculated the CPB as follows:

- Assume the rate of undetected MDD decreases from 25% to 15% (Table 6, row *ae*): CPB = 126
- Assume the rate of undetected MDD increases from 25% to 35% (Table 6, row *ae*): CPB = 318
- Assume a second round of screening (with BDI) is introduced, with a sensitivity of 86.9% and a specificity of 83.5% (Table 6, rows *am & an*): CPB = 206
- Assume the rate of treatment seeking increases from 50.5% to 69% (Table 6, row *aq*): CPB = 239
- Assume the rate of treatment seeking decreases from 50.5% to 32% (Table 6, row *aq*): CPB = 204
- Assume the QoL decrement for depression is reduced from 31% to 15% (Table 6, row *z*) and the QoL decrement for anti-depressant maintenance therapy is reduced from 8% to 0% (i.e. no decrement) (Table 6, row *bg*): CPB = 144
- Assume the QoL decrement for depression is increased from 31% to 45% (Table 6, row *z*) and the QoL decrement for anti-depressant maintenance therapy is increased from 8% to 26% (Table 6, row *bg*): CPB = 264
- Assume that the screening rate is only applied to one visit per year per patient, rather than 2.07 (Table 6, row *ag*): CPB = 107

CPB for Males

Based on the above assumptions for males, the CPB associated with screening for major depressive disorder in male adolescents' ages 12 to 18 is 83 QALYs (see Table 6a, row *da*).

Table 6a: CPB of Screening for MDD in Male Adolescents Ages 12 - 18
In a BC Birth Cohort of 40,000

Row Label	Variable	Base case	Data Source
a	Number of life years, 12 year olds	19,896	BC Life Table
b	Annual rate of MDD, 12 year olds	5.2%	√
c	Life years with MDD, 12 year olds	1,035	= a * b
d	Life years without MDD, 12 year olds	18,862	= a - c
e	Number of life years, 13 year olds	19,894	BC Life Table
f	Annual rate of MDD, 13 year olds	9.3%	√
g	Life years with MDD, 13 year olds	1,850	= e * f
h	Life years without MDD, 13 year olds	18,044	= e - g
i	Number of life years, 14 year olds	19,892	BC Life Table
j	Annual rate of MDD, 14 year olds	11.7%	√
k	Life years with MDD, 14 year olds	2,327	= i * j
l	Life years without MDD, 14 year olds	17,564	= i - k
m	Number of life years, 15 year olds	19,888	BC Life Table
n	Annual rate of MDD, 15 year olds	15.0%	√
o	Life years with MDD, 15 year olds	2,983	= m * n
p	Life years without MDD, 15 year olds	16,905	= m - o
q	Number of life years, 16 year olds	19,884	BC Life Table
r	Annual rate of MDD, 16 year olds	16.0%	√
s	Life years with MDD, 16 year olds	3,181	= q * r
t	Life years without MDD, 16 year olds	16,703	= q - s
u	Number of life years, 17 and 18 year olds	39,750	BC Life Table
v	Annual rate of MDD, 17 and 18 year olds	16.5%	√
w	Life years with MDD, 17 and 18 year olds	6,559	= u * v
x	Life years without MDD, 17 and 18 year olds	33,191	= u - w
y	**Life years with MDD between 12 and 18**	**17,935**	= c + g + k + o + s + w
z	QoL decrement due to depression	0.31	√
aa	QALYs lost during adolescence due to depression	5,560	= y * z
ab	Deaths attributable to ISH between the ages of 12 and 34	45	Table 4
ac	QALYS lost due to deaths attributable to ISH between the ages of 12 and 34	2,159	Table 4
ad	**Total QALYs lost due to depression in adolescence**	**7,719**	= aa + ac
ae	% MDD undetected in lifetime	25.0%	√
af	Life years with undetected MDD in cohort between 12 - 18 years of age	4,484	= y * ae
ag	Number of well care visits per year	1.75	√
ah	Depression screening rate	6.9%	√
ai	Sensitivity (rate of true positives), initial test	73.0%	√
aj	Specificity (rate of true negatives), initial test	94.0%	√
ak	Number of MDD cases correctly identified, initial test	395	= af * ag * ah * ai
al	Number of MDD cases diagnosed incorrectly, initial test	879	= (d + h + l + p + t + x) * ag * ah * (1 - aj)
am	Sensitivity (rate of true positives), 2nd test	100.0%	No second test in base model
an	Specificity (rate of true negatives), 2nd test	0.0%	No second test in base model
	Incorrectly Diagnosed MDD cases		
ao	Number of MDD cases diagnosed incorrectly, overall	879	= al * (1 - an)
ap	Rate of anti-depressants, months 0 - 3	17.5%	√
aq	Number taking anti-depressants months 0 - 3	154	= ao * ap
ar	Rate of anti-depressants, months 4 - 6	19.5%	√
as	Number taking anti-depressants months 4 - 6	171	= ao * ar
at	Life years on anti-depressants	81	= (aq * 0.25) + (as * 0.25)
au	QoL decrement due to antidepressant therapy	0.08	√
av	**QALYs Gained (or Lost), Incorrectly Diagnosed MDD**	**-6.5**	= - (at * au)

Table 6a: CPB of Screening for MDD in Male Adolescents Ages 12 - 18 In a BC Birth Cohort of 40,000			
	Correctly Diagnosed MDD cases		
	Single Event MDD		
aw	Number of MDD cases correctly identified, overall	395	= ak * am
ax	Rate of single event MDD in correct diagnoses	50.0%	√
ay	Number of single event MDD cases	198	= aw * ax
az	Rate of 6-month anti-depressant use	19.5%	√
ba	Number on anti-depressants	39	= ay * az
bb	Clinical improvement rate due to anti-depressants	25.7%	√
bc	Length of single event MDD, years	0.5	√
bd	**Depression-free life years gained due to anti-depressants**	**5.0**	= ab * bb * bc
be	Treatment seeking rate	43.5%	√
bf	Rate counselling among treatment seekers	50.7%	√
bg	Overall counselling rate	22.1%	= be * bf
bh	Number in counselling	44	= ay * bg
bi	Clinical improvement rate due to counselling	12.1%	√
bj	Length of single event MDD counselling, years	0.25	√
bk	**Depression-free life years gained due to counselling**	**1.3**	= bh * bi * bj
	Recurrent MDD		
bl	Number of MDD cases correctly identified, overall	395	= ak * am
bm	Rate of recurrent MDD in correct diagnoses	45.3%	√
bn	Number of recurrent MDD cases	179	= bl * bm
bo	Rate of 12-month anti-depressant use	19.5%	√
bp	Number on anti-depressants	35	= bn * bo
bq	Clinical improvement rate due to anti-depressants	25.7%	√
br	Length of recurrent MDD event, years	1.0	√
bs	Number of recurrent episodes, lifetime	8.0	√
bt	**Depression-free life years gained due to anti-depressants**	**72**	= bp * bq * br * bs
bu	Treatment seeking rate	43.5%	√
bv	Rate counselling among treatment seekers	50.7%	√
bw	Overall counselling rate	22.1%	= bu * bv
bx	Number in counselling	39	= bn * bw
by	Clinical improvement rate due to counselling	12.1%	√
bz	Length of recurrent MDD counselling, years	0.75	√
ca	**Depression-free life years gained due to counselling**	**29**	= bx * by * bz *bs
	Persistent MDD		
cb	Number of MDD cases correctly identified, overall	395	= ak * am
cc	Rate of persistent MDD in correct diagnoses	4.7%	√
cd	Number of persistent MDD cases	19	= cb * cc
ce	Rate of first year anti-depressant use	19.5%	√
cf	Number on anti-depressants	4	= cd * ce
cg	Clinical improvement rate due to anti-depressants	25.7%	√
ch	Length of treatment	1.0	√
ci	**Depression-free life years gained due to anti-depressants, year 1**	**0.9**	= cf * cg * ch
cj	Rate of anti-depressant use years 2 - 20	100.0%	√
ck	Number on anti-depressants	19	= cd * cj
cl	Clinical improvement rate due to anti-depressants	25.7%	√
cm	Length of treatment	19.0	√
cn	**Depression-free life years gained due to anti-depressants, years 2 - 20**	**91**	= ck * cl * cm
co	Treatment seeking rate	43.5%	√
cp	Rate counselling among treatment seekers	50.7%	√
cq	Overall counselling rate	22.1%	= co * cp
cr	Number in counselling	4	= cd * cq
cs	Clinical improvement rate due to counselling	12.1%	√
ct	Length of effect persistent event MDD counselling, years	20.0	√
cu	**Depression-free life years gained due to counselling**	**10**	= cr * cs * ct
	Summary of QALYs Gained with Screening		
cv	Individuals with MDD helped by treatment	30	= aw * ((az * bb) + (bg * bi))
cw	Depression free life years due to screening, correctly diagnosed MDD	208	= (bd + bk) + (bt + ca) + (ci + cn + cu)
cx	Reduction in % of total life years with MDD due to screening	1.16%	= cw / y
cy	QALYs gained due to screening, correctly diagnosed MDD	90	= cx * ad
cz	QALYs due to treating incorrectly diagnosed MDD	-7	= av
da	**Net QALYs as a result of screening (CPB)**	**83**	= cy + cz

√ = Estimates from the literature

For the sensitivity analysis of the base model for males, we modified a number of major assumptions and recalculated the CPB as follows:

- Assume the rate of undetected MDD decreases from 25% to 15% (Table 6a, row *ae*): CPB = 47
- Assume the rate of undetected MDD increases from 25% to 35% (Table 6a, row *ae*): CPB = 119
- Assume a second round of screening (with BDI) is introduced, with a sensitivity of 86.9% and a specificity of 83.5% (Table 6a, rows *am & an*): CPB = 77
- Assume the rate of treatment seeking increases from 43.5% to 65.2% (Table 6a, row *aq*): CPB = 92
- Assume the rate of treatment seeking decreases from 43.5% to 21.8% (Table 6a, row *aq*): CPB = 75
- Assume the QoL decrement for depression is reduced from 31% to 15% (Table 6a, row *z*) and the QoL decrement for anti-depressant maintenance therapy is reduced from 8% to 0% (i.e. no decrement) (Table 6a, row *bg*): CPB = 56
- Assume the QoL decrement for depression is increased from 31% to 45% (Table 6a, row *z*) and the QoL decrement for anti-depressant maintenance therapy is increased from 8% to 26% (Table 6a, row *bg*): CPB = 98
- Assume that the screening rate is only applied to one visit per year per patient, rather than 1.75 (Table 6a, row *ag*): CPB = 48

CPB for Females

Based on the above assumptions for females, the CPB associated with screening for major depressive disorder in female adolescents' ages 12 to 18 is 135 QALYs (see Table 6b, row *da*).

Table 6b: CPB of Screening for MDD in Female Adolescents Ages 12 - 18
In a BC Birth Cohort of 40,000

Row Label	Variable	Base case	Data Source
a	Number of life years, 12 year olds	19,911	BC Life Table
b	Annual rate of MDD, 12 year olds	5.2%	√
c	Life years with MDD, 12 year olds	1,035	= a * b
d	Life years without MDD, 12 year olds	18,876	= a - c
e	Number of life years, 13 year olds	19,910	BC Life Table
f	Annual rate of MDD, 13 year olds	9.3%	√
g	Life years with MDD, 13 year olds	1,852	= e * f
h	Life years without MDD, 13 year olds	18,059	= e - g
i	Number of life years, 14 year olds	19,909	BC Life Table
j	Annual rate of MDD, 14 year olds	11.7%	√
k	Life years with MDD, 14 year olds	2,329	= i * j
l	Life years without MDD, 14 year olds	17,580	= i - k
m	Number of life years, 15 year olds	19,907	BC Life Table
n	Annual rate of MDD, 15 year olds	15.0%	√
o	Life years with MDD, 15 year olds	2,986	= m * n
p	Life years without MDD, 15 year olds	16,921	= m - o
q	Number of life years, 16 year olds	19,904	BC Life Table
r	Annual rate of MDD, 16 year olds	16.0%	√
s	Life years with MDD, 16 year olds	3,185	= q * r
t	Life years without MDD, 16 year olds	16,720	= q - s
u	Number of life years, 17 and 18 year olds	39,794	BC Life Table
v	Annual rate of MDD, 17 and 18 year olds	16.5%	√
w	Life years with MDD, 17 and 18 year olds	6,566	= u * v
x	Life years without MDD, 17 and 18 year olds	33,228	= u - w
y	**Life years with MDD between 12 and 18**	**17,953**	= c + g + k + o + s + w
z	QoL decrement due to depression	0.31	√
aa	QALYs lost during adolescence due to depression	5,565	= y * z
ab	Deaths attributable to ISH between the ages of 12 and 34	20	Table 5
ac	QALYS lost due to deaths attributable to ISH between the ages of 12 and 34	1,030	Table 5
ad	**Total QALYs lost due to depression in adolescence**	**6,596**	= aa + ac
ae	% MDD undetected in lifetime	25.0%	√
af	Life years with undetected MDD in cohort between 12 - 18 years of age	4,488	= y * ae
ag	Number of well care visits per year	2.42	√
ah	Depression screening rate	8.0%	√
ai	Sensitivity (rate of true positives), initial test	73.0%	√
aj	Specificity (rate of true negatives), initial test	94.0%	√
ak	Number of MDD cases correctly identified, initial test	630	= af * ag * ah * ai
al	Number of MDD cases diagnosed incorrectly, initial test	1,401	= (d + h + l + p + t + x) * ag * ah * (1 - aj)
am	Sensitivity (rate of true positives), 2nd test	100.0%	No second test in base model
an	Specificity (rate of true negatives), 2nd test	0.0%	No second test in base model
	Incorrectly Diagnosed MDD cases		
ao	Number of MDD cases diagnosed incorrectly, overall	1,401	= al * (1 - an)
ap	Rate of anti-depressants, months 0 - 3	20.9%	√
aq	Number taking anti-depressants months 0 - 3	293	= ao * ap
ar	Rate of anti-depressants, months 4 - 6	23.6%	√
as	Number taking anti-depressants months 4 - 6	331	= ao * ar
at	Life years on anti-depressants	156	= (aq * 0.25) + (as * 0.25)
au	QoL decrement due to antidepressant therapy	0.08	√
av	**QALYs Gained (or Lost), Incorrectly Diagnosed MDD**	**-12.5**	= - (at * au)

Table 6b: CPB of Screening for MDD in Female Adolescents Ages 12 - 18 In a BC Birth Cohort of 40,000			
	Correctly Diagnosed MDD cases		
	Single Event MDD		
aw	Number of MDD cases correctly identified, overall	630	= ak * am
ax	Rate of single event MDD in correct diagnoses	50.0%	√
ay	Number of single event MDD cases	315	= aw * ax
az	Rate of 6-month anti-depressant use	23.6%	√
ba	Number on anti-depressants	74	= ay * az
bb	Clinical improvement rate due to anti-depressants	25.7%	√
bc	Length of single event MDD, years	0.5	√
bd	**Depression-free life years gained due to anti-depressants**	**9.6**	= ab * bb * bc
be	Treatment seeking rate	52.0%	√
bf	Rate counselling among treatment seekers	50.7%	√
bg	Overall counselling rate	26.4%	= be * bf
bh	Number in counselling	83	= ay * bg
bi	Clinical improvement rate due to counselling	12.1%	√
bj	Length of single event MDD counselling, years	0.25	√
bk	**Depression-free life years gained due to counselling**	**2.5**	= bh * bi * bj
	Recurrent MDD		
bl	Number of MDD cases correctly identified, overall	630	= ak * am
bm	Rate of recurrent MDD in correct diagnoses	44.3%	√
bn	Number of recurrent MDD cases	279	= bl * bm
bo	Rate of 12-month anti-depressant use	23.6%	√
bp	Number on anti-depressants	66	= bn * bo
bq	Clinical improvement rate due to anti-depressants	25.7%	√
br	Length of recurrent MDD event, years	1.0	√
bs	Number of recurrent episodes, lifetime	8.0	√
bt	**Depression-free life years gained due to anti-depressants**	**135**	= bp * bq * br * bs
bu	Treatment seeking rate	52.0%	√
bv	Rate counselling among treatment seekers	50.7%	√
bw	Overall counselling rate	26.4%	= bu * bv
bx	Number in counselling	74	= bn * bw
by	Clinical improvement rate due to counselling	12.1%	√
bz	Length of recurrent MDD counselling, years	0.75	√
ca	**Depression-free life years gained due to counselling**	**53**	= bx * by * bz *bs
	Persistent MDD		
cb	Number of MDD cases correctly identified, overall	630	= ak * am
cc	Rate of persistent MDD in correct diagnoses	5.7%	√
cd	Number of persistent MDD cases	36	= cb * cc
ce	Rate of first year anti-depressant use	23.6%	√
cf	Number on anti-depressants	8	= cd * ce
cg	Clinical improvement rate due to anti-depressants	25.7%	√
ch	Length of treatment	1.0	√
ci	**Depression-free life years gained due to anti-depressants, year 1**	**2.2**	= cf * cg * ch
cj	Rate of anti-depressant use years 2 - 20	100.0%	√
ck	Number on anti-depressants	36	= cd * cj
cl	Clinical improvement rate due to anti-depressants	25.7%	√
cm	Length of treatment	19.0	√
cn	**Depression-free life years gained due to anti-depressants, years 2 - 20**	**175**	= ck * cl * cm
co	Treatment seeking rate	52.0%	√
cp	Rate counselling among treatment seekers	50.7%	√
cq	Overall counselling rate	26.4%	= co * cp
cr	Number in counselling	9	= cd * cq
cs	Clinical improvement rate due to counselling	12.1%	√
ct	Length of effect persistent event MDD counselling, years	20.0	√
cu	**Depression-free life years gained due to counselling**	**23**	= cr * cs * ct
	Summary of QALYs Gained with Screening		
cv	Individuals with MDD helped by treatment	58	= aw * ((az * bb) + (bg * bi))
cw	Depression free life years due to screening, correctly diagnosed MDD	402	= (bd + bk) + (bt + ca) + (ci + cn + cu)
cx	Reduction in % of total life years with MDD due to screening	2.24%	= cw / y
cy	QALYs gained due to screening, correctly diagnosed MDD	148	= cx * ad
cz	QALYs due to treating incorrectly diagnosed MDD	-12	= av
da	**Net QALYs as a result of screening (CPB)**	**135**	= cy + cz

√ = Estimates from the literature

For the sensitivity analysis of the base model for females, we modified a number of major assumptions and recalculated the CPB as follows:

- Assume the rate of undetected MDD decreases from 25% to 15% (Table 6b, row *ae*): CPB = 76
- Assume the rate of undetected MDD increases from 25% to 35% (Table 6b, row *ae*): CPB = 194
- Assume a second round of screening (with BDI) is introduced, with a sensitivity of 86.9% and a specificity of 83.5% (Table 6b, rows *am & an*): CPB = 126
- Assume the rate of treatment seeking increases from 52.0% to 70.7% (Table 6b, row *aq*): CPB = 145
- Assume the rate of treatment seeking decreases from 52.0% to 33.3% (Table 6b, row *aq*): CPB = 125
- Assume the QoL decrement for depression is reduced from 31% to 15% (Table 6b, row *z*) and the QoL decrement for anti-depressant maintenance therapy is reduced from 8% to 0% (i.e. no decrement) (Table 6b, row *bg*): CPB = 83
- Assume the QoL decrement for depression is increased from 31% to 45% (Table 6b, row *z*) and the QoL decrement for anti-depressant maintenance therapy is increased from 8% to 26% (Table 6b, row *bg*): CPB = 163
- Assume that the screening rate is only applied to one visit per year per patient, rather than 2.42 (Table 6b, row *ag*): CPB = 56

Modelling Cost-Effectiveness

In this section, we will calculate the CE associated with screening for major depressive disorder in adolescents.

In modelling CE, we made the following assumptions:

- An adolescent depression screening rate of 7.4% (Table 7, row *c*), completed at each well-care visit, or 2.07 times per year (Table 7, row *b)*,[128] during the seven years of an adolescent's life between 12 and 18 years of age. We model the number available for screening as the sum of adolescents of each age in the cohort (Table 7, row *a)*.
- The cost of each 10 minute primary care provider office visit is $34.85 (see Reference Document) (Table 7, row *e)*.
- The value of patient time for each visit to a primary care office is $59.38 (see Reference Document) (Table 7, row *f)*.
- The proportion of each office visit attributable to screening is 50% (see Reference Document) (Table 7, row *g)*.
- If a second screening is applied (Table 7, row *k*), then all individuals with a positive screen on the first test make another visit to their primary care provider for the second screen. 50% of the office visit time is assumed to be used for the second screen (Table 7, row *g)*.
- Both the PHQ-A[129] and BDI are available online. The PHQ-A is free, but the BDI is copyright (though unlicensed copies exist online) and therefore each use of the BDI is considered to occur through properly licensed channels and cost $4.40 per use (Table 7, row *n*).[130]
- We have assumed that each positive depression diagnosis results in one (1) follow-up visit to the primary care provider. It is assumed that the entire visit is devoted to the depression diagnosis (100% of office visit cost and patient cost) (Table 7, row *r).*
- We have assumed that each depression diagnosis resulting in a course of anti-depressant medication results in two (2) additional visits to a primary care provider to monitor prescription effectiveness (Table 7, row *ab*).
- We model treatment for those with a positive MDD screen by time period as follows:
    - 0 – 3 months after screening: 19.7% of positive screened adolescents are taking anti-depressants (Table 7, row *t*).
        - For males this rate is 17.5% (Table 7a, row *t*)
        - For females this rate is 20.9% (Table 7b, row *t*)
    - 4 – 6 months after screening: 22.2% of positive screen adolescents are taking anti-depressants and 25.6% are in counselling or therapy (Table 7 row *ad*), with half of the therapy group in individual sessions and half in group sessions.

[128] Sekhar DL, Ba DM, Liu G et al. Major depressive disorder screening remains low even among privately insured adolescents. *Journal of Pediatrics*. 2018: Available at https://www-sciencedirect-com.ezproxy.library.ubc.ca/science/article/pii/S0022347618310850. Accessed December 2018.
[129] PHQ-9 modified for Adolescents (PHQ-A) Available at http://www.uacap.org/uploads/3/2/5/0/3250432/phq-a.pdf. Accessed November 2018.
[130] Pearson Clinical Assessment Canada. *Beck Depression Inventory®—II.* 2018. Available at https://www.pearsonclinical.ca/en/products/product-master/item-139.html. Accessed January 2019.

        - For males the counselling rate is 22.1% (Table 7a row *ad*).
        - For females the counselling rate is 26.4% (Table 7b row *ad*).
    - 7 – 12 months after screening: 22.2% of **correctly diagnosed** adolescents with **recurrent or persistent MDD** are on anti-depressants and 25.6% are in counselling or therapy, with half of the therapy group in individual sessions and half in group sessions (To avoid double-counting, counselling for these individuals is modelled in the 4 – 6 month time period).
    - 13+ months after screening: all of the **correctly diagnosed** adolescents with **persistent MDD** are on anti-depressants. We assume that the 25.6% in counselling or therapy receive four (4) individual sessions annually (Table 7 row *bk*).
        - For males the counselling rate is 22.1% (Table 7a row *bk*).
        - For females the counselling rate is 26.4% (Table 7b row *bk*).
    - Recurrent MDD: for each year of recurrent MDD, 22.2% of individuals with recurrent MDD take anti-depressants and 25.6% receive therapy (Table 7 row *cc*).
        - For males the counselling rate is 22.1% (Table 7a row *cc*).
        - For females the counselling rate is 26.4% (Table 7b row *cc*).

<table>
<tr><th colspan="6">Treatment Modeling for Positive MDD Screens</th></tr>
<tr><th colspan="2" rowspan="2"></th><th colspan="3">True Positive Screens</th><th rowspan="2">False Positive Screens</th></tr>
<tr><th>Single Event</th><th>Recurrent</th><th>Persistent</th></tr>
<tr><td rowspan="2">0 - 3 Months</td><td>Pharmacological</td><td colspan="3">19.7% anti-depressant rate</td><td rowspan="2"></td></tr>
<tr><td>Therapeutic</td><td colspan="3">None</td></tr>
<tr><td rowspan="2">4 - 6 Months</td><td>Pharmacological</td><td colspan="3">22.2% anti-depressant rate</td><td rowspan="2"></td></tr>
<tr><td>Therapeutic</td><td colspan="3">25.6% receiving therapy</td></tr>
<tr><td rowspan="2">7 -12 Months</td><td>Pharmacological</td><td rowspan="4">No treatment</td><td colspan="2">22.2% anti-depressant rate</td><td rowspan="4">No treatment</td></tr>
<tr><td>Therapeutic</td><td colspan="2">25.6% receiving therapy</td></tr>
<tr><td rowspan="2">13+ Months</td><td>Pharmacological</td><td rowspan="2">No Treatment</td><td>100% anti-depressant rate</td></tr>
<tr><td>Therapeutic</td><td>25.6% receiving therapy</td></tr>
</table>

- 50% of the MDD cases are single events and 50% will be recurrent (Table 7, row *ax*), split into 5.3% (Table 7, row *bf*) of the total that are persistent (i.e. requiring continuing treatment) and 44.7% of the total that occur on a recurrent basis (Table 7, row *bu*).
- For males, 50% of MDD cases will be recurrent (Table 7a, row *ax*), split into 4.7% (Table 7a, row *bf*) of the total that are persistent (i.e. requiring continuing treatment) and 45.3% of the total that occur on a recurrent basis (Table 7a, row *bu*).
- For females, 50% of MDD cases will be recurrent (Table 7, row *ax*), split into 5.7% (Table 7, row *bf*) of the total that are persistent (i.e. requiring continuing treatment) and 44.3% of the total that occur on a recurrent basis (Table 7, row *bu*).

- Each patient with persistent MDD visits their primary care provider an additional 2 times each year for mental health related matters.[131,132] (Table 7, row *bs*)
- Treatment length for persistent MDD is modelled at 20 years, in keeping with Tables 4 & 5.
- For recurrent cases, there are an additional 7 episodes after the index MDD episode (Table 7, row *bw*). For discounting purposes, we model these as occurring eight years apart throughout the lifetime of the affected individuals.
- When group CBT is given, it is typically provided in a group setting of 10 individuals and lasts between 10 – 15 sessions. Each session is approximately 1.5 hours long (Table 7, row *an*).[133]
- We assume one hour of total travel time per patient to attend each CBT session (Table 7, row *ao*).
- We assume that each session is provided by a grade VI clinical social worker, Level 16 with 6 years of experience. We assume 25% benefits and 40% non-worked hours and a wage rate of $48.65 / hr[134] for a total cost per *worked* hour of $80.27 ($48.65 + ($48.65 * 0.25) + ($48.65 * 0.40)).
- We assume that each of 12 group CBT sessions lasts 1.5 hours and that the preparation time is also 1.5 hours, for a total cost of $240.82 (3 hours * $80.27) per session for the clinical social worker (Table 7, row *ai, bm & ch*).
- We model that half (50%) of adolescents receiving counselling interventions receive 12 group CBT sessions (Table 7, rows *aq*) lasting 1.5 hours in groups of 10 (Table 7, rows *ar*) for their initial sessions. Subsequent CBT requirements as a result of recurring MDD are reduced to 5 sessions each time (Table 7, row *cp*).
- We model that the other half (50%) of adolescents receiving counselling interventions receive 12 individual counselling sessions with a clinical social worker (Table 7, rows *ah*). These sessions also last 1.5 hours.
- Individuals with persistent MDD receive four sessions of individual counselling each year (Table 7, row *bl*).
- March and colleagues' report, upon which the USPSTF recommendation was based, started the treatment at 10mg of fluoxetine daily, increased to 20mg/day after one week and, if necessary, up to a maximum of 40mg/day by week eight of the twelve week trial.[135]

[131] Wong ST, Manca D, Barber D et al. The diagnosis of depression and its treatment in Canadian primary care practices: an epidemiological study. *Canadian Medical Association Journal Open*. 2014; 2(4): e337-42.
[132] Valenstein M, Vijan S, Zeber JE et al. The cost–utility of screening for depression in primary care. *Annals of Internal Medicine.* 2001; 134(5): 345-60.
[133] Dr. Kelly Price, Senior Psychologist, Child and Youth Mental Health Branch, B.C. Ministry of Children and Families. January 8, 2019. Personal communication.
[134] Health Employers Association of BC. *Provincial Agreement between the Health Science Professionals Bargaining Association and Health Employers Association of BC April 1, 2012 – March 31, 2019.* Available at http://www.heabc.bc.ca/public/CAs/HSP/HSP2012-2019_FINAL_3.pdf. Accessed January 2019.
[135] March J, Silva S, Petrycki S et al. Fluoxetine, cognitive-behavioral therapy, and their combination for adolescents with depression: Treatment for Adolescents With Depression Study (TADS) randomized controlled trial. *Journal of the American Medical Association*. 2004; 292(7): 807-20.

- Fluoxetine is available in 10mg and 20mg doses.[136] We model daily treatment with 20mg fluoxetine (or generic equivalent). The cost ranges between $0.35 – 0.88 per 20mg pill for the "BC, Canada" and "Vancouver, BC" geographies. The dispensing fee ranges from $10 – 13.99.[137] Using the mid-point of the above ranges and assuming a 30-day dose is dispensed each time, the modelled annual cost of treatment is $368.48 (($0.615 * 365) + (12 * $12.00)) (Table 7, row *aj*). Using the high and low numbers of the ranges above, we use a high of $489 and low of $248 / year in our sensitivity analysis.
- Clayton and Barcelo estimated the direct costs associated with a completed suicide in the province of New Brunswick to be $5,693 (in 1996 CAD) or $8,129 in 2017 CAD, including ambulance, hospital, physician, autopsy, and funeral services plus the cost of police investigations.[138]
- Kinchin and Doran estimated the direct costs per youth suicide in Australia to be $9,721 (in 2014 AUD) or $8,336 in 2017 CAD.[139]
- Shepard et al estimated that the direct costs per nonfatal suicide attempt are 10% higher than the direct costs per completed suicide in the US.[140]
- For modelling purposes, we have assumed the direct costs per completed suicide in BC to be $8,233 ($8,129 + $8,336 / 2) (Table 7, row *db*) and the direct cost per suicide attempt to be $9,056 ($8,233 * 1.1) (Table 7, row *dc*).
- The ratio of attempted suicides to completed suicides among adolescents is estimated to be 50:1 to 100:1.[141] One-third (33%) of suicide attempts in adolescents require medical attention.[142] For modelling purposes, we assumed that there would be 25 attempted suicides requiring medical attention per completed suicide (Table 7, row *df*) (based on the midpoint between 50 and 100 times 33%) and varied this from 17 to 33 in the sensitivity analysis.
- In a US study by Wright and colleagues, adolescents ages 13-17 who screened negative for depression utilized $2,357 (in 2013 USD) in health care services in the 12-month period following the screening. By comparison, adolescents who screened positive for moderate to severe depression utilized $8,173 in health care services in the 12-month period following the screening.[143] We assumed that the difference of $5,816 ($8,173 - $2,357) would be avoided in those adolescents for whom treatment for MDD was effective. This comes to $5,251 (2017) CAD (Table 7, row *di*).

[136] Pacific Blue Cross. *Pharmacy Compass*. 2018. Available at https://www.pac.bluecross.ca/pharmacycompass. Accessed January 2019.
[137] Pacific Blue Cross. *Pharmacy Compass*. 2018. Available at https://www.pac.bluecross.ca/pharmacycompass. Accessed January 2019.
[138] Clayton D and Barcel A. The cost of suicide mortality in New Brunswick, 1996. *Chronic Diseases in Canada.* 1999; 20(2): 89-95.
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CE for Both Sexes

Based on these assumptions, the CE associated with screening for major depressive disorder in adolescents ages 12 to 18 is $28,215 / QALY (Table 7, row *dp*).

Table 7: CE of Screening for MDD in Adolescents Ages 12 - 18
In a BC Birth Cohort of 40,000

Row Label	Variable	Base case	Source
a	Life years, 12 to 18 year olds	278,512	Table 6, rows a + e + l + m + q + u
b	Number of well care visits per year	2.07	√
c	Depression screening rate	7.4%	√
d	Number of screens conducted, cohort total	42,662	= a * b * c
e	Cost of 10 minute office visit	$34.85	Ref Doc
f	Value of patient time and travel for office visit	$59.38	Ref Doc
g	Portion of 10-minute visit for screening	50%	Ref Doc
h	Initial screening cost	$2,010,042	= d * (e + f) * g
i	Number of MDD cases correctly identified, initial test	1,003	Table 6, row ak
j	Number of MDD cases diagnosed incorrectly, initial test	2,230	Table 6, row al
k	Second screen applied	NO	Table 6, row am
l	Number to be re-screened	0	= i + j (if applicable)
m	Cost of second screening test, each	$4.40	√
n	Cost of second screening	$0	= l * (((e + f) * g) + m)
o	Number of MDD cases correctly identified, overall	1,003	Table 6, row ao
p	Number of MDD cases diagnosed incorrectly, overall	2,230	Table 6, row ap
q	Total number of MDD cases diagnosed	3,233	= o + p
r	Follow up visits, each diagnosed depression	1	Assumed
s	Follow up visit cost	$304,656	= q * (e + f) * r
	Treatment 0 - 3 months post diagnosis (All positive screens)		
t	Anti-depressant rate, 0 - 3 months	19.7%	√
u	Number on anti-depressants	637	= q * t
v	Cost of medication, per year	$368	√
w	Cost of medication, 0 - 3 months	$58,673	= u * v * 0.25
	Treatment 4 - 6 months post diagnosis (All positive screens)		
x	Anti-depressant rate, 4 - 6 months	22.2%	√
y	Number on anti-depressants	718	= q * x
z	Cost of medication, per year	$368	√
aa	Cost of medication, 4 - 6 months	$66,118	= y * z * 0.25
ab	Follow up visits for medication review, per patient	1	√
ac	Cost of medication follow-up	$67,634	= y * ab * (e + f)
ad	Counselling rate	25.6%	Table 6
ae	Number receiving counselling	828	= q * ad
af	Rate of individual counselling	50.0%	√
ag	Number receiving individual counselling	414	= ae * af
ah	Number of CBT sessions	12	√
ai	Cost of clinical social worker per session	$240.82	√
aj	Cost of offering individual CBT (social worker)	$1,196,090	= ag * ah * ai
ak	Session length, in hours	1.5	√
al	Travel time, in hours	1.0	√
am	Patient time, cost per hour	$29.69	Ref Doc
an	Patient time cost, individual CBT treatment sessions	$368,656	= ag * ah * (ak + al) * am
ao	Rate of group counselling	50.0%	√
ap	Number receiving individual counselling	414	= ae * ao
aq	Number of CBT sessions	12	√
ar	Number of individuals in each session	10	√
as	Cost of offering group CBT (social worker)	$119,609	= (ap / ar) * aq * ai
at	Session length, in hours	1.5	√
au	Travel time, in hours	1.0	√
av	Patient time cost per hour	$29.69	Ref Doc
aw	Patient time cost, group CBT treatment sessions	$368,656	= ap *aq * (at + au) * av
	Treatment 7 - 12 months post diagnosis (recurrent and persistent MDD only)		
ax	Rate of recurrent and persistent MDD, correctly diagnosed	50.0%	√
ay	Anti-depressant rate, 7 - 12 months	22.2%	√
az	Number on anti-depressants	111	= o * ax * ay
ba	Cost of medication, per year	$368	√
bb	Cost of medication, 7 - 12 months	$20,515	= az * ba * 0.5
bc	Counselling costs	$0	Included in 4 - 6 month counselling costs

Table 7: CE of Screening for MDD in Adolescents Ages 12 - 18 In a BC Birth Cohort of 40,000			
	Treatment 13+ months post diagnosis (persistent MDD only)		
be	Anti-depressant rate, 13+ months	100.0%	√
bf	Rate of persistent MDD, correctly diagnosed	5.3%	√
bg	Number on anti-depressants	53	= o * be * bf
bh	Cost of medication, per year	$368	√
bi	Additional years of medication	19	√
bj	Cost of medication, 2 - 20 years	$374,198	= bg * bh * bi
bk	Counselling rate, for persistent MDD	25.6%	√
bl	Number of CBT sessions, per year	4	√
bm	Cost of clinical social worker per session	$240.82	√
bn	Cost of offering individual CBT (social worker), years 2 - 20	$250,464	= bg * bi * bl * bk * bm
bo	Session length, in hours	1.5	√
bp	Travel time, in hours	1.0	√
bq	Patient time cost per hour	$29.69	Ref Doc
br	Patient time cost, first CBT treatment sessions	$301,512	= bg * bi * bl * (bo + bp) * bq
bs	Additional physician visits due to anti-depressant medication, each year	2	√
bt	Cost of additional physician visits, persistent MDD	$191,387	= bg * bi * bs * (e + f)
	Treatment for Recurrent MDD (after index event)		
bu	Rate of recurrent MDD, correctly diagnosed	44.7%	√
bv	Number of individuals with recurrent MDD	448	= o * bu
bw	Number of additional recurrent MDD events after index event	7	√
bx	Length of each recurrent MDD event, years	1	√
by	Anti-depressant rate, recurrent MDD	22.2%	√
bz	Number on anti-depressants	99	= bv * by
ca	Cost of medication, per year	$368	√
cb	Cost of medication, recurrent MDD	$256,608	= bz * ca * bw * bx
cc	Counselling rate, for recurrent MDD	25.6%	√
cd	Number individuals in therapy, per recurrent MDD event	115	= bv * cc
ce	Rate of individual counselling	50.0%	√
cf	Number receiving individual counselling	57	= cd * ce
cg	Number of CBT sessions	5	√
ch	Cost of clinical social worker per session	$240.82	√
ci	Cost of offering individual CBT (social worker)	$483,550	= cf * cg * ch * bw
cj	Session length, in hours	1.5	√
ck	Travel time, in hours	1.0	√
cl	Patient time cost per hour	$29.69	Ref Doc
cm	Patient time cost, individual CBT sessions, recurrent MDD	$149,039	= cf * cg * (cj + ck) * cl * bw
cn	Rate of group counselling	50.0%	√
co	Number receiving group counselling	57	= cd * cn
cp	Number of CBT sessions	5	√
cq	Number of individuals in each session	10	√
cr	Cost of offering group CBT (social worker)	$48,355	= (co / cq) * cp * ch * bw
cs	Session length, in hours	1.5	√
ct	Travel time, in hours	1.0	√
cu	Patient time cost per hour	$29.69	Ref Doc
cv	Patient time cost, group CBT, recurrent MDD	$149,039	= co * cp * (cs + ct) * cu * bw
cw	Sub-total, Screening & Screening Follow-up Cost	$2,314,698	= h + n + s
cx	Sub-total, Medication and Medication Follow-up Cost	$1,035,133	= w + aa + ac + bb + bj + bt + cb
cy	Sub-total, Individual Counselling Cost	$2,749,310	= aj + an + bn + br + ci + cm
cz	Sub-total, Group Counselling Cost	$685,659	= as + aw + cr + cv
da	**Total Cost of Intervention**	**$6,784,800**	= cw + cx + cy + cz
	Potential Costs Avoided		
db	Direct costs per completed suicide	$8,233	√
dc	Direct cost per attempted suicide	$9,056	√
dd	Completed suicides avoided due to screening	1.09	Table 6, row ab * Table 6, row cx
de	Costs avoided due to suicides avoided	$8,988	= db * dd
df	Attempted suicides requiring medical attention per completed suicide	25	√
dg	Costs avoided due to suicide attempts avoided	$247,171	= dc * dd * df
dh	Number of people for whom treatment is effective	88.3	Table 6, row cv
di	Health care cost avoided in first 12 months after screening due to effective treatment	$5,251	√
dj	Health care cost avoided, total	$463,735	= dh * di
dk	**Net Costs of Intervention**	**$6,064,907**	= da - de - dg - dj
dl	Net QALYs Gained	221.9	Table 6, row da
dm	Cost Effectiveness (CE) of Intervention, $/QALY	$27,331	= dk / dl
dn	Net Cost of Intervention (1.5% Discount)	$5,375,723	Calculated
do	Net QALYs Gained (1.5% Discount)	190.5	Calculated
dp	Cost Effectiveness (CE) of Intervention, $/QALY (1.5% Discount)	**$28,215**	= dn /do

√ = Estimates from the literature

For the sensitivity analysis, we modified a number of major assumptions and recalculated the CE as follows:

- Assume the rate of undetected MDD decreases from 25% to 15% (Table 6, row *ae*): CE = $43,932
- Assume the rate of undetected MDD increases from 25% to 35% (Table 6, row *ae*): CE = $22,091
- Assume a second round of screening (with BDI) is introduced, with a sensitivity of 86.9% and a specificity of 83.5% (Table 6, rows *am & am*): CE = $21,555
- Assume the rate of treatment seeking increases from 50.5% to 69% (Table 6, row *aq*): CE = $30,645
- Assume the rate of treatment seeking decreases from 50.5% to 32% (Table 6, row *aq*): CE = $25,361
- Assume the QoL decrement for depression is reduced from 31% to 15% (Table 6, row *z*) and the QoL decrement for anti-depressant maintenance therapy is reduced from 8% to 0% (i.e. no decrement) (Table 6, row *bg*): CE = $45,994
- Assume QoL decrement for depression is increased from 31% to 45% (Table 6, row *z*) and the QoL decrement for anti-depressant maintenance therapy is increased from 8% to 26% (Table 6, row *bg*): CE = $23,446
- Assume number of visits after depression diagnosis increases from 1 to 2 (Table 7, row *r*): CE = $29,745
- Assume the cost of medication increases from $368/year to $489/year (Table 7, rows *v, z, ba, bh & ca*): CE = $29,251
- Assume the cost of medication decreases from $368/year to $248/year (Table 7, rows *v, z, ba, bh & ca*): CE = $27,177
- Assume the number of suicide attempts per completed suicide is increased from 25 to 33 (Table 7, row *df*): CE = $27,869
- Assume the number of suicide attempts per completed suicide is reduced from 25 to 17 (Table 7, row *df*): CE = $28,561
- Assume the direct cost of completed suicide doubles from $8,233 to $16,466 (Table 7, row *db*) and the direct cost of attempted suicide doubles from $9,056 to $18,112 (Table 7, row *dc*): CE = $27,094
- Assume that the screening rate is only applied to one visit per year per patient, rather than 2.07 (Table 6, row *ag*): CE = $28,215 (i.e. no change)

CE for Males

Based on the above assumptions for males, the CE associated with screening for major depressive disorder in male adolescents' ages 12 to 18 is $27,595 (see Table 7a, row *dp*).

Table 7a: CE of Screening for MDD in Male Adolescents Ages 12 - 18
In a BC Birth Cohort of 40,000

Row Label	Variable	Base case	Source
a	Life years, 12 to 18 year olds	139,204	Table 6, rows a + e + l + m + q + u
b	Number of well care visits per year	1.75	√
c	Depression screening rate	6.9%	√
d	Number of screens conducted, cohort total	16,809	= a * b * c
e	Cost of 10 minute office visit	$34.85	Ref Doc
f	Value of patient time and travel for office visit	$59.38	Ref Doc
g	Portion of 10-minute visit for screening	50%	Ref Doc
h	Initial screening cost	$791,951	= d * (e + f) * g
i	Number of MDD cases correctly identified, initial test	395	Table 6, row ak
j	Number of MDD cases diagnosed incorrectly, initial test	879	Table 6, row al
k	Second screen applied	NO	Table 6, row am
l	Number to be re-screened	0	= i + j (if applicable)
m	Cost of second screening test, each	$4.40	√
n	Cost of second screening	$0	= l * (((e + f) * g) + m)
o	Number of MDD cases correctly identified, overall	395	Table 6, row ao
p	Number of MDD cases diagnosed incorrectly, overall	879	Table 6, row ap
q	Total number of MDD cases diagnosed	1,274	= o + p
r	Follow up visits, each diagnosed depression	1	Assumed
s	Follow up visit cost	$120,033	= q * (e + f) * r
	Treatment 0 - 3 months post diagnosis (All positive screens)		
t	Anti-depressant rate, 0 - 3 months	17.5%	√
u	Number on anti-depressants	223	= q * t
v	Cost of medication, per year	$368	√
w	Cost of medication, 0 - 3 months	$20,535	= u * v * 0.25
	Treatment 4 - 6 months post diagnosis (All positive screens)		
x	Anti-depressant rate, 4 - 6 months	19.5%	√
y	Number on anti-depressants	248	= q * x
z	Cost of medication, per year	$368	√
aa	Cost of medication, 4 - 6 months	$22,882	= y * z * 0.25
ab	Follow up visits for medication review, per patient	1	√
ac	Cost of medication follow-up	$23,406	= y * ab * (e + f)
ad	Counselling rate	22.1%	Table 6
ae	Number receiving counselling	281	= q * ad
af	Rate of individual counselling	50.0%	√
ag	Number receiving individual counselling	140	= ae * af
ah	Number of CBT sessions	12	√
ai	Cost of clinical social worker per session	$240.82	√
aj	Cost of offering individual CBT (social worker)	$405,932	= ag * ah * ai
ak	Session length, in hours	1.5	√
al	Travel time, in hours	1.0	√
am	Patient time, cost per hour	$29.69	Ref Doc
an	Patient time cost, individual CBT treatment sessions	$125,115	= ag * ah * (ak + al) * am
ao	Rate of group counselling	50.0%	√
ap	Number receiving individual counselling	140	= ae * ao
aq	Number of CBT sessions	12	√
ar	Number of individuals in each session	10	√
as	Cost of offering group CBT (social worker)	$40,593	= (ap / ar) * aq * ai
at	Session length, in hours	1.5	√
au	Travel time, in hours	1.0	√
av	Patient time cost per hour	$29.69	Ref Doc
aw	Patient time cost, group CBT treatment sessions	$125,115	= ap *aq * (at + au) * av
	Treatment 7 - 12 months post diagnosis (recurrent and persistent MDD only)		
ax	Rate of recurrent and persistent MDD, correctly diagnosed	50.0%	√
ay	Anti-depressant rate, 7 - 12 months	19.5%	√
az	Number on anti-depressants	39	= o * ax * ay
ba	Cost of medication, per year	$368	√
bb	Cost of medication, 7 - 12 months	$7,100	= az * ba * 0.5
bc	Counselling costs	$0	Included in 4 - 6 month counselling costs

Table 7a: CE of Screening for MDD in Male Adolescents Ages 12 - 18 In a BC Birth Cohort of 40,000			
	Treatment 13+ months post diagnosis (persistent MDD only)		
be	Anti-depressant rate, 13+ months	100.0%	√
bf	Rate of persistent MDD, correctly diagnosed	4.7%	√
bg	Number on anti-depressants	19	= o * be * bf
bh	Cost of medication, per year	$368	√
bi	Additional years of medication	19	√
bj	Cost of medication, 2 - 20 years	$130,053	= bg * bh * bi
bk	Counselling rate, for persistent MDD	22.1%	√
bl	Number of CBT sessions, per year	4	√
bm	Cost of clinical social worker per session	$240.82	√
bn	Cost of offering individual CBT (social worker), years 2 - 20	$74,983	= bg * bi * bl * bk * bm
bo	Session length, in hours	1.5	√
bp	Travel time, in hours	1.0	√
bq	Patient time cost per hour	$29.69	Ref Doc
br	Patient time cost, first CBT treatment sessions	$104,791	= bg * bi * bl * (bo + bp) * bq
bs	Additional physician visits due to anti-depressant medication, each year	2	√
bt	Cost of additional physician visits, persistent MDD	$66,517	= bg * bi * bs * (e + f)
	Treatment for Recurrent MDD (after index event)		
bu	Rate of recurrent MDD, correctly diagnosed	45.3%	√
bv	Number of individuals with recurrent MDD	179	= o * bu
bw	Number of additional recurrent MDD events after index event	7	√
bx	Length of each recurrent MDD event, years	1	√
by	Anti-depressant rate, recurrent MDD	19.5%	√
bz	Number on anti-depressants	35	= bv * by
ca	Cost of medication, per year	$368	√
cb	Cost of medication, recurrent MDD	$90,054	= bz * ca * bw * bx
cc	Counselling rate, for recurrent MDD	22.1%	√
cd	Number individuals in therapy, per recurrent MDD event	39	= bv * cc
ce	Rate of individual counselling	50.0%	√
cf	Number receiving individual counselling	20	= cd * ce
cg	Number of CBT sessions	5	√
ch	Cost of clinical social worker per session	$240.82	√
ci	Cost of offering individual CBT (social worker)	$166,413	= cf * cg * ch * bw
cj	Session length, in hours	1.5	√
ck	Travel time, in hours	1.0	√
cl	Patient time cost per hour	$29.69	Ref Doc
cm	Patient time cost, individual CBT sessions, recurrent MDD	$51,292	= cf * cg * (cj + ck) * cl * bw
cn	Rate of group counselling	50.0%	√
co	Number receiving group counselling	20	= cd * cn
cp	Number of CBT sessions	5	√
cq	Number of individuals in each session	10	√
cr	Cost of offering group CBT (social worker)	$16,641	= (co / cq) * cp * ch * bw
cs	Session length, in hours	1.5	√
ct	Travel time, in hours	1.0	√
cu	Patient time cost per hour	$29.69	Ref Doc
cv	Patient time cost, group CBT, recurrent MDD	$51,292	= co * cp * (cs + ct) * cu * bw
cw	Sub-total, Screening & Screening Follow-up Cost	$911,984	= h + n + s
cx	Sub-total, Medication and Medication Follow-up Cost	$360,547	= w + aa + ac + bb + bj + bt + cb
cy	Sub-total, Individual Counselling Cost	$928,526	= aj + an + bn + br + ci + cm
cz	Sub-total, Group Counselling Cost	$233,641	= as + aw + cr + cv
da	**Total Cost of Intervention**	**$2,434,699**	= cw + cx + cy + cz
	Potential Costs Avoided		
db	Direct costs per completed suicide	$8,233	√
dc	Direct cost per attempted suicide	$9,056	√
dd	Completed suicides avoided due to screening	0.53	Table 6, row ab * Table 6, row cx
de	Costs avoided due to suicides avoided	$4,326	= db * dd
df	Attempted suicides requiring medical attention per completed suicide	25	√
dg	Costs avoided due to suicide attempts avoided	$118,972	= dc * dd * df
dh	Number of people for whom treatment is effective	30.4	Table 6, row cv
di	Health care cost avoided in first 12 months after screening due to effective treatment	$5,251	√
dj	Health care cost avoided, total	$159,394	= dh * di
dk	**Net Costs of Intervention**	**$2,152,006**	= da - de - dg - dj
dl	Net QALYs Gained	83.1	Table 6, row da
dm	Cost Effectiveness (CE) of Intervention, $/QALY	$25,887	= dk / dl
dn	Net Cost of Intervention (1.5% Discount)	$1,916,383	Calculated
do	Net QALYs Gained (1.5% Discount)	69.4	Calculated
dp	Cost Effectiveness (CE) of Intervention, $/QALY (1.5% Discount)	**$27,595**	= dn /do

√ = Estimates from the literature

For the sensitivity analysis of the base model for males, we modified a number of major assumptions and recalculated the CE as follows:

- Assume the rate of undetected MDD decreases from 25% to 15% (Table 6a, row *ae*): CE = $43,386
- Assume the rate of undetected MDD increases from 25% to 35% (Table 6a, row *ae*): CE = $21,415
- Assume a second round of screening (with BDI) is introduced, with a sensitivity of 86.9% and a specificity of 83.5% (Table 6a, rows *am & am*): CE = $21,583
- Assume the rate of treatment seeking increases from 43.5% to 65.2% (Table 6a, row *aq*): CE = $30,523
- Assume the rate of treatment seeking decreases from 43.5% to 21.8% (Table 6a, row *aq*): CE = $23,984
- Assume the QoL decrement for depression is reduced from 31% to 15% (Table 6a, row *z*) and the QoL decrement for anti-depressant maintenance therapy is reduced from 8% to 0% (i.e. no decrement) (Table 6a, row *bg*): CE = $43,489
- Assume QoL decrement for depression is increased from 31% to 45% (Table 6a, row *z*) and the QoL decrement for anti-depressant maintenance therapy is increased from 8% to 26% (Table 6a, row *bg*): CE = $23,168
- Assume number of visits after depression diagnosis increases from 1 to 2 (Table 7a, row *r*): CE = $29,249
- Assume the cost of medication increases from $368/year to $489/year (Table 7a, rows *v, z, ba, bh & ca*): CE = $28,586
- Assume the cost of medication decreases from $368/year to $248/year (Table 7a, rows *v, z, ba, bh & ca*): CE = $26,603
- Assume the number of suicide attempts per completed suicide is increased from 25 to 33 (Table 7a, row *df*): CE = $27,138
- Assume the number of suicide attempts per completed suicide is reduced from 25 to 17 (Table 7a, row *df*): CE = $28,052
- Assume the direct cost of completed suicide doubles from $8,233 to $16,466 (Table 7a, row *db*) and the direct cost of attempted suicide doubles from $9,056 to $18,112 (Table 7a, row *dc*): CE = $26,116
- Assume that the screening rate is only applied to one visit per year per patient, rather than 1.75 (Table 6a, row *ag*): CE = $27,595 (i.e. no change)

CE for Females

Based on the above assumptions for males, the CE associated with screening for major depressive disorder in male adolescents' ages 12 to 18 is $29,368 (see Table 7b, row *dp*).

Table 7b: CE of Screening for MDD in Female Adolescents Ages 12 - 18
In a BC Birth Cohort of 40,000

Row Label	Variable	Base case	Source
a	Life years, 12 to 18 year olds	139,335	Table 6, rows a + e + l + m + q + u
b	Number of well care visits per year	2.42	√
c	Depression screening rate	8.0%	√
d	Number of screens conducted, cohort total	26,807	= a * b * c
e	Cost of 10 minute office visit	$34.85	Ref Doc
f	Value of patient time and travel for office visit	$59.38	Ref Doc
g	Portion of 10-minute visit for screening	50%	Ref Doc
h	Initial screening cost	$1,262,998	= d * (e + f) * g
i	Number of MDD cases correctly identified, initial test	630	Table 6, row ak
j	Number of MDD cases diagnosed incorrectly, initial test	1,401	Table 6, row al
k	Second screen applied	NO	Table 6, row am
l	Number to be re-screened	0	= i + j (if applicable)
m	Cost of second screening test, each	$4.40	√
n	Cost of second screening	$0	= l * (((e + f) * g) + m)
o	Number of MDD cases correctly identified, overall	630	Table 6, row ao
p	Number of MDD cases diagnosed incorrectly, overall	1,401	Table 6, row ap
q	Total number of MDD cases diagnosed	2,032	= o + p
r	Follow up visits, each diagnosed depression	1	Assumed
s	Follow up visit cost	$191,430	= q * (e + f) * r
	Treatment 0 - 3 months post diagnosis (All positive screens)		
t	Anti-depressant rate, 0 - 3 months	20.9%	√
u	Number on anti-depressants	425	= q * t
v	Cost of medication, per year	$368	√
w	Cost of medication, 0 - 3 months	$39,112	= u * v * 0.25
	Treatment 4 - 6 months post diagnosis (All positive screens)		
x	Anti-depressant rate, 4 - 6 months	23.6%	√
y	Number on anti-depressants	479	= q * x
z	Cost of medication, per year	$368	√
aa	Cost of medication, 4 - 6 months	$44,165	= y * z * 0.25
ab	Follow up visits for medication review, per patient	1	√
ac	Cost of medication follow-up	$45,177	= y * ab * (e + f)
ad	Counselling rate	26.4%	Table 6
ae	Number receiving counselling	536	= q * ad
af	Rate of individual counselling	50.0%	√
ag	Number receiving individual counselling	268	= ae * af
ah	Number of CBT sessions	12	√
ai	Cost of clinical social worker per session	$240.82	√
aj	Cost of offering individual CBT (social worker)	$773,883	= ag * ah * ai
ak	Session length, in hours	1.5	√
al	Travel time, in hours	1.0	√
am	Patient time, cost per hour	$29.69	Ref Doc
an	Patient time cost, individual CBT treatment sessions	$238,524	= ag * ah * (ak + al) * am
ao	Rate of group counselling	50.0%	√
ap	Number receiving individual counselling	268	= ae * ao
aq	Number of CBT sessions	12	√
ar	Number of individuals in each session	10	√
as	Cost of offering group CBT (social worker)	$77,388	= (ap / ar) * aq * ai
at	Session length, in hours	1.5	√
au	Travel time, in hours	1.0	√
av	Patient time cost per hour	$29.69	Ref Doc
aw	Patient time cost, group CBT treatment sessions	$238,524	= ap *aq * (at + au) * av
	Treatment 7 - 12 months post diagnosis (recurrent and persistent MDD only)		
ax	Rate of recurrent and persistent MDD, correctly diagnosed	50.0%	√
ay	Anti-depressant rate, 7 - 12 months	23.6%	√
az	Number on anti-depressants	74	= o * ax * ay
ba	Cost of medication, per year	$368	√
bb	Cost of medication, 7 - 12 months	$13,704	= az * ba * 0.5
bc	Counselling costs	$0	Included in 4 - 6 month counselling costs

Table 7b: CE of Screening for MDD in Female Adolescents Ages 12 - 18 In a BC Birth Cohort of 40,000			
	Treatment 13+ months post diagnosis (persistent MDD only)		
be	Anti-depressant rate, 13+ months	100.0%	√
bf	Rate of persistent MDD, correctly diagnosed	5.7%	√
bg	Number on anti-depressants	36	= o * be * bf
bh	Cost of medication, per year	$368	√
bi	Additional years of medication	19	√
bj	Cost of medication, 2 - 20 years	$251,548	= bg * bh * bi
bk	Counselling rate, for persistent MDD	26.4%	√
bl	Number of CBT sessions, per year	4	√
bm	Cost of clinical social worker per session	$240.82	√
bn	Cost of offering individual CBT (social worker), years 2 - 20	$173,371	= bg * bi * bl * bk * bm
bo	Session length, in hours	1.5	√
bp	Travel time, in hours	1.0	√
bq	Patient time cost per hour	$29.69	Ref Doc
br	Patient time cost, first CBT treatment sessions	$202,685	= bg * bi * bl * (bo + bp) * bq
bs	Additional physician visits due to anti-depressant medication, each year	2	√
bt	Cost of additional physician visits, persistent MDD	$128,656	= bg * bi * bs * (e + f)
	Treatment for Recurrent MDD (after index event)		
bu	Rate of recurrent MDD, correctly diagnosed	44.3%	√
bv	Number of individuals with recurrent MDD	279	= o * bu
bw	Number of additional recurrent MDD events after index event	7	√
bx	Length of each recurrent MDD event, years	1	√
by	Anti-depressant rate, recurrent MDD	23.6%	√
bz	Number on anti-depressants	66	= bv * by
ca	Cost of medication, per year	$368	√
cb	Cost of medication, recurrent MDD	$169,983	= bz * ca * bw * bx
cc	Counselling rate, for recurrent MDD	26.4%	√
cd	Number individuals in therapy, per recurrent MDD event	74	= bv * cc
ce	Rate of individual counselling	50.0%	√
cf	Number receiving individual counselling	37	= cd * ce
cg	Number of CBT sessions	5	√
ch	Cost of clinical social worker per session	$240.82	√
ci	Cost of offering individual CBT (social worker)	$310,262	= cf * cg * ch * bw
cj	Session length, in hours	1.5	√
ck	Travel time, in hours	1.0	√
cl	Patient time cost per hour	$29.69	Ref Doc
cm	Patient time cost, individual CBT sessions, recurrent MDD	$95,628	= cf * cg * (cj + ck) * cl * bw
cn	Rate of group counselling	50.0%	√
co	Number receiving group counselling	37	= cd * cn
cp	Number of CBT sessions	5	√
cq	Number of individuals in each session	10	√
cr	Cost of offering group CBT (social worker)	$31,026	= (co / cq) * cp * ch * bw
cs	Session length, in hours	1.5	√
ct	Travel time, in hours	1.0	√
cu	Patient time cost per hour	$29.69	Ref Doc
cv	Patient time cost, group CBT, recurrent MDD	$95,628	= co * cp * (cs + ct) * cu * bw
cw	Sub-total, Screening & Screening Follow-up Cost	$1,454,427	= h + n + s
cx	Sub-total, Medication and Medication Follow-up Cost	$692,346	= w + aa + ac + bb + bj + bt + cb
cy	Sub-total, Individual Counselling Cost	$1,794,354	= aj + an + bn + br + ci + cm
cz	Sub-total, Group Counselling Cost	$442,567	= as + aw + cr + cv
da	**Total Cost of Intervention**	**$4,383,695**	= cw + cx + cy + cz
	Potential Costs Avoided		
db	Direct costs per completed suicide	$8,233	√
dc	Direct cost per attempted suicide	$9,056	√
dd	Completed suicides avoided due to screening	0.44	Table 6, row ab * Table 6, row cx
de	Costs avoided due to suicides avoided	$3,627	= db * dd
df	Attempted suicides requiring medical attention per completed suicide	25	√
dg	Costs avoided due to suicide attempts avoided	$99,741	= dc * dd * df
dh	Number of people for whom treatment is effective	58.3	Table 6, row cv
di	Health care cost avoided in first 12 months after screening due to effective treatment	$5,251	√
dj	Health care cost avoided, total	$306,347	= dh * di
dk	**Net Costs of Intervention**	**$3,973,980**	= da - de - dg - dj
dl	Net QALYs Gained	135.1	Table 6, row da
dm	Cost Effectiveness (CE) of Intervention, $/QALY	$29,425	= dk / dl
dn	Net Cost of Intervention (1.5% Discount)	$3,514,247	Calculated
do	Net QALYs Gained (1.5% Discount)	119.7	Calculated
dp	Cost Effectiveness (CE) of Intervention, $/QALY (1.5% Discount)	**$29,368**	= dn /do

√ = Estimates from the literature

For the sensitivity analysis of the base model for females, we modified a number of major assumptions and recalculated the CE as follows:

- Assume the rate of undetected MDD decreases from 25% to 15% (Table 6b, row *ae*): CE = $45,560
- Assume the rate of undetected MDD increases from 25% to 35% (Table 6b, row *ae*): CE = $23,098
- Assume a second round of screening (with BDI) is introduced, with a sensitivity of 86.9% and a specificity of 83.5% (Table 6b, rows *am & am*): CE = $22,321
- Assume the rate of treatment seeking increases from 52.0% to 70.7% (Table 6b, row *aq*): CE = $31,878
- Assume the rate of treatment seeking decreases from 52.0% to 33.3% (Table 6b, row *aq*): CE = $26,434
- Assume the QoL decrement for depression is reduced from 31% to 15% (Table 6b, row *z*) and the QoL decrement for anti-depressant maintenance therapy is reduced from 8% to 0% (i.e. no decrement) (Table 6b, row *bg*): CE = $49,734
- Assume QoL decrement for depression is increased from 31% to 45% (Table 6b, row *z*) and the QoL decrement for anti-depressant maintenance therapy is increased from 8% to 26% (Table 6b, row *bg*): CE = $24,171
- Assume number of visits after depression diagnosis increases from 1 to 2 (Table 7b, row *r*): CE = $30,899
- Assume the cost of medication increases from $368/year to $489/year (Table 7b, row *aj*): CE = $30,472
- Assume the cost of medication decreases from $368/year to $248/year (Table 7b, row *aj*): CE = $28,264
- Assume the number of suicide attempts per completed suicide is increased from 25 to 33 (Table 7b, row *df*): CE = $29,146
- Assume the number of suicide attempts per completed suicide is reduced from 25 to 17 (Table 7b, row *df*): CE = $29,591
- Assume the direct cost of completed suicide doubles from $8,233 to $16,466 (Table 7b, row *db*) and the direct cost of attempted suicide doubles from $9,056 to $18,112 (Table 7b, row *dc*): CE = $28,649
- Assume that the screening rate is only applied to one visit per year per patient, rather than 2.42 (Table 6b, row *ag*): CE = $29,368 (i.e. no change)

Summary

Applying a 1.5% discount rate, the clinically preventable burden (CPB) associated with screening for, and treatment of, major depressive disorder (MDD) in adolescents ages 12 to 18 is estimated to be 191 quality-adjusted life years (QALYs) while the cost-effectiveness (CE) is estimated at $28,215 per QALY (see Table 8).

In male adolescents ages 12-18, the CPB with screening for, and treatment of, MDD is estimated to be 69 QALYs while the CE is estimated at $27,595 per QALY (see Table 8a).

In female adolescents ages 12-18, the CPB with screening for, and treatment of, MDD is estimated to be 120 QALYs while the CE is estimated at $29,368 per QALY (see Table 8b).

Table 8: Screening for MDD in Adolescents Ages 12 - 18 in a BC Birth Cohort of 40,000
Summary

	Base Case	Range	
CPB (Potential QALYs Gained)			
Assume No Current Service			
1.5% Discount Rate	**191**	92	274
3% Discount Rate	171	83	247
0% Discount Rate	222	107	318
CE ($/QALY) ***including*** patient time costs			
1.5% Discount Rate	**$28,215**	$21,555	$45,994
3% Discount Rate	$28,892	$21,422	$48,789
0% Discount Rate	$27,331	$21,661	$42,094
CE ($/QALY) ***excluding*** patient time costs			
1.5% Discount Rate	$14,063	$9,656	$22,925
3% Discount Rate	$14,201	$9,298	$23,981
0% Discount Rate	$13,998	$10,199	$21,558

Table 8a: Screening for MDD in Male Adolescents Ages 12 - 18 in a BC Birth Cohort of 40,000
Summary

	Base Case	Range	
CPB (Potential QALYs Gained)			
Assume No Current Service			
1.5% Discount Rate	**69**	39	100
3% Discount Rate	61	34	88
0% Discount Rate	83	47	119
CE ($/QALY) ***including*** patient time costs			
1.5% Discount Rate	**$27,595**	$21,415	$43,489
3% Discount Rate	$28,858	$22,004	$47,491
0% Discount Rate	$25,887	$2,061	$38,218
CE ($/QALY) ***excluding*** patient time costs			
1.5% Discount Rate	$13,264	$10,301	$20,904
3% Discount Rate	$13,693	$10,395	$22,535
0% Discount Rate	$12,788	$10,264	$18,879

Table 8b: Screening for MDD in Female Adolescents Ages 12 - 18 in a BC Birth Cohort of 40,000

Summary

	Base Case	Range	
CPB (Potential QALYs Gained)			
Assume No Current Service			
1.5% Discount Rate	**120**	49	173
3% Discount Rate	110	45	158
0% Discount Rate	135	56	194
CE ($/QALY) ***including*** patient time costs			
1.5% Discount Rate	**$29,368**	$22,321	$49,734
3% Discount Rate	$29,432	$21,724	$51,078
0% Discount Rate	$29,425	$23,174	$47,720
CE ($/QALY) ***excluding*** patient time costs			
1.5% Discount Rate	$14,934	$10,282	$25,291
3% Discount Rate	$14,742	$9,689	$25,585
0% Discount Rate	$15,378	$11,210	$24,940

Behavioural Counselling Interventions

Promotion of Breastfeeding

Canadian Task Force on Preventive Health Care (2004)

Breastfeeding has been shown in both developing and developed countries to improve the health of infants and their mothers, making it the optimal method of infant nutrition.

The CTFPHC concludes that there is good evidence to recommend providing structured antepartum educational programs and postpartum support to promote breastfeeding initiation and duration. (A recommendation)

Unfortunately, advice from a woman's primary clinician (such as family physician, obstetrician or midwife) has not been sufficiently evaluated, and a research gap remains in this area.

The CTFPHC concludes that there is insufficient evidence to make a recommendation regarding advice by primary caregivers to promote breastfeeding. (I Recommendation)[144]

United States Preventive Services Task Force Recommendations (2008)

The USPSTF recommends interventions during pregnancy and after birth to promote and support breastfeeding. This is a grade B recommendation.

There is convincing evidence that breastfeeding provides substantial health benefits for children and adequate evidence that breastfeeding provides moderate health benefits for women.

Adequate evidence indicates that interventions to promote and support breastfeeding increase the rates of initiation, duration, and exclusivity of breastfeeding.

The USPSTF concludes that there is moderate certainty that interventions to promote and support breastfeeding have a moderate net benefit.

Interventions may include multiple strategies, such as formal breastfeeding education for mothers and families, direct support of mothers during breastfeeding observations, and the training of health professional staff about breastfeeding and techniques for breastfeeding support.

Although the activities of individual clinicians to promote and support breastfeeding are likely to be positive, additional benefit may result from efforts that are integrated into systems of care.[145]

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[144] Palda VA, Guise J-M and Wathen CN. Interventions to promote breast-feeding: applying the evidence in clinical practice. *Canadian Medical Association Journal*. 2004; 170(6): 976-8.

[145] US Preventive Services Task Force. Primary care interventions to promote breastfeeding: US Preventive Services Task Force recommendation statement. *Annals of Internal Medicine*. 2008; 149(8): 560-4.

Modelling the Clinically Preventable Burden

In this section, we will calculate the CPB associated with interventions aimed at improving longer term (6 months) exclusive breastfeeding rates in a British Columbia birth cohort of 40,000.

Breastfeeding promotion interventions in developed countries are associated with a 28% increase (odds ratio or OR = 1.28, 95% CI of 1.11 – 1.48) in short-term (1–3 months) exclusive breastfeeding and a 44% increase (OR = 1.44, 95% CI of 1.13 – 1.84) in long-term (6–8 months) exclusive breastfeeding.[146]

Research evidence does not clearly identify which types or components of breastfeeding promotion interventions are effective. In their review for the USPSTF, Chung and colleagues "did not find that formal or structured breastfeeding education or individual-level professional support significantly affected the breastfeeding outcomes. [They] did find that lay support significantly increased the rate of any and exclusive breastfeeding in the short-term." They also noted that interventions including both pre- and post-natal components are important. Finally, "the BFHI (Baby Friendly Hospital Initiative) is effective in increasing exclusive breastfeeding rates, at least up to 6 months after delivery." [147]

From the perspective of a CPS, then, it may be most important for the clinician to refer their pregnant patient or new mother to an intervention including lay support.

Breastfeeding is associated with the following health benefits for the infant:

- Any breastfeeding is associated with a 40% reduction (OR = 0.60, 95% CI of 0.46 – 0.78) in the risk of otitis media (OM) compared to no breastfeeding (Table 2, row *k*). [148] The overall incidence of OM is 1.9 episodes in the first year of life (Table 2, row *j*).[149]

- Exclusive breastfeeding for 3 months or longer is associated with a 42% reduction (OR = 0.58, 95% CI of 0.41 – 0.92) in the risk of atopic dermatitis (AD) compared to exclusive breastfeeding for less than 3 months (Table 2, row *n*). [150] AD has a cumulative incidence of 0.165 in the first two years of life (Table 2, row *m*). [151]

- Any breastfeeding is associated with a 64% reduction (OR = 0.36, 95% CI of 0.32 – 0.41) in the risk of gastrointestinal infection (GI) compared to no breastfeeding (Table 2, row *q*). [152] GI is associated with 0.222 ambulatory visits (Table 2, row *p*) and 0.00298 hospitalizations per infant < 1 year old. [153]

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[146] Chung M, Raman G, Trikalinos T et al. Interventions in primary care to promote breastfeeding: an evidence review for the US Preventive Services Task Force. *Annals of Internal Medicine*. 2008; 149(8): 565-82.
[147] Ibid.
[148] Ibid.
[149] Bartick M and Reinhold A. The burden of suboptimal breastfeeding in the United States: a pediatric cost analysis. *Pediatrics*. 2010; 125(5): e1048-e56.
[150] Chung M, Raman G, Trikalinos T et al. Interventions in primary care to promote breastfeeding: an evidence review for the US Preventive Services Task Force. *Annals of Internal Medicine*. 2008; 149(8): 565-82.
[151] Bartick M and Reinhold A. The burden of suboptimal breastfeeding in the United States: a pediatric cost analysis. *Pediatrics*. 2010; 125(5): e1048-e56.
[152] Chung M, Raman G, Trikalinos T et al. Interventions in primary care to promote breastfeeding: an evidence review for the US Preventive Services Task Force. *Annals of Internal Medicine*. 2008; 149(8): 565-82.
[153] Bartick M and Reinhold A. The burden of suboptimal breastfeeding in the United States: a pediatric cost analysis. *Pediatrics*. 2010; 125(5): e1048-e56.

- Exclusive breastfeeding for 4 months or longer is associated with a 72% reduction (OR = 0.28, 95% CI of 0.14 – 0.54) in the risk of lower respiratory tract infection (LRTI) compared to formula feeding (Table 2, row *t*). [154] The overall incidence of LRTI in infants is 0.0409 cases (Table 2, row *s*) with a death rate of 0.0000732 (Table 2, row *v*). [155]

- Breastfeeding for 3 months or longer is associated with a 27% reduction (OR = 0.73, 95% CI of 0.59 – 0.92) in the risk of asthma compared to no breastfeeding in families without a history of asthma (Table 2, row *aa*). [156] The cumulative incidence of asthma during childhood is 0.127 (Table 2, row *z*) with a death rate of 0.00000273 (Table 2, row *cc*). [157]

- Any breastfeeding is associated with a 24% reduction (OR = 0.76, 95% CI of 0.67 – 0.86) in the risk of overweight or obesity compared to no breastfeeding (Table 2, row *hh & mm*). Each month of breastfeeding is associated with a 4% reduced risk of overweight or obesity. [158] The 2010 rate of overweight and obesity by age group in BC is detailed in Figure 1.[159] Based on this rate and mean survival rates by age group, a birth cohort of 40,000 in BC would be expected to include 878,446 years in a 'state' of overweight and 348,584 years in a 'state' of obesity (see Table 1). Overweight/obesity is associated with a reduced life expectancy of approximately 0.6 and 2.6 years, respectively (see Reference Document). Given the average life expectancy in BC of 82.2 years, this represents a reduction in life expectancy of 0.73% (0.6 / 82.2) associated with overweight (Table 2, row *jj*) and 3.16% (2.6 / 82.2) for obesity (Table 2, row *oo*).

[154] Chung M, Raman G, Trikalinos T et al. Interventions in primary care to promote breastfeeding: an evidence review for the US Preventive Services Task Force. *Annals of Internal Medicine*. 2008; 149(8): 565-82.
[155] Bartick M and Reinhold A. The burden of suboptimal breastfeeding in the United States: a pediatric cost analysis. *Pediatrics*. 2010; 125(5): e1048-e56.
[156] Chung M, Raman G, Trikalinos T et al. Interventions in primary care to promote breastfeeding: an evidence review for the US Preventive Services Task Force. *Annals of Internal Medicine*. 2008; 149(8): 565-82.
[157] Bartick M and Reinhold A. The burden of suboptimal breastfeeding in the United States: a pediatric cost analysis. *Pediatrics*. 2010; 125(5): e1048-e56.
[158] Chung M, Raman G, Trikalinos T et al. Interventions in primary care to promote breastfeeding: an evidence review for the US Preventive Services Task Force. *Annals of Internal Medicine*. 2008; 149(8): 565-82.
[159] Statistics Canada. *Canadian Community Health Survey Public Use Microdata File 2009-2010 and 2010.* All computations, use and interpretation of these data are entirely that of H. Krueger & Associates Inc.

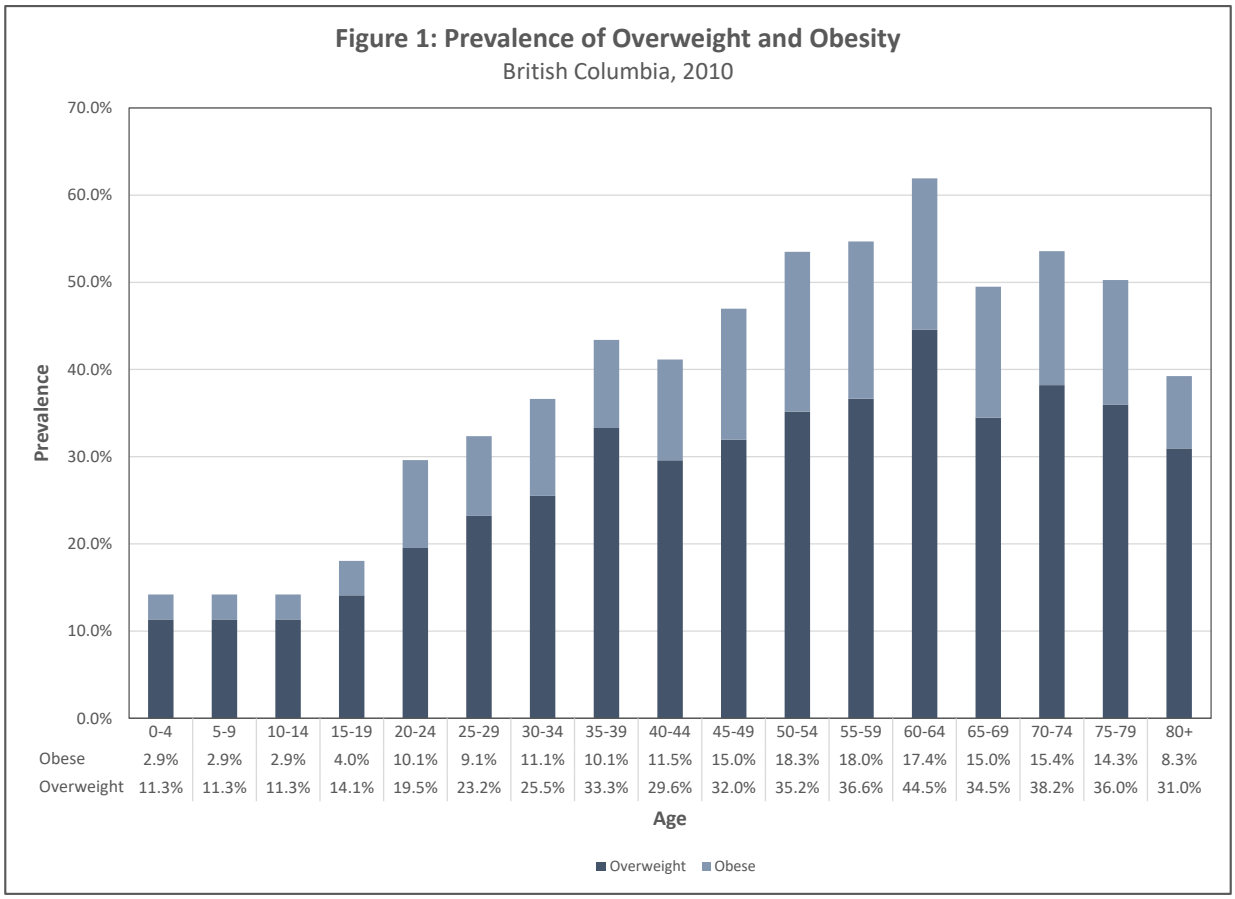

Table 1: Years of Life as Overweight or Obese in a Birth Cohort of 40,000

Age Group	Mean Survival Rate	Years of Life in Birth Cohort	% Overweight	Years of Life Overweight	% Obese	Years of Life Obese
0-4	99.6%	199,198	11.3%	22,572	2.9%	5,711
5-9	99.5%	199,088	11.3%	22,560	2.9%	5,708
10-14	99.5%	199,022	11.3%	22,552	2.9%	5,706
15-19	99.4%	198,868	14.1%	28,034	4.0%	7,856
20-24	99.2%	198,408	19.5%	38,776	10.1%	19,990
25-29	98.9%	197,850	23.2%	45,921	9.1%	18,075
30-34	98.6%	197,290	25.5%	50,330	11.1%	21,927
35-39	98.3%	196,550	33.3%	65,453	10.1%	19,818
40-44	97.8%	195,526	29.6%	57,851	11.5%	22,580
45-49	97.0%	194,070	32.0%	62,018	15.0%	29,161
50-54	96.0%	191,948	35.2%	67,489	18.3%	35,177
55-59	94.4%	188,786	36.6%	69,177	18.0%	34,041
60-64	92.0%	183,998	44.5%	81,961	17.4%	31,970
65-69	88.3%	176,658	34.5%	60,915	15.0%	26,517
70-74	82.7%	165,362	38.2%	63,193	15.4%	25,408
75-79	74.1%	148,142	36.0%	53,308	14.3%	21,158
80+	59.5%	214,284	31.0%	66,334	8.3%	17,784
Total		**3,245,048**	**27.1%**	**878,446**	**10.7%**	**348,584**

- Breastfeeding for 3 months or longer is associated with a 19% reduction (OR = 0.81, 95% CI of 0.74 – 0.89) in the risk of type 1 diabetes compared to breastfeeding for less than 3 months (Table 2, row *rr*). [160] The overall incidence of type 1 diabetes is 0.000186 (Table 2, row *qq*) with a death rate of 0.00000121 (Table 1-2, row *tt*). [161]

- Breastfeeding for less than 6 months is associated with a 12% reduction (OR = 0.88, 95% CI of 0.80 – 0.96) in the risk of childhood leukemia while breastfeeding for more than 6 months is associated with a 24% reduction (OR = 0.76, 95% CI of 0.68 – 0.84) in the risk of childhood leukemia compared to no breastfeeding (Table 2, row *yy*). [162][147] The overall incidence of childhood leukemia is 0.0000321 (Table 2, row *xx*) with a five-year death rate 39.8% (Table 2, row *aaa*) for children younger than 15. [163]

- Any breastfeeding is associated with a 36% reduction (OR = 0.64, 95% CI of 0.51 – 0.81) in the risk of sudden infant death syndrome (SIDS) compared to no breastfeeding (Table 2, row *fff*). [164] The overall incidence of SIDS is 0.00054 (Table 2, row *eee*). [165]

Breastfeeding is associated with the following health benefits for the mother:

- The risk of breast cancer is reduced by 4.3% for each year of breastfeeding. [166] We have assumed a reduced risk of 2.15% for each 6 months of breastfeeding (Table 2, row *jjj*). The lifetime probability of developing (female) breast cancer is 11.5% (Table 2, row *iii*).[167] Breast cancer is associated with a reduced life expectancy of 12.9 years (see Reference Document, Table 2, row *mmm*).

- Any breastfeeding is associated with a 21% reduction (OR = 0.79, 95% CI of 0.68–0.91) in the risk of ovarian cancer compared to no breastfeeding (Table 1-2, row *ppp*). Cumulative breastfeeding of at least 12 months is associated with a 28% reduction (OR = 0.72, 95% CI of 0.54–0.97) in the risk of ovarian cancer compared to no breastfeeding. [168][147] Ovarian cancer is associated with a reduced life expectancy of 16.5 years (see reference Document, Table 2, row *sss*).

- Other assumptions used in assessing the clinically preventable burden are detailed in the Reference Document.

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[160] Chung M, Raman G, Trikalinos T et al. Interventions in primary care to promote breastfeeding: an evidence review for the US Preventive Services Task Force. *Annals of Internal Medicine*. 2008; 149(8): 565-82.
[161] Bartick M and Reinhold A. The burden of suboptimal breastfeeding in the United States: a pediatric cost analysis. *Pediatrics*. 2010; 125(5): e1048-e56.
[162] Chung M, Raman G, Trikalinos T et al. Interventions in primary care to promote breastfeeding: an evidence review for the US Preventive Services Task Force. *Annals of Internal Medicine*. 2008; 149(8): 565-82.
[163] Bartick M and Reinhold A. The burden of suboptimal breastfeeding in the United States: a pediatric cost analysis. *Pediatrics*. 2010; 125(5): e1048-e56.
[164] Chung M, Raman G, Trikalinos T et al. Interventions in primary care to promote breastfeeding: an evidence review for the US Preventive Services Task Force. *Annals of Internal Medicine*. 2008; 149(8): 565-82.
[165] Bartick M and Reinhold A. The burden of suboptimal breastfeeding in the United States: a pediatric cost analysis. *Pediatrics*. 2010; 125(5): e1048-e56.
[166] Chung M, Raman G, Trikalinos T et al. Interventions in primary care to promote breastfeeding: an evidence review for the US Preventive Services Task Force. *Annals of Internal Medicine*. 2008; 149(8): 565-82.
[167] Canadian Cancer Society's Advisory Committee on Cancer Statistics. *Canadian Cancer Statistics 2014.* 2014. Canadian Cancer Society. Available at www.cancer.ca/statistics. Accessed February 2015.
[168] Chung M, Raman G, Trikalinos T et al. Interventions in primary care to promote breastfeeding: an evidence review for the US Preventive Services Task Force. *Annals of Internal Medicine*. 2008; 149(8): 565-82.

Based on these assumptions, the CPB associated with interventions aimed at improving rates of exclusive breastfeeding at 6 months from 0% to 60% is 5,002 QALYs (Table 2, row *vvv*).

Table 2: CPB of Promotion of Breastfeeding in a Birth Cohort of 40,000

Row Label	Variable	Base Case	Data Source
a	Infants in birth cohort	40,000	
b	Current proportion exclusively breastfed for 6 months	41%	√
c	Number exclusively breastfed for 6 months	16,400	= (a * c)
d	Effectiveness of breastfeeding promotion interventions in increasing adherence to breastfeeding for 6 months	44%	√
e	Increase in exclusive 6-month breastfeeding with 100% adherence	10,384	= (a - c) * d
f	Estimated adherence with intervention	75%	Assumed
g	Increase in exclusive 6-month breastfeeding with intervention	7,788	= (e * f)
h	Total proportion exclusively breastfed for 6 months with intervention	60%	= (c + g)/a
	Health Benefits for the Infant		
i	Average life expectancy of an infant in BC	82.2	√
j	Average cases of otitis media (OM) in first year	1.90	√
k	Effectiveness of breastfeeding in reducing risk of OM	40.0%	√
l	Reduced cases of OM with intervention	5,919	= (g * j) * k
m	Average cases of atopic dermatitis (AD) in first 2 years	0.165	√
n	Effectiveness of breastfeeding in reducing risk of AD	42.0%	√
o	Reduced cases of AD with intervention	540	= (g * m) * n
p	Average cases of gastrointestinal infection (GI) in first year	0.222	√
q	Effectiveness of breastfeeding in reducing risk of GI	64.0%	√
r	Reduced cases of GI with intervention	1,107	= (g * p) * q
s	Average cases of lower respiratory tract infection (LTRI) in first year	0.041	√
t	Effectiveness of breastfeeding in reducing risk of LTRI	72.0%	√
u	Reduced cases of LTRI with intervention	229	= (g * s) * t
v	Average rate of death due to LTRI	0.0000732	√
w	Effectiveness of breastfeeding in reducing risk of LTRI	72.0%	√
x	Reduced deaths due to LTRI with intervention	0.41	= (g * v) * w
y	Life years gained with intervention	33.7	= x * i
z	Average cases of childhood asthma	0.127	√
aa	Effectiveness of breastfeeding in reducing risk of asthma	27.0%	√
bb	Reduced cases of asthma with intervention	267	= (g * z) * aa
cc	Average rate of death due to asthma	0.0000027	√
dd	Effectiveness of breastfeeding in reducing risk of asthma	27.0%	√
ee	Reduced deaths due to asthma with intervention	0.01	= (g * cc) * dd
ff	Life years gained with intervention	0.5	= ee * i
gg	Average % of years as overweight	27.1%	Table 1-1
hh	Effectiveness of breastfeeding in reducing risk of overweight	24%	√
ii	Reduced years as overweight with intervention	41,591	= g * i * gg* hh
jj	% of life years lost with overweight	0.73%	√
kk	Life years gained with intervention	304	= ii * jj
ll	Average % of years as obese	10.7%	Table 1
mm	Effectiveness of breastfeeding in reducing risk of obesity	24%	√
nn	Reduced years as obese with intervention	16,504	= g * i * ll* mm
oo	% of life years lost with obesity	3.16%	√
pp	Life years gained with intervention	522	= nn * oo
qq	Average cases of type 1 diabetes in children	0.0001860	√
rr	Effectiveness of breastfeeding in reducing risk of type 1 diabetes	19.0%	√
ss	Reduced cases of type 1 diabetes with intervention	0.28	= (g * qq) * rr
tt	Average rate of death due to type 1 diabetes	0.0000012	√
uu	Effectiveness of breastfeeding in reducing risk of type 1 diabetes	19.0%	√
vv	Reduced deaths due to type 1 diabetes with intervention	0.002	= (g * tt) * uu
ww	Life years gained with intervention	0.15	= vv * i

Table 2: CPB of Promotion of Breastfeeding in a Birth Cohort of 40,000			
Row Label	Variable	Base Case	Data Source
xx	Average cases of childhood leukemia	0.0000321	√
yy	Effectiveness of breastfeeding in reducing risk of childhood leukemia	24.0%	√
zz	Reduced cases of childhood leukemia with intervention	0.06	= (g * xx) * yy
aaa	5 year death rate due to childhood leukemia	39.8%	√
bbb	Effectiveness of breastfeeding in reducing risk of childhood leukemia	24.0%	√
ccc	Reduced deaths due to childhood leukemia with intervention	0.006	= zz * aaa * bbb
ddd	Life years gained with intervention	0.47	= ccc * i
eee	Average rate of death due to Sudden Infant Death Syndrome (SIDS)	0.00054	√
fff	Effectiveness of breastfeeding in reducing risk of SIDS	36.0%	√
ggg	Reduced deaths due to SIDS with intervention	1.514	= (g * eee) * fff
hhh	Life years gained with intervention	124.4	= ggg * i
	Health Benefits for the Mother		
iii	Lifetime probability of developing breast cancer	11.5%	√
jjj	Effectiveness of breastfeeding in reducing risk of breast cancer	2.15%	√
kkk	Reduced breast cancer cases due to intervention	19.3	= (g * iii) * jjj
lll			
mmm	Life years lost per breast cancer	12.9	Ref Doc
nnn	Life years gained with intervention	248.4	= kkk * mmm
ooo	Lifetime probability of developing ovarian cancer	1.4%	√
ppp	Effectiveness of breastfeeding in reducing risk of ovarian cancer	21%	√
qqq	Reduced ovarian cancer cases due to intervention	22.9	= (g * ooo) * ppp
rrr			
sss	Life years lost per ovarian cancer	16.5	Ref Doc
ttt	Life years gained with intervention	377.8	= qqq * sss
uuu	**Potential QALYs gained, Intervention increasing from 41% to 60%**	**1,611**	= y + ff + kk + pp + ww + ddd + hhh + nnn + ttt
vvv	**Potential QALYs gained, Intervention increasing from 0% to 60%**	**5,002**	=(uuu/g) * (c+g)

√ = Estimates from the literature

We also modified a number of major assumptions and recalculated the CPB as follows:

- Assume the effectiveness of interventions aimed at improving rates of exclusive breastfeeding at 6 months is reduced from 44% to 13% (Table 2, row *d*): CPB = 3,868 QALYs
- Assume the effectiveness of interventions aimed at improving rates of exclusive breastfeeding at 6 months is increased from 44% to 84% (Table 2, row *d*): CPB = 6,466 QALYs
- Assume the effectiveness of breastfeeding in reducing overweight and obesity is reduced from 24% to 14% (Table 2, row *hh* & *mm*): CPB = 3,934 QALYs
- Assume the effectiveness of breastfeeding in reducing overweight and obesity is increased from 24% to 33% (Table 2, row *hh* & *mm*): CPB = 5,963 QALYs

Modelling Cost-Effectiveness

In this section, we will calculate the CPB associated with interventions aimed at improving longer term (6 months) exclusive breastfeeding rates in a British Columbia birth cohort of 40,000.

In modelling CE, we made the following assumptions:

- **Patient time costs for office visit** – We assumed that two hours of patient time would be required, including travel to and from the appointment.
- **Patient time costs for breastfeeding support groups** - We assumed that a new mother would attend a breastfeeding support group once per month (lasting two hours) for six months. We assumed an additional hour for travel time for a total patient time commitment of 18 hours.

- **Otitis media** - Two estimates from the US suggest a direct cost (ambulatory care and antibiotics) per case of $156 (2007 USD)[169] and $106 (2004 USD).[170] A Canadian study suggested additional hospital costs over and above physician and drug costs of 15.6%.[171] We have converted the $156 to 2017 Canadian dollars and then added 15.6% to this cost per case to reflect hospital costs for a total cost per case of $251 (Table 3, row *p*).
- **Atopic dermatitis** - The mean duration of atopic dermatitis is 10 years with 45% of cases being mild in severity, 45% moderate and 10% severe.[172] The direct annual costs per mild, moderate and severe case are $175, $300, and $405, respectively. The average weighted cost totalled $254 CAD in 2001[173] or $342 (in 2017 CAD) per case per year. Lifetime costs were estimated at $3,420 (Table 3, row *s*).
- **Gastrointestinal infection** - A US study suggests the direct costs for gastrointestinal infections and lower respiratory tract infections are $331 per case (in 1995 USD)[174] or $462 in 2017 CAD (Table 3, rows *v*).
- **Lower respiratory tract infection** - See above (Table 3, rows y).
- **Asthma** - A BC study estimated the annual direct costs attributable to asthma at $444 per person year (in 2006 CAD)[175] or $523 in 2017 CAD. Based on an average treatment duration of 10 years,[176] the total costs attributable to childhood asthma would be $5,230 per case (Table 3, row *bb*).
- **Type 1 diabetes** - The lifetime cost per case in the US has been estimated at $77,463 (in 2007 USD)[177] or $76,598 in 2017 CAD (Table 3, row *kk*).
- **Childhood leukemia** - The lifetime cost per case in the US has been estimated at $136,444 (in 2007 USD)[178] or $134,920 in 2017 CAD (Table 3, row *nn*).
- Other costs and assumptions used in assessing cost-effectiveness are detailed in the Reference Document.
- Discount rate of 1.5%, varied from 0% to 3% in the sensitivity analysis.

Based on these assumptions, the CE associated with interventions aimed at improving rates of exclusive breastfeeding at 6 months is -$9,021 per QALY (Table 3, row *bbb*).

[169] Bartick M and Reinhold A. The burden of suboptimal breastfeeding in the United States: a pediatric cost analysis. *Pediatrics*. 2010; 125(5): e1048-e56.
[170] Zhou F, Shefer A, Kong Y et al. Trends in acute otitis media-related health care utilization by privately insured young children in the United States, 1997–2004. *Pediatrics*. 2008; 121(2): 253-60.
[171] Coyte PC, Asche CV and Elden LM. The economic cost of otitis media in Canada. *International Journal of Pediatric Otorhinolaryngology*. 1999; 49(1): 27-36.
[172] Barbeau M and Bpharm HL. Burden of atopic dermatitis in Canada. *International Journal of Dermatology*. 2006; 45(1): 31-6.
[173] Ibid.
[174] Ball TM and Wright AL. Health care costs of formula-feeding in the first year of life. *Pediatrics*. 1999; 103(Suppl. 1): 870-6.
[175] Sadatsafavi M, Lynd L, Marra C et al. Direct health care costs associated with asthma in British Columbia. *Canadian Respiratory Journal*. 2010; 17(2): 74-80.
[176] Bartick M and Reinhold A. The burden of suboptimal breastfeeding in the United States: a pediatric cost analysis. *Pediatrics*. 2010; 125(5): e1048-e56.
[177] Ibid.
[178] Ibid.

Table 3: CE of Promotion of Breastfeeding in a Birth Cohort of 40,000			
Row Label	**Variable**	**Base Case**	**Data Source**
a	Women eligible for screening/referral in primary care	40,000	
b	Proportion already exclusively breastfeeding for 6 months	41%	Table 2, row b
c	Number exclusively breastfeeding for 6 months	16,400	= a * b
d	Women eligible for intervention (support group)	23,600	= a - c
e	Estimated adherence with intervention	75%	Assumed
f	Women attending intervention (support group)	17,700	= d * f
g	Effectiveness of breastfeeding promotion interventions in increasing adherence to breastfeeding for 6 months	44%	Table 2, row d
h	# of women attending intervention (support group) who exclusively breastfeed for 6 months	7,788	= f * g
	Costs of intervention		
i	Cost of 10-minute office visit	$34.85	Ref Doc
j	Value of patient time and travel for office visit	$59.38	=2 * $29.69
k	Portion of 10-minute office visit for screen/referral	50%	Ref Doc
l	Estimated cost of screening	$1,884,600	= a * (I + j) * k
m	Value of patient time and travel for intervention	$534	=18 * $29.69
n	Estimated cost of intervention over lifetime of birth cohort	$9,451,800	= f * m
	Cost avoided		
o	Cases of otitis media avoided	5,919	Table 2, row l
p	Cost per case	$251	√
q	Costs avoided	$1,485,639	= o * p
r	Cases of atopic dermatitis avoided	540	Table 2, row o
s	Cost per person with atopic dermatitis	$3,420	√
t	Costs avoided	$1,845,803	= r * s
u	Cases of gastrointestinal infection avoided	1,107	Table 2, row r
v	Cost per case	$462	√
w	Costs avoided	$511,212	= u * v
x	Cases of lower respiratory tract infection avoided	229	Table 2, row u
y	Cost per case	$462	√
z	Costs avoided	$105,956	= x * y
aa	Cases of asthma avoided	267	Table 2, row bb
bb	Cost per case	$5,230	√
cc	Costs avoided	$1,396,674	= aa * bb
dd	Years of overweight avoided	41,591	Table 2, row ii
ee	Cost per year	$227	Ref Doc
ff	Costs avoided	$9,441,234	= dd * ee
gg	Years of obesity avoided	16,504	Table 2, row nn
hh	Cost per year	$805	Ref Doc
ii	Costs avoided	$13,285,924	= gg * hh
jj	Cases of type 1 diabetes avoided	0.3	Table 2, row ss
kk	Cost per case	$76,598	√
ll	Costs avoided	$21,082	= jj * kk
mm	Cases of childhood leukemia avoided	0.06	Table 2, row zz
nn	Cost per case	$134,920	√
oo	Costs avoided	$8,095	= mm * nn
pp	Cases of breast cancer avoided	19.3	Table 2, row kkk
qq	Cost per case	$29,707	Ref Doc
rr	Costs avoided	$572,033	= pp * qq
ss	Cases of ovarian cancer avoided	22.9	Table 2, row qqq
tt	Cost per case	$84,534	Ref Doc
uu	Costs avoided	$1,935,551	= ss * tt
	CE calculation		
vv	Cost of intervention over lifetime of birth cohort	$11,336,400	= l + n
ww	Costs avoided	$30,609,203	= q + t + w + z + cc + ff + ii + ll + oo + rr + uu
xx	QALYs saved	1,611	Table 2, row uuu
yy	Cost of intervention over lifetime of birth cohort (1.5% discount)	$11,336,400	Calculated
zz	Costs avoided (1.5% discount)	$19,827,768	Calculated
aaa	QALYs saved (1.5% discount)	941	Calculated
bbb	**CE ($/QALY saved)**	**-$9,021**	= (yy-zz)/aaa

√ = Estimates from the literature

We also modified several major assumptions and recalculated the cost per QALY as follows:

- Assume the effectiveness of interventions aimed at improving rates of exclusive breastfeeding at 6 months is reduced from 44% to 13% (Table 2, row *d*): CE = $19,699 per QALY
- Assume the effectiveness of interventions aimed at improving rates of exclusive breastfeeding at 6 months is increased from 44% to 84% (Table 2, row *d*): CE = -$14,757 per QALY
- Assume the effectiveness of breastfeeding in reducing overweight and obesity is reduced from 24% to 14% (Table 2, rows *hh* & *mm*): CE = -$3,995 per QALY
- Assume the effectiveness of breastfeeding in reducing overweight and obesity is increased from 24% to 33% (Table 2, rows *hh* & *mm*): CE = -$12,006 per QALY
- Assume the proportion of an office visit required for screening/referral is reduced from 50% to 33% (Table 3, row *k)*: CE = -$9,702 per QALY
- Assume the proportion of an office visit required for screening/referral is increased from 50% to 67% (Table 3, row *k)*: CE = -$8,341 per QALY

Summary

Applying a 1.5% discount rate, the clinically preventable burden (CPB) associated with interventions aimed at improving rates of exclusive breastfeeding at 6 months is estimated to be 2,923 quality-adjusted life years (QALYs) while the cost-effectiveness (CE) is estimated to result in cost savings of $9,021 per QALY (see Table 4).

Table 4: Promotion of Breastfeeding in a Birth Cohort of 40,000
Summary

	Base Case	Range	
CPB (Potential QALYs Gained)			
Assume No Current Service			
1.5% Discount Rate	**2,923**	2,260	3,779
3% Discount Rate	1,853	1,433	2,396
0% Discount Rate	5,002	3,868	6,466
Gap between B.C. Current and Best in the World			
1.5% Discount Rate	**941**	278	1,797
3% Discount Rate	597	176	1,139
0% Discount Rate	1,611	476	3,075
CE ($/QALY) **including** patient time costs			
1.5% Discount Rate	**-$9,021**	-$14,757	$19,699
3% Discount Rate	-$4,745	-$13,791	$40,557
0% Discount Rate	-$11,966	-$15,318	$4,818
CE ($/QALY) **excluding** patient time costs			
1.5% Discount Rate	-$20,325	-$20,678	-$18,599
3% Discount Rate	-$22,574	-$23,130	-$19,789
0% Discount Rate	-$18,572	-$18,778	-$17,540

Growth Monitoring and Healthy Weight Management in Children and Youth

Canadian Task Force on Preventive Health Care (2015)[179]

> *We recommend growth monitoring[180] at all appropriate[181] primary care visits using the 2014 WHO Growth Charts for Canada. (Strong recommendation; very low quality evidence)*

This growth monitoring recommendation applies to all children and youth 0–17 years of age who present to primary care.

> *We recommend that primary care practitioners not routinely offer structured interventions[182] aimed at preventing overweight and obesity in healthy weight children and youth. (Weak recommendation; very low quality evidence)*

This prevention recommendation applies to all children and youth 0–17 years of age who have a healthy weight. They do not apply to children and youth with eating disorders, or who are underweight, overweight, or obese.

> *For children and youth aged 2 to 17 years who are overweight or obese, we recommend that primary care practitioners offer or refer to structured behavioural interventions aimed at healthy weight management. (Weak recommendation; moderate quality evidence)*
>
> *For children and youth aged 2 to 11 years who are overweight or obese, we recommend that primary care practitioners not offer Orlistat[183] aimed at healthy weight management. (Strong recommendation; very low quality evidence)*
>
> *For children and youth aged 12 to 17 years who are overweight or obese, we recommend that primary care practitioners not routinely offer Orlistat aimed at healthy weight management. (Weak recommendation; moderate quality evidence)*
>
> *For children and youth aged 2 to 17 years who are overweight or obese, we recommend that primary care practitioners not routinely refer for surgical interventions. (Strong recommendation; very low quality evidence)*

These management recommendations apply to children and youth 2–17 years of age who are overweight or obese. Children and youth with health conditions where weight management is inappropriate are excluded.

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[179] Canadian Task Force on Preventive Health Care. Recommendations for growth monitoring, and prevention and management of overweight and obesity in children and youth in primary care. *Canadian Medical Association Journal*. 2015; 187(6): 411-21.

[180] **Growth monitoring** consists of measurement of height or length, weight and BMI calculation or weight for length according to age.

[181] **Appropriate primary care visits** include scheduled health supervision visits, visits for immunizations or medication renewal, episodic care or acute illness, and other visits where the primary care practitioner deems it appropriate. Primary care visits are completed at primary health care settings, including those outside of a physician's office (e.g. public health nurses carrying out a well-child visit at a community setting).

[182] **Structured interventions** are behavioural modification programs that involve several sessions that take place over weeks to months, follow a comprehensive-approach delivered by a specialized inter-disciplinary team, involve group sessions, and incorporate family and parent involvement. Behaviourally-based interventions may focus on diet, increasing exercise, making lifestyle changes, or any combination of these. These can be delivered by a primary health care team in the office or through a referral to a formal program within or outside of primary care, such as hospital-based, school-based or community programs.

[183] **Orlistat** is a prescription drug designed as an aid for weight loss.

The CTFPHC concludes that "the most effective behavioural interventions were those that were delivered by a specialized interdisciplinary team, involved group sessions, and incorporated family and parent involvement". Furthermore, "where structured behavioural interventions for weight management in children and youth are not yet available in Canada, primary care practitioners and policy makers should consider their development a priority."[184]

United States Preventive Services Task Force Recommendations (2017)

> *The USPSTF recommends that clinicians screen for obesity in children and adolescents 6 years and older and offer or refer them to comprehensive, intensive behavioral interventions to promote improvements in weight status. (Grade B recommendation)* [185]

Modelling the Clinically Preventable Burden

In this section, we model CPB associated with growth monitoring in children and youth ages 0-17 and the offer of, or referral to, structured behavioural interventions aimed at healthy weight management for children and youth aged 2 to 17 years who are overweight or obese.

In modelling CPB, we made the following assumptions:

- There were 865,080 children and youth ages 0-17 living in BC in 2017. The majority of these children and youth would be eligible for growth monitoring. Based on *measured height and weight* as calculated for the 2004 Canadian Community Health Survey (CCHS), 26.5% of BC children and youth ages 1-17 are either overweight or obese.[186] An estimated 19.9% are overweight (or 172,583 individuals) while a further 6.6% are obese (or 56,749 individuals) (see Table 1). The 56,749 children and youth with obesity are most likely to be offered structured behavioural interventions aimed at healthy weight management.

[184] Canadian Task Force on Preventive Health Care. Recommendations for growth monitoring, and prevention and management of overweight and obesity in children and youth in primary care. *Canadian Medical Association Journal*. 2015; 187(6): 411-21.
[185] US Preventive Services Task Force. Screening for obesity in children and adolescents: US Preventive Services Task Force Recommendation Statement. *Journal of American Medical Association*. 2017; 317(23): 2417-26.
[186] Statistics Canada. Canadian Community Health Survey (CCHS) - Nutrition, 2004 Public Use Microdata file (Catalogue number 82M0024GPE). 2004: All computations, use and interpretation of these data are entirely that of H. Krueger & Associates Inc.

Table 1: Estimated Number of Overweight and Obese Children and Youth In British Columbia

By Sex and Age, 2017

Prevalence Based on 2004 CCHS Data

	Male		Female		Total	
Population						
<1	23,780		22,580		46,360	
1 to 3	71,340		67,740		139,080	
4 to 8	121,140		113,540		234,680	
9 to 13	122,260		114,340		236,600	
14 to 17	107,640		100,720		208,360	
Total	**446,160**		**418,920**		**865,080**	
	Overweight	**Obese**	**Overweight**	**Obese**	**Overweight**	**Obese**
Prevalence						
<1	-	-	-	-	-	-
1 to 3	11.5%	8.5%	13.9%	2.1%	12.9%	4.7%
4 to 8	17.3%	2.2%	11.4%	13.6%	14.2%	8.2%
9 to 13	32.8%	6.1%	22.2%	4.7%	27.6%	5.4%
14 to 17	20.0%	10.1%	18.5%	3.8%	19.2%	6.8%
Total	23.1%	6.3%	17.1%	6.8%	19.9%	6.6%
	Overweight	**Obese**	**Overweight**	**Obese**	**Overweight**	**Obese**
# of Individuals						
<1	-	-	-	-	-	-
1 to 3	8,177	6,042	9,447	1,454	18,003	6,532
4 to 8	21,016	2,704	12,930	15,463	33,336	19,332
9 to 13	40,084	7,515	25,427	5,323	65,281	12,806
14 to 17	21,502	10,884	18,643	3,851	40,010	14,155
Total	**102,881**	**28,249**	**71,665**	**28,356**	**172,583**	**56,749**

- Evidence suggests that excess weight in children/youth often persists into adulthood.[187,188,189] We assumed that, without any intervention, the 20.0% of 14-17 year old males and 18.5% of 14-17 year old females who are overweight would remain so for the rest of their lives (see Table 1). A similar assumption was made for the 10.1% of 14-17 year old males and 3.8% of 14-17 year old females who are obese. Based on this assumption, of the total 1.5 million life years in the male birth cohort (see Table 3, row *a*), 310,760 would be lived as overweight (see Table 3, row *b*) and 143,044 as obese (see Table 3, row *c*). Similarly, of the total 1.6 million life years in the female birth cohort (see Table 3, row *d*), 287,637 would be lived as overweight (see Table 3, row *e*) and 69,962 as obese (see Table 3, row *f*).

[187] Whitaker RC, Wright JA, Pepe MS et al. Predicting obesity in young adulthood from childhood and parental obesity. *New England Journal of Medicine*. 1997; 337(13): 869-73.

[188] Freedman DS, Khan LK, Serdula M et al. The relation of childhood BMI to adult adiposity: the Bogalusa Heart Study. *Pediatrics*. 2005; 115(1): 22-7.

[189] Herman KM, Craig CL, Gauvin L et al. Tracking of obesity and physical activity from childhood to adulthood: the Physical Activity Longitudinal Study. *International Journal of Pediatric Obesity*. 2009; 4(4): 281-8.

Table 2: Years of Life as Overweight or Obese in a Birth Cohort of 40,000														
	Mean Survival		Individuals in		Years of Life in Birth				Years of Life				Years of Life	
Age	Rate		Birth Cohort		Cohort		% Overweight		Overweight		% Obese		Obese	
Group	Male	Female	Male	Female	Male	Female	Male	Female	Male	Female	Male	Female	Male	Female
0-4	99.55%	99.63%	19,910	19,926	99,551	99,629	11.5%	13.9%	11,411	13,894	8.5%	2.1%	8,432	2,138
5-9	99.51%	99.58%	19,903	19,915	99,513	99,577	17.3%	11.4%	17,264	11,340	2.2%	13.6%	2,221	13,561
10-14	99.48%	99.55%	19,895	19,911	99,476	99,553	32.8%	22.2%	32,614	22,139	6.1%	4.7%	6,115	4,635
15-19	99.37%	99.48%	19,875	19,897	99,374	99,484	20.0%	18.5%	19,851	18,415	10.1%	3.8%	10,048	3,804
20-24	99.07%	99.32%	19,813	19,865	99,065	99,323	20.0%	18.5%	19,789	18,385	10.1%	3.8%	10,017	3,797
25-29	98.67%	99.16%	19,734	19,833	98,672	99,163	20.0%	18.5%	19,711	18,355	10.1%	3.8%	9,977	3,791
30-34	98.29%	98.98%	19,658	19,795	98,289	98,975	20.0%	18.5%	19,634	18,320	10.1%	3.8%	9,938	3,784
35-39	97.80%	98.71%	19,560	19,741	97,798	98,706	20.0%	18.5%	19,536	18,271	10.1%	3.8%	9,889	3,774
40-44	97.13%	98.31%	19,427	19,662	97,134	98,311	20.0%	18.5%	19,403	18,197	10.1%	3.8%	9,822	3,759
45-49	96.20%	97.73%	19,241	19,546	96,203	97,730	20.0%	18.5%	19,217	18,090	10.1%	3.8%	9,727	3,737
50-54	94.86%	96.87%	18,971	19,375	94,855	96,873	20.0%	18.5%	18,948	17,931	10.1%	3.8%	9,591	3,704
55-59	92.85%	95.59%	18,570	19,118	92,852	95,591	20.0%	18.5%	18,548	17,694	10.1%	3.8%	9,389	3,655
60-64	89.84%	93.63%	17,967	18,726	89,835	93,630	20.0%	18.5%	17,945	17,331	10.1%	3.8%	9,083	3,580
65-69	85.26%	90.57%	17,052	18,113	85,261	90,567	20.0%	18.5%	17,032	16,764	10.1%	3.8%	8,621	3,463
70-74	78.34%	85.72%	15,668	17,144	78,342	85,720	20.0%	18.5%	15,650	15,867	10.1%	3.8%	7,921	3,277
75-79	68.08%	78.04%	13,616	15,608	68,078	78,041	20.0%	18.5%	13,599	14,445	10.1%	3.8%	6,884	2,984
80+	53.10%	65.90%	10,620	13,180	53,100	65,900	20.0%	18.5%	10,607	12,198	10.1%	3.8%	5,369	2,520
Total					**1,547,398**	**1,596,773**	**20.1%**	**18.0%**	**310,760**	**287,637**	**9.2%**	**4.4%**	**143,044**	**69,962**

- The systematic review and meta-analysis for the CTFPHC found that the overall effectiveness of interventions resulted in a -0.53 drop in BMI (95% CI from -0.69 to -0.36). This decrease, however, was not maintained 6-12 months after the intervention (0.08 change in BMI, 95% CI from -0.07 to 0.23). The most effective interventions included a focus on both diet and exercise (-1.09 drop in BMI, 95% CI from -1.84 to -0.34). The review also found a statistically significant improvement in QoL.[190]
- Interventions reduced the prevalence of overweight from 40% to 35% and obesity from 33% to 31% over a duration of up to 36 months.[191]
- Improvements in QoL appear to be positively correlated with weight loss.[192] One small study found a clinically important improvement in 22% (4 of 18) of the children/youth who successfully completed a multidisciplinary lifestyle program.[193]
- For modelling purposes, we assumed that a weight management program would reduce overweight by 12.5% (Table 3, row *ak*) and obesity by 6.1% (Table 3, row al) (based on the reduction in the prevalence of overweight from 40% to 35% and obesity from 33% to 31% noted above[194]). We also assumed the increase in QoL associated with the successful completion of a weight management program would be maintained long-term for 22% of participants (Table 3, rows *an* & *ao*). This

[190] Peirson L, Fitzpatrick-Lewis D, Morrison K et al. Treatment of overweight and obesity in children and youth: a systematic review and meta-analysis. *Canadian Medical Association Open Access Journal*. 2015; 3(1): e35-e46.
[191] Canadian Task Force on Preventive Health Care. Recommendations for growth monitoring, and prevention and management of overweight and obesity in children and youth in primary care. *Canadian Medical Association Journal*. 2015; 187(6): 411-21.
[192] Dreimane D, Safani D, MacKenzie M et al. Feasibility of a hospital-based, family-centered intervention to reduce weight gain in overweight children and adolescents. *Diabetes Research and Clinical Practice*. 2007; 75(2): 159-68.
[193] Vignolo M, Rossi F, Bardazza G et al. Five-year follow-up of a cognitive-behavioural lifestyle multidisciplinary programme for childhood obesity outpatient treatment. *European Journal of Clinical Nutrition*. 2008; 62(9): 1047-57.
[194] Canadian Task Force on Preventive Health Care. Recommendations for growth monitoring, and prevention and management of overweight and obesity in children and youth in primary care. *Canadian Medical Association Journal*. 2015; 187(6): 411-21.

assumption was varied in the sensitivity analysis from 12.5% for overweight and 6.1% for obese to 30% for both overweight and obese.

- Children in families that do not have a regular primary care provider (PCP) are unlikely to enter a weight monitoring/management process. Based on 2012 CCHS data, 89% of families in BC have a regular PCP (Table 3, row *ad*).[195]
- We noted earlier that the regular assessment of BMI by primary care providers is relatively poor. For modelling purposes, we assumed that 13% of PCPs would regularly monitor BMI (Table 3, row *ae*) and that 70% of these PCPs would refer overweight and obese children youth to a weight management program (Table 3, row *af*). Furthermore, we assumed that 39% of families referred to a weight management program would successfully complete the program (Table 3, row *ag* with a range from 29% to 49%). Between January 2013 and June 2015, 1,071 children and their parent(s) were referred to Shapedown BC.[196] Between January and June of 2015, 39% of those referred to the program ultimately completed it.
- The USPSTF review grouped interventions by intensity as follows: very low (<10 hours), low (10-25 hours), moderate (26-75 hours) or high (>75 hours). The comprehensiveness of the interventions was determined by a focus on both diet and physical activity as well as instruction in and support for the use of behavioural management techniques. Only comprehensive interventions of moderate to high intensity were effective (a reduction of between 1.9 to 3.3kg/m^2 at 12 months).[197,198]
- Other assumptions used in assessing the clinically preventable burden are detailed in the Reference Document.

Based on these assumptions, the CPB associated with growth monitoring in children and youth ages 0-17 along with the offer of, or referral to, structured behavioural interventions aimed at healthy weight management for children and youth aged 2 to 17 years who are overweight or obese is 80 QALYs (see Table 3, row *ar*). The CPB of 80 represents the gap between no coverage and the 'best in the world' growth monitoring coverage, which was estimated at 13%.

[195] Statistics Canada. Canadian Community Health Survey (CCHS), 2012 Public Use Microdata file (Catalogue number 82M0013X2013001). 2013: All computations, use and interpretation of these data are entirely that of H. Krueger & Associates Inc.

[196] HealthyFamiliesBC. *Provincial Management and Evaluation Report Cycles I-VII: January 2013 – June 2015*. September 2015.

[197] US Preventive Services Task Force. Screening for obesity in children and adolescents: US Preventive Services Task Force recommendation statement. *Pediatrics*. 2010; 125(2): 361-7.

[198] Whitlock EP, O'Connor EA, Williams SB et al. Effectiveness of weight management interventions in children: a targeted systematic review for the USPSTF. *Pediatrics*. 2010; 125(2): e396-e418.

Table 3: CPB of Growth Monitoring and Healthy Weight Management in Children / Youth in a Birth Cohort of 40,000			
Row Label	**Variable**	**Base Case**	**Data Source**
	Current State		
a	Years of life lived in the birth cohort - males	1,547,398	Table 2
b	Years of life lived with overweight in the birth cohort - males	310,760	Table 2
c	Years of life lived with obesity in the birth cohort - males	143,044	Table 2
d	Years of life lived in the birth cohort - females	1,596,773	Table 2
e	Years of life lived with overweight in the birth cohort - females	287,637	Table 2
f	Years of life lived with obesity in the birth cohort - females	69,962	Table 2
g	Disutility associated with overweight	0.0%	Ref Doc
h	Disutility associated with obesity	5.9%	Ref Doc
i	QALYs lost due to overweight - males	0	= b * g
j	QALYs lost due to obesity - males	8,440	= c * h
k	QALYs lost due to overweight - females	0	= e * g
l	QALYs lost due to obesity - females	4,128	= f * h
m	Overweight males at age 18	3,970	Table 2
n	Obese males at age 18	2,010	Table 2
o	Overweight females at age 18	3,683	Table 2
p	Obese females at age 18	761	Table 2
q	Life years lost due to overweight per individual	0.6	Ref Doc
r	Life years lost due to obesity per individual	2.6	Ref Doc
s	Life years lost due to overweight - males	2,382	= m * q
t	Life years lost due to obesity - males	5,225	= n * r
u	Life years lost due to overweight - females	2,210	= o * q
v	Life years lost due to obesity - females	1,978	= p * r
w	Total QALYs lost due to overweight - males	2,382	= i + s
x	Total QALYs lost due to obesity - males	13,665	= j + t
y	Total QALYs lost due to excess weight in males	16,047	= w + x
z	Total QALYs lost due to overweight - females	2,210	= k + u
aa	Total QALYs lost due to obesity - females	6,106	= l + v
ab	Total QALYs lost due to excess weight in females	8,315	= z + aa
ac	Total QALYs lost due to excess weight in birth cohort	24,362	= y + ab
	Effect of Intervention		
ad	BC families with a regular primary care provider (PCP)	89%	√
ae	Proportion of PCPs who regularly assess BMI	13%	Ref Doc
af	Proportion of PCPs who regularly assess BMI who would refer children/youth with excess weight to a weight management program	70%	Assumed
ag	Proportion of children/youth who would successfully complete a weight management program	39%	√
ah	Number of overweight individuals who would successfully complete a weight management program	125	= m * ad * ae * af * ag
ai	Number of obese individuals who would successfully complete a weight management program	63	= n * ad * ae * af * ag
aj	Years of life lived by an 8-year old in this subgroup	74	√
ak	Decrease in prevalence of overweight associated with intervention	12.5%	√
al	Decrease in prevalence of obesity associated with intervention	6.1%	√
am	Life-years gained with intervention	19	= (ah * q * ak)+(ai * r * al)
an	Proportion of individuals with overweight benefitting from an improvement in QoL	22.0%	√
ao	Proportion of individuals with obesity benefitting from an improvement in QoL	22.0%	√
ap	QALYs gained due to intervention	61	= (ah * aj * g * an)+(ai * aj * h *ao)
ar	**Potential QALYs gained, Intervention increasing from 0% to 13%**	**80**	= am + ap

√ = Estimates from the literature

We also modified a number of major assumptions and recalculated the CPB as follows:

- Assume that the proportion of children/youth who successfully complete a weight management program after being referred is reduced from 39% to 29% (Table 3, row *ag*): CPB = 60.
- Assume that the proportion of children/youth who would successfully complete a weight management program after being referred is increased from 39% to 49% (Table 3, row *ag*): CPB = 101.
- Assume that the proportion of children/youth who maintain improvement in QoL after successfully completing a weight management program is reduced from 22% to 12.5% and 6.1% for children / youth who are overweight/obese (Table 3, row *an* & *ao*): CPB = 36.
- Assume that the proportion of children/youth who maintain improvement in QoL after successfully completing a weight management program is increased from 22% to 30% (Table 3, row *an* & *ao*): CPB = 103.

Modelling Cost-Effectiveness

In modelling CE, we made the following assumptions:

- **Frequency of screening** – The CTFPHC recommends growth monitoring at all appropriate primary care visits. Appropriate primary care visits are defined as "scheduled health supervision visits, visits for immunizations or medication renewal, episodic care or acute illness, and other visits where the primary care practitioner deems it appropriate. Primary care visits are completed at primary health care settings, including those outside of a physician's office (e.g. public health nurses carrying out a well-child visit at a community setting)."[199] The Canadian Paediatric Association recommends that well-child visits take place at 1 week, at 2, 4, 6 and 12 months, annually from ages 2-5 and then every year or two until the child is 18 years of age.[200] For modelling purposes, we have assumed that growth monitoring would occur annually between the ages of 0-17 at a well-child visit (Table 4, row *d*).
- **Program costs** - Holingworth and colleagues estimated a range of program costs between £108 and £662 (in 2009 British pounds) per child based on a review of ten lifestyle interventions to treat overweight and obesity in children.[201] We converted these costs to equivalent Canadian health care costs in 2017, for a cost of $214 to $1,310 per child. For modelling purposes we used the mid-point for the base case scenario ($762) and the range in the sensitivity analysis (Table 4, row *l* & *m*).
- We assumed that the excess costs associated with overweight and obesity would be avoided during the remaining lifetime of the individual after a successful weight management program. We also modified this assumption so that costs would only be avoided for a five year period after a successful weight management program.
- Other costs and assumptions used in assessing cost-effectiveness are detailed in the Reference Document.

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[199] Canadian Task Force on Preventive Health Care. Recommendations for growth monitoring, and prevention and management of overweight and obesity in children and youth in primary care. *Canadian Medical Association Journal*. 2015; 187(6): 411-21.

[200] Canadian Paediatric Association. *Caring for Kids: Information for parents from Canada's paediatricians*. Available at http://www.caringforkids.cps.ca/handouts/schedule_of_well_child_visits. Accessed April 2016.

[201] Hollingworth W, Hawkins J, Lawlor D et al. Economic evaluation of lifestyle interventions to treat overweight or obesity in children. *International Journal of Obesity*. 2012; 36(4): 559-66.

- Discount rate of 1.5%, varied from 0% to 3% in the sensitivity analysis.

Based on these assumptions, the CE associated with growth monitoring in children and youth ages 0-17 and the offer of, or referral to, structured behavioural interventions aimed at healthy weight management for children and youth ages 2 to 17 years who are overweight or obese is $77,441 / QALY (Table 4, row *ac*).

Table 4: CE of Growth Monitoring and Healthy Weight Management in Children / Youth in a Birth Cohort of 40,000

Row Label	Variable	Base Case	Data Source
a	Years of life lived in birth cohort from 0-17	716,614	Table 2
b	BC families with a regular primary care provider (PCP)	89%	Table 3, row ad
c	Proportion of PCPs who regularly assess BMI	13%	Table 3, row ae
d	Number of assessments per year	1	Assumed
e	Total number of screens	82,912	= a * b * c * d
	Costs of Screening		
f	Cost of 10-minute office visit	$34.85	Ref Doc
g	Value of patient time and travel for office visit	$59.38	Ref Doc
h	Portion of 10-minute office visit for screen/referral	50%	Assumed
i	Estimated cost of screening	**$3,906,409**	= (e * f * h)+(e * g * h)
	Costs of Intervention		
j	Number of obese individuals successfully completing a weight management program	63	Table 3, row ai
k	Number of overweight individuals successfully completing a weight management program	125	Table 3, row ah
l	Cost of intervention per obese individual	$762	√
m	Cost of intervention per overweight individual	$762	√
n	Cost of intervention	**$143,925**	= (j * l)+(k *m)
o	Value of patient time and travel per intervention	$891	√
p	Total value of patient time and travel for interventions	**$168,290**	= (j + k) *o
	Cost avoided		
q	Years of overweight avoided	1,160	Table 3, row ah * Table 3, row aj * Table 3, row ak
r	Medical care costs per year associated with overweight	$227	Ref Doc
s	Costs avoided	$263,314	= q * r
t	Years of obesity avoided	287	Table 3, row ai * Table 3, row aj * Table 3, row al
u	Medical care costs per year associated with obesity	$805	Ref Doc
v	Costs avoided	$230,655	= t * u
	CE calculation		
w	Cost of intervention over lifetime of birth cohort	$4,218,624	= i + n + p
x	Costs avoided	$493,969	= s + v
y	QALYs saved	80	Table 3, row ar
z	Cost of intervention over lifetime of birth cohort (1.5% discount)	$3,704,213	Calculated
aa	Costs avoided (1.5% discount)	$272,147	Calculated
ab	QALYs saved (1.5% discount)	44	Calculated
ac	**CE ($/QALY saved)**	**$77,441**	= (z - aa) / ab

√ = Estimates from the literature

We also modified a number of major assumptions and recalculated the CE as follows:

- Assume that the proportion of children/youth who successfully complete a weight management program after being referred is reduced from 39% to 29% (Table 3, row *ag*): CE = $104,129.
- Assume that the proportion of children/youth who would successfully complete a weight management program after being referred is increased from 39% to 49% (Table 3, row *ag*): CE = $61,646.

- Assume that the proportion of children/youth who maintain improvement in QoL after successfully completing a weight management program is reduced from 22% to 12.5% and 6.1% for children/youth who are overweight/obese (Table 3, rows an & *ao*): CE = $171,245.
- Assume that the proportion of children/youth who maintain improvement in QoL after successfully completing a weight management program is increased from 22% to 30% (Table 3, rows *an* & *ao*): CE = $60,709.
- Assume that the proportion of an office visit for weight measurement is decreased from 50% to 33% (Table 4, row *h*): CE = $51,126.
- Assume that the proportion of an office visit for weight measurement is increased from 50% to 67% (Table 4, row *h*): CE = $103,755.
- Assume that the cost of the weight management program per individual is reduced from $762 to $214 (Table 4, row *l* & *m*): CE = $75,390.
- Assume that the cost of the weight management program per individual is increased from $762 to $1,310 (Table 4, row *l* & *m*): CE = $79,491.
- Assume that costs avoided would only last for five years, rather than a lifetime, after a successful weight management program (Table 3, rows *aj*): CE = $283,574.

Summary

Applying a 1.5% discount rate, the clinically preventable burden (CPB) associated with growth monitoring in children and youth ages 0-17 and the offer of, or referral to, structured behavioural interventions aimed at healthy weight management for children and youth ages 2 to 17 years who are overweight or obese is estimated to be 44 quality-adjusted life years (QALYs) while the cost-effectiveness (CE) is estimated to be $77,441 per QALY (see Table 5).

Table 5: Growth Monitoring and Healthy Weight Management in Children / Youth in a Birth Cohort of 40,000

Summary

	Base Case	Range	
CPB (Potential QALYs Gained)			
Assume No Current Service			
1.5% Discount Rate	**44**	13	57
3% Discount Rate	26	8	33
0% Discount Rate	80	24	103
CE ($/QALY) **including** patient time costs			
1.5% Discount Rate	**$77,441**	$51,126	$283,574
3% Discount Rate	$119,993	$80,282	$428,667
0% Discount Rate	$46,302	$29,791	$177,402
CE ($/QALY) **excluding** patient time costs			
1.5% Discount Rate	$25,335	$15,603	$105,908
3% Discount Rate	$41,360	$26,673	$160,547
0% Discount Rate	$13,609	$7,502	$65,925

Preventing Tobacco Use

Canadian Task Force on Preventive Health Care Recommendations (2017)

> *We recommend asking children and youth (age 5–18 yr) or their parents about tobacco use by the child or youth and offering brief information and advice, as appropriate, during primary care visits to **prevent** tobacco smoking among children and youth (weak recommendation, low-quality evidence).*
>
> *We recommend asking children and youth (age 5–18 yr) or their parents about tobacco use by the child or youth and offering brief information and advice, as appropriate, during primary care visits to **treat** tobacco smoking among children and youth (weak recommendation, low-quality evidence).*[202]

United States Preventive Services Task Force Recommendations (2013)

> *The USPSTF recommends that primary care clinicians provide interventions, including education or brief counselling, to prevent initiation of tobacco use in school-aged children and adolescents. (B Recommendation)*[203]

In their review of the evidence,[204] the USPSTF noted that the 2012 Surgeon General's Report concluded that there is a "large, robust, and consistent" evidence base that documents known effective strategies for reducing tobacco use among youths and young adults.[205] These strategies include coordinated, multi-component campaigns that combine media campaigns, price increases, school-based policies and programs and community-wide changes in policies and norms. The purpose of the USPSTF review was not to reconsider the evidence covered by the Surgeon General's Report, but rather "to review the evidence for the efficacy and harms of primary-care relevant interventions that aim to reduce tobacco use among children and adolescents."[206]

Modelling the Clinically Preventable Burden

In this section, we model CPB associated with asking children and youth or their parents about tobacco use by the child or youth and offering brief information and advice, as appropriate, during primary care visits to prevent and / or treat tobacco smoking among children and youth.

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[202] Canadian Task Force on Preventive Health Care. Recommendations on behavioural interventions for the prevention and treatment of cigarette smoking among school-aged children and youth. *Canadian Medical Association Journal*. 2017;189 (8): E310-16.

[203] Moyer VA. Primary care interventions to prevent tobacco use in children and adolescents: U.S. Preventive Services Task Force recommendation statement. *Annals of Internal Medicine*. 2013; 159(8): 552-7.

[204] Patnode CD, O'Connor E, Whitlock EP et al. Primary care-relevant interventions for tobacco use prevention and cessation in children and adolescents: a systematic evidence review for the U.S. Preventive Services Task Force. *Annals of Internal Medicine*. 2013; 158(4): 253-60.

[205] U.S. Department of Health and Human Services. *Preventing Tobacco Use Among Youth and Young Adults: A Report of the Surgeon General*. 2012. Available at http://www.cdc.gov/tobacco/data_statistics/sgr/2012/consumer_booklet/pdfs/consumer.pdf. Accessed January 2014.

[206] Patnode CD, O'Connor E, Whitlock EP et al. Primary care-relevant interventions for tobacco use prevention and cessation in children and adolescents: a systematic evidence review for the U.S. Preventive Services Task Force. *Annals of Internal Medicine*. 2013; 158(4): 253-60.

In modelling CPB, we made the following assumptions:

- Interventions aimed at reducing smoking initiation among non-smoking children and adolescents have an effectiveness of 18% (RR 0.82, 95% CI of 0.72 to 0.94).[207]
- Interventions aimed at smoking cessation among children and adolescents have an effectiveness of 34% (RR 1.34, 95% CI of 1.05 to 1.69).[208]
- An estimated 12.34% of 19 year-olds were daily or occasional smokers in BC in 2010 (see Table 1).[209]

Table 1: Smokers in British Columbia in 2010
Based on 2010 CCHS Data
Ages 12 to 19

	Total Population			Daily Smokers			Occasional Smokers			Current Smokers as % of Pop.		
Age Group	Males	Females	Total	Males	Females	Total	Males	Females	Total	Males	Females	Total
12-14	73,171	68,779	**141,950**	459	-	**459**	97	-	**97**	0.76%	0.00%	0.39%
15-17	81,088	74,831	**155,919**	4,383	2,994	**7,377**	1,274	208	**1,482**	6.98%	4.28%	5.68%
18-19	57,055	55,256	**112,311**	4,661	4,479	**9,140**	3,541	1,175	**4,716**	14.38%	10.23%	12.34%
Total	**211,314**	**198,866**	**410,180**	**9,503**	**7,473**	**16,976**	**4,912**	**1,383**	**6,295**	**6.82%**	**4.45%**	**5.67%**

- On average, 57.3% of smokers would quit (become former smokers) by the age of 25-34 (Table 3, row *e*), 60.4% by age 35-44 (Table 3, row *h*) and 68.9% by age 45-54 (Table 3, row *k*) (see Table 2).[210]

Table 2: Smoking Occurrence
British Columbia, 2010

SMOKING CATEGORY	AGE GROUP					
	18-24	25-34	35-44	45-54	55-64	65+
DAILY SMOKER	50,238	91,696	94,232	114,679	70,612	47,346
OCCASIONAL SMOKER (FORMER DAILY SMOKER)	17,203	27,935	21,481	18,486	9,914	12,950
ALWAYS AN OCCASIONAL SMOKER	31,786	18,272	15,056	7,787	6,320	296
FORMER DAILY SMOKER	27,365	77,671	110,446	203,967	183,720	256,094
FORMER OCCASIONAL SMOKER	53,224	107,195	89,353	108,870	83,717	92,489
NEVER SMOKED	225,389	267,255	288,143	265,911	209,738	223,185
SMOKERS	179,816	322,769	330,568	453,789	354,283	409,175
% of FORMER SMOKERS	44.8%	57.3%	60.4%	68.9%	75.5%	85.2%

- An average of 11.5 life years lost per smoker (Table 3, row *c*). An average of 10.5 of those life-years can be regained by stopping smoking at age 30 (Table 3, row *g*), 9.5 by stopping smoking at age 40 (Table 3, row *j*) and 6.5 by stopping smoking at age 50 (Table 3, row *l*).[211]
- Other assumptions used in assessing the clinically preventable burden are detailed in the Reference Document.

[207] Canadian Task Force on Preventive Health Care. Recommendations on behavioural interventions for the prevention and treatment of smoking among school-aged children and youth. *Canadian Medical Association Journal*. 2017; 189(8): e310-6.
[208] Canadian Task Force on Preventive Health Care. Recommendations on behavioural interventions for the prevention and treatment of smoking among school-aged children and youth. *Canadian Medical Association Journal*. 2017; 189(8): e310-6.
[209] This analysis is based on the Statistics Canada's Canadian Community Health 2010 Public Use Microdata File. All computations, use and interpretation of these data are entirely that of H. Krueger & Associates Inc.
[210] This analysis is based on the Statistics Canada's Canadian Community Health 2010 Public Use Microdata File. All computations, use and interpretation of these data are entirely that of H. Krueger & Associates Inc.
[211] Jha P, Ramasundarahettige C, Landsman V et al. 21st-century hazards of smoking and benefits of cessation in the United States. *New England Journal of Medicine*. 2013; 368(4): 341-50.

Based on these assumptions, the CPB associated with interventions aimed at preventing and / or treating tobacco smoking among children and youth is 4,123 QALYs (Table 3, row *gg*). The CPB of 4,123 represents the gap between no coverage and the 'best in the world' coverage, which was estimated at 53%.

Table 3: CPB of Interventions for Tobacco Use Prevention and Cessation in Children and Youth for Birth Cohort of 40,000 Individuals (B.C.)

	Estimate of Life Years Lost without Intervention	**Base Case**	**Data Source**
a	% of 19 year-olds who smoke in B.C.	12.34%	Table 1
b	Estimated # in birth cohort initiating smoking by age 19	4,935	= a* 40,000
c	Life-years lost per smoker	11.5	√
d	Potential life-years lost	56,751	= c * b
e	Proportion former smokers at age 30	57.3%	Table 2
f	Former smokers at age 30	2,828	= e * b
g	Life-years gained by stopping smoking at age 30	10.5	√
h	Proportion former smokers at age 40	60.4%	Table 2
i	Former smokers at age 40	2,981	= h * b
j	Life-years gained by stopping smoking at age 40	9.5	√
k	Proportion former smokers at age 50	68.9%	Table 2
l	Life-years gained by stopping smoking at age 50	6.5	√
m	Former smokers at age 50	3,400	= k * b
n	Life-years gained by stopping smoking	33,871	= (f*g)+(i-f)*j+(m-i)*l
o	**Estimated Life Years Lost without Intervention**	**22,881**	= d - n
	Estimate of Life Years Lost with Intervention		
p	Effectiveness of intervention	34.0%	√
q	Estimated # in birth cohort initiating smoking by age 19	3,257	= a * (1 - p) *40,000
r	Life-years lost per smoker	11.5	√
s	Potential life-years lost	37,456	= r * q
t	Proportion former smokers at age 30	57.3%	Table 2
u	Former smokers at age 30	1,866	= t * q
v	Life-years gained by stopping smoking at age 30	10.5	√
w	Proportion former smokers at age 40	60.4%	Table 2
x	Former smokers at age 40	1,967	= w * q
y	Life-years gained by stopping smoking at age 40	9.5	√
z	Proportion former smokers at age 50	68.9%	Table 2
aa	Life-years gained by stopping smoking at age 50	6.5	√
bb	Former smokers at age 50	2,244	= z * q
cc	Life-years gained by stopping smoking	22,355	= (u*v)+(x-u)*y+(bb-x)*aa
dd	**Estimated Life Years Lost with Intervention**	**15,101**	= s - cc
	Calculation of CPB		
ee	Life-years gained with 100% adherence	7,779	= o - dd
ff	Potential coverage of this service	53%	Ref Doc
gg	Potential CPB in BC	**4,123**	= ee * ff

√ = Estimates from the literature

We also modified a major assumption and recalculated the CPB as follows:

- Assume the effectiveness of interventions aimed at smoking cessation among children and adolescents is reduced from 34% to 5% (Table 3, row *p*): CPB = 606.

- Assume the effectiveness of interventions aimed at smoking cessation among children and adolescents is increased from 34% to 69% (Table 3, row *p*): CPB = 8,367.

Modelling Cost-Effectiveness

In this section, we model CE associated with asking children and youth or their parents about tobacco use by the child or youth and offering brief information and advice, as appropriate, during primary care visits to prevent and/or treat tobacco smoking among children and youth.

In estimating CE, we made the following assumptions:

- The USPSTF evidence review suggests that the effectiveness of the intervention lasts for at least two years.[212] We have assumed that an intervention would be required seven times between the ages of 5 and 19 for maximum effect (Table 4, row *d*).
- Other costs and assumptions used in assessing cost-effectiveness are detailed in the Reference Document.
- Discount rate of 1.5%, varied from 0% to 3% in the sensitivity analysis.

Based on these assumptions, the CE associated with interventions to prevent and/or treat tobacco smoking among children and youth is -$7,349 per QALY (Table 4, row *p*).

Table 4: Cost Effectiveness of Interventions for Tobacco Use Prevention in Children and Youth for Birth Cohort of 40,000 Individuals (B.C.)

		Base Case	Data Source
Cost of counseling			
a	Cost of 10-minute office visit	$34.85	Ref Doc
b	Cost of patient time and travel for office visit	$59.38	Ref Doc
c	Portion of office visit needed for counseling	50%	Ref Doc
d	# of interventions	7.0	√
e	Total cost of counseling per individual	$329.81	= (a+b)*c*d
f	Estimated Cost of Counselling	$13,192,200	= e * 40,000
Estimated Cost Avoidance			
g	Annual medical costs avoided per additional year as never smoker	$1,195	Ref Doc
h	Years of smoking avoided due to intervention	43,950	Calculated
i	Costs avoided	$52,520,012	= g * h
CE calculation			
j	Estimated Cost of Counselling	$13,192,200	= f
k	Costs avoided	$52,520,012	= i
l	Potential QALYs saved	4,123	= Table 3, row gg
m	Estimated Cost of Counselling (1.5% discount rate)	$11,830,577	Calculated
n	Costs avoided (1.5% discount rate)	$27,965,774	Calculated
o	Potential QALYs saved (1.5% discount rate)	2,195	Calculated
p	**Cost per QALY (CE)**	**-$7,349**	= (m - n) / o

Notes: *√ = Estimates from the literature*

[212] Patnode CD, O'Connor E, Whitlock EP et al. Primary care-relevant interventions for tobacco use prevention and cessation in children and adolescents: a systematic evidence review for the U.S. Preventive Services Task Force. *Annals of Internal Medicine*. 2013; 158(4): 253-60.

We also modified several major assumptions and recalculated the cost per QALY as follows:

- Assume the effectiveness of interventions aimed at smoking cessation among children and adolescents is reduced from 34% to 5% (Table 3, row *p*): $/QALY = $23,905.
- Assume the effectiveness of interventions aimed at smoking cessation among children and adolescents is increased from 34% to 69% (Table 3, row *p*): $/QALY = -$10,083.
- Assume the portion of an office visit needed for counselling is reduced from 50% to 33% (Table 4, row *c*): $/QALY = -$9,182.
- Assume the portion of an office visit needed for counselling is increased from 50% to 67% (Table 4, row *c*): $/QALY = -$5,517.

Summary

Applying a 1.5% discount rate, the clinically preventable burden (CPB) associated with interventions to prevent and/or treat tobacco smoking among children and youth is estimated to be 2,195 quality-adjusted life years (QALYs) while the cost-effectiveness (CE) is estimated to result in cost savings of $7,349 per QALY (see Table 5).

Table 5: Interventions for Tobacco Use Prevention and Cessation in Children and Youth for Birth Cohort of 40,000
Summary

	Base Case	Range	
CPB (Potential QALYs Gained)			
Assume No Current Service			
1.5% Discount Rate	**2,195**	323	4,455
3% Discount Rate	1,206	177	2,447
0% Discount Rate	4,123	606	8,367
CE ($/QALY) **including** patient time costs			
1.5% Discount Rate	**-$7,349**	-$10,083	$23,905
3% Discount Rate	-$3,909	-$8,388	$47,299
0% Discount Rate	-$9,538	-$11,161	$9,019
CE ($/QALY) **excluding** patient time costs			
1.5% Discount Rate	-$10,745	-$11,756	$814
3% Discount Rate	-$9,473	-$11,129	$9,466
0% Discount Rate	-$11,555	-$12,155	-$4,691

Preventive Medication / Devices

Fluoride Varnish and Fissure Sealants for Dental Health in Children

United States Preventive Service Task Force Recommendations (2014)

Dental caries is the most common chronic disease in children in the United States. According to the 1999–2004 National Health and Nutrition Examination Survey (NHANES), ~ 42% of children ages 2 to 11 years have dental caries in their primary teeth. After decreasing from the early 1970s to the mid-1990s, the prevalence of dental caries in children has been increasing, particularly in young children ages 2 to 5 years.

The U.S. Preventive Services Task Force recommends that primary care clinicians prescribe oral fluoride supplementation starting at age 6 months for children whose water supply is deficient in fluoride. (B recommendation)

The U.S. Preventive Services Task Force recommends that primary care clinicians apply fluoride varnish to the primary teeth of all infants and children starting at the age of primary tooth eruption. (B recommendation)[213]

Canadian Task Force on Preventive Health Care Recommendations (1994)

Lower dental caries prevalence and the need for efficiency in the provision of preventive and therapeutic dental services require selective use of dental caries preventives and targeting of services toward persons at greatest risk. The following recommendations are based on a review of the available evidence.

There is good evidence of effectiveness of the following measures in preventing dental caries (A Recommendation):

1. Water fluoridation for preventing coronal and root caries;

2. Fluoride supplements in low fluoride areas with careful adherence to low dosage schedules;

3. Professional topical fluoride applications and self-administered fluoride mouth rinses for those with very active decay or at high future risk for dental caries;

4. Fluoride dentifrices, with special supervision and the use of small amounts for young children;

5. Professionally-applied fissure sealants for selective use on permanent molar teeth soon after their eruption.[214]

The Cochrane Oral Health Group (2017)

Resin-based sealants applied on occlusal surfaces of permanent molars are effective for preventing caries in children and adolescents. Our review found

[213] Moyer VA. Prevention of dental caries in children from birth through age 5 years: US Preventive Services Task Force recommendation statement. *Pediatrics*. 2014; 133(5): 1-10.

[214] Lewis DW and Ismail AI. *Canadian Guide to Clinical Preventive Health Care: Chapter 36: Prevention of Dental Caries*. 1994. Available at http://canadiantaskforce.ca/wp-content/uploads/2013/03/Chapter36_dental_caries94.pdf?0136ff. Accessed November 2013.

moderate-quality evidence that resin-based sealants reduced caries by between 11% and 51% compared to no sealant, when measured at 24 months.[215]

Fluoride Varnish – Modelling the Clinically Preventable Burden

In this section, we model the CPB associated with applying fluoride varnish every six months between the ages of one and five for the prevention of dental caries in children.

In modelling CPB, we made the following assumptions:

- In 2012/13, 91.8% of BC kindergarten children were screened for dental health. Of these, 67.3% were caries free, 18.1% had treated caries and 14.6% had visible decay (Table 1, row *a*).[216]
- The effectiveness of fluoride varnish in reducing decayed, missing and filled teeth is 37% with a 95% CI of 24% to 51% (Table 1, row *b*).[217]
- Other assumptions used in assessing the clinically preventable burden are detailed in the Reference Document.

Based on these assumptions, the CPB associated with applying fluoride varnish every six months between the ages of one and five for the prevention of dental caries in children is 150 (Table 1, row *i*).

Table 1: CPB of Flouride Varnish for the Prevention of Dental Caries in Children < 5 Years of Age in a Birth Cohort of 40,000 (B.C.)

Row Label	Variable	Base Case	Data Source
a	Proportion of B.C. kindergarten children caries free	67.3%	√
b	Effectiveness of fluoride varnish in reducing decayed, missing and filled tooth surfaces	37.0%	√
c	Adherence with intervention	62%	Ref Doc
d	Children with treated caries or visible decay	13,080	= (1-a)*40,000
e	Children benefitting from intervention	3,001	= (d * c) * b
f	Years of benefits (from ages 1 to 5) per child	5.0	√
g	Life-years lived with poor oral health	15,003	= e * f
h	Change in QoL associated with improved oral health	0.01	Ref Doc
i	**Potential QALYs gained, CPB**	**150**	= g * h

√ = Estimates from the literature

We also modified several major assumptions and recalculated the CPB as follows:

- Assume the effectiveness of fluoride varnish in reducing decayed, missing and filled teeth is reduced from 37% to 24% (Table 1, row *b*): CPB = 97
- Assume the effectiveness of fluoride varnish in reducing decayed, missing and filled teeth is increased from 37% to 51% (Table 1, row *b*): CPB = 207

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[215] Cochrane Oral Health Group. *Pit and fissure sealants for preventing dental decay in permanent teeth*. The Cochrane Library. July 31, 2017. Available online at http://www.cochrane.org/CD001830/ORAL_sealants-preventing-tooth-decay-permanent-teeth. Accessed September 2017.

[216] Healthy Development and Women's Health Directorate - BC Ministry of Health. *BC Dental Survey of Kindergarten Children 2012-2013: A Provincial and Regional Analysis* 2014. Available at http://www.health.gov.bc.ca/women-and-children/pdf/provincial-kindergarten-dental-survey-2012-13.pdf. Accessed July 2014.

[217] Marinho VC, Worthington HV, Walsh T et al. Fluoride varnishes for preventing dental caries in children and adolescents. *Cochrane Database of Systematic Reviews.* 2013.

- Assume the change in QoL associated with improved oral health is reduced from 0.01 to 0.005 (Table 1, row *h*): CPB = 75
- Assume the change in QoL associated with improved oral health is increased from 0.01 to 0.019 (Table 1, row *h*): CPB = 285

Fluoride Varnish – Modelling Cost-Effectiveness

In this section, we model the CE associated with applying fluoride varnish every six months between the ages of one and five for the prevention of dental caries in children.

In modelling CE, we made the following assumptions:

- Fluoride varnish would be available for application to all children in BC with a 62% adherence rate (Table 2, row *b*).
- Assume fluoride varnish would need to be applied once every six months from age 1 to age 5 for a total of 9 applications (Table 2, row *f*).[218]
- For patient time and travel costs, we assumed an hour of patient time required per dental visit and three hours of patient time for dental day surgery. Dental day surgery in BC lasts an average of 83 minutes.[219]
- Assume 2.9 new carious surfaces per untreated 5 year-old (Table 2, row *g*).[220]
- The prevalence for day surgery for dental cavities in BC is estimated to be 1.38% of children (Table 2, row *l*).[221]
- Other costs and assumptions used in assessing cost-effectiveness are detailed in the Reference Document.
- Discount rate of 1.5%, varied from 0% to 3% in the sensitivity analysis.

Based on these assumptions, the CE associated with applying fluoride varnish every six months between the ages of one and five for the prevention of dental caries in children is $43,048 per QALY (Table 2, row *y*).

[218] Fluoride Recommendations Work Group. Recommendations for using fluoride to prevent and control dental caries in the United States. *Morbidity and Mortality Weekly Report Recommendations and Reports*. 2001; 50(RR-14): 1-42.
[219] Canadian Institute for Health Information. *Treatment of Preventable Dental Cavities in Preschoolers: A Focus on Day Surgery Under General Anesthesia*. 2013. Available at https://secure.cihi.ca/free_products/Dental_Caries_Report_en_web.pdf. Accessed January 2014.
[220] Ramos-Gomez FJ and Shepard DS. Cost-effectiveness model for prevention of early childhood caries. *Journal of the California Dental Association*. 1999; 27(7): 539-44.
[221] Canadian Institute for Health Information. *Treatment of Preventable Dental Cavities in Preschoolers: A Focus on Day Surgery Under General Anesthesia*. 2013. Available at https://secure.cihi.ca/free_products/Dental_Caries_Report_en_web.pdf. Accessed January 2014.

Table 2: CE of Flouride Varnish for the Prevention of Dental Caries in Children < 5 Years of Age in a Birth Cohort of 40,000 (B.C.)			
Label	**Variable**	**Base Case**	**Data Source**
a	Children eligible for intervention	40,000	√
b	Adherence with intervention	62%	= Table 1 row c
c	Children with treated caries or visible decay	13,080	= Table 1 row d
	Costs of intervention		
d	Cost of flouride varnish application	$10.61	Ref Doc
e	Value of patient time and travel for office visit	$29.69	Ref Doc
f	# of times flouride varnish applied from age 1 to 5	9	√
g	Estimated cost of intervention over lifetime of birth cohort	$8,994,960	= (d + e) * f *a *b
	Cost avoided		
h	New carious surfaces per untreated 5 year-old	2.9	√
i	Dental caries avoided	14,035	= g * c * Table 1 row b
j	Cost per filling	$92.75	Ref Doc
k	Value of patient time and travel for office visit	$59.38	Ref Doc
l	Filling costs avoided	-$2,135,120	= (i + j) * h
m	Prevalence of day surgery for caries	1.38%	√
n	Day surgeries without intervention in birth cohort	552	= a * m
o	Day surgeries avoided with intervention in birth cohort	204	= m * Table 1 row b
p	Cost of day surgery	$1,884	Ref Doc
q	Value of patient time and travel for day surgery	$89.07	Ref Doc
r	Day surgery costs avoided	-$402,980	= (p + q) * o
	CE calculation		
s	Cost of intervention over lifetime of birth cohort	$8,994,960	= g
t	Costs avoided	-$2,538,100	= l + r
u	QALYs saved	150	Table 8-1 row i
v	Cost of intervention over lifetime of birth cohort (1.5% discount)	$8,605,388	Calculated
w	Costs avoided (1.5% discount)	-$2,428,175	Calculated
x	QALYs saved (1.5% discount)	144	Calculated
y	**CE ($/QALY saved)**	**$43,038**	= (v + w) / x

√ = Estimates from the literature

We also modified several major assumptions and recalculated the cost per QALY as follows:

- Assume the effectiveness of fluoride varnish in reducing decayed, missing and filled teeth is reduced from 37% to 24% (Table 1, row *b*): CE = $75,514
- Assume the effectiveness of fluoride varnish in reducing decayed, missing and filled teeth is increased from 37% to 51% (Table 1, row *b*): CE = $26,579
- Assume the change in QoL associated with improved oral health is reduced from 0.01 to 0.005 (Table 1, row *h*): CE = $86,076
- Assume the change in QoL associated with improved oral health is increased from 0.01 to 0.019 (Table 1, row *h*): CE = $22,651
- Assume that the application of fluoride varnish is equally effective if applied annually (versus every six months) (Table 2, row *f*). The evidence on frequency of applications is inconclusive[222]: CE = $16,391
- Assume that the cost per filling is reduced from $92.75 to $83.10 (Table 2, row *j*): CE = $43,941

[222] Marinho VC, Worthington HV, Walsh T et al. Fluoride varnishes for preventing dental caries in children and adolescents. *Cochrane Database of Systematic Reviews.* 2013.

- Assume that the cost per filling is increased from $92.75 to $102.40 (Table 2, row *j*): CE = $42,135

Fluoride Varnish – Summary

Applying a 1.5% discount rate, the clinically preventable burden (CPB) associated with applying fluoride varnish every six months between the ages of one and five for the prevention of dental caries in children is estimated to be 144 quality-adjusted life years (QALYs) while the cost-effectiveness (CE) is estimated to be $43,038 per QALY (see Table 3).

Table 3: Application of Fluoride Varnish for Children < 5 Years of Age in a Birth Cohort of 40,000

Summary

	Base Case	Range	
CPB (Potential QALYs Gained)			
Assume No Current Service			
1.5% Discount Rate	**144**	72	273
3% Discount Rate	137	69	261
0% Discount Rate	150	75	285
CE ($/QALY) **including** patient time costs			
1.5% Discount Rate	**$43,038**	$16,391	$86,076
3% Discount Rate	$43,038	$16,391	$86,076
0% Discount Rate	$43,038	$16,391	$86,076
CE ($/QALY) **excluding** patient time costs			
1.5% Discount Rate	$4,543	-$2,472	$9,087
3% Discount Rate	$4,543	-$2,472	$9,087
0% Discount Rate	$4,543	-$2,472	$9,087

Dental Sealants - Modelling the Clinically Preventable Burden

While the focus of the USPSTF is on improving dental health in preschool children, there is also a body of evidence indicating that the use of dental sealants is effective in preventing decayed, missing and filled teeth in children six years of age and older with permanent teeth.[223]

In this section, we model the CPB associated with applying dental sealants for the prevention of dental caries in children and youth with permanent teeth.

In modelling CPB, we made the following assumptions:

- Dental sealants would be placed on the 1st molars at age six, the 1st and 2nd bicuspids at age 10 and the 2nd molars at age 12.
- The effectiveness of dental sealants in reducing decayed, missing and filled teeth is 84% at year 1, decreasing to 55% at year 9. Effectiveness beyond nine years is unknown.[224]
- An estimated 12.2% of Canadians avoid certain foods because of problems with their teeth or mouth, and 11.6% of Canadians sometimes or always have pain in their

[223] Cochrane Oral Health Group. *Pit and fissure sealants for preventing dental decay in permanent teeth*. The Cochrane Library. July 31, 2017. Available online at http://www.cochrane.org/CD001830/ORAL_sealants-preventing-tooth-decay-permanent-teeth. Accessed September 2017.

[224] Ahovuo-Saloranta A, Forss H, Walsh T et al. Sealants for preventing dental decay in the permanent teeth. *Cochrane Database of Systematic Reviews.* 2013.

mouth.[225] Based on this information, we assumed that 12% of children/youth with caries would have significant enough pain to reduce their quality of life (Table 4, row *j*).

- Other assumptions used in assessing the clinically preventable burden are detailed in the Reference Document.

Based on these assumptions, the CPB associated with preventing decayed, missing and filled teeth in children with permanent teeth is 157 (Table 4, row *m*). The CPB of 157 represents the gap between no coverage and improving coverage to 59%.

Table 4: CPB of Dental Sealants in Children/Youth with Permanent Teeth in a Birth Cohort of 40,000 (B.C.)

Row Label	Variable	Base Case	Data Source
a	# of 6-year olds in a birth cohort of 40,000	39,818	Ref Doc
b	Adherence with intervention	59%	Ref Doc
c	Children 'accepting' intervention	23,492	= a * b
d	Estimated new caries between ages 6-20 per child - untreated	7.69	Calculated
e	Estimated new caries between ages 6-20 per child - treated	2.46	Calculated
f	Estimated new caries without intervention	180,615	= c * d
g	Estimated new caries with intervention	57,718	= c * e
h	New caries avoided with intervention	122,898	= f - g
i	Life-years lived without caries due to intervention	130,643	Calculated
j	Proportion of children living with caries with significant pain	12.0%	√
k	Life-years lived without caries or pain due to intervention	15,677	= I * j
l	Change in QoL associated with improved oral health	0.01	Ref Doc
m	Potential QALYs gained, Intervention increasing from 0% to 59%	157	= k * l

√ = Estimates from the literature

We also modified a major assumption and recalculated the CPB as follows:

- Assume the change in QoL associated with improved oral health is reduced from 0.01 to 0.005 (Table 4, row *l*): CPB = 78
- Assume the change in QoL associated with improved oral health is increased from 0.01 to 0.019 (Table 4, row *l*): CPB = 298

Dental Sealants - Modelling Cost-Effectiveness

In this section, we model the CE associated with applying dental sealants for the prevention of dental caries in children and youth with permanent teeth.

In modelling CE, we made the following assumptions:

- The cost of applying sealants is estimated at $19.74 for the first tooth in a quadrant and $10.83 for each additional tooth in the quadrant (see Reference Document). The costs of applying dental sealants on the 1st molars at age six would therefore be $78.96, the 1st and 2nd bicuspids at age 10 would be $122.32 and the 2nd molars at age 12 would be $78.96 for a total cost of $280.24 (Table 5, row *d*).
- For patient time and travel costs, we estimated two hours of patient time per dental visit.

[225] Canadian Dental Association. *Dental Health Services in Canada: Facts and Figures 2010*. 2010. Available at http://www.med.uottawa.ca/sim/data/Dental/Dental_Health_Services_in_Canada_June_2010.pdf. Accessed January 2014.

- An average of 1.84 fillings would be treated each time fillings are required (Table 5, row *l*).[226]
- Other costs and assumptions used in assessing cost-effectiveness are detailed in the Reference Document.
- Discount rate of 1.5%, varied from 0% to 3% in the sensitivity analysis.

Based on these assumptions, the CE associated with preventing dental caries in children with permanent teeth by applying dental sealants is -$24,690 per QALY (Table 5, row *v*).

Table 5: CE of Dental Sealants in Children/Youth with Permanent Teeth in a Birth Cohort of 40,000 (B.C.)

Label	Variable	Base Case	Data Source
a	Children eligible for intervention	39,818	= Table 4, row a
b	Adherence with intervention	59%	= Table 4, row b
c	Children 'accepting' intervention	23,492	= Table 4, row c
	Costs of intervention		
d	Cost of dental sealant applications	$280.24	√
e	Value of patient time and travel for office visit	$59.38	Ref Doc
f	# of sealant applications (at age 6, 10 and 12)	3	√
g	Estimated cost of intervention over lifetime of birth cohort	$6,583,506	= c * d
h	Estimated cost of patient time over lifetime of birth cohort	$4,184,933	= c * e * f
	Cost avoided		
i	Dental caries avoided with intervention	122,898	Calculated
j	Cost per filling	$92.75	Ref Doc
k	Value of patient time and travel for office visit	$59.38	Ref Doc
l	# of fillings per visit	1.84	√
m	# of dental visits avoided	66,792	= i / l
n	Filling costs avoided	-$11,398,770	= i * j
o	Patient costs avoided	-$3,966,125	= m * k
	CE calculation		
p	Cost of intervention over lifetime of birth cohort	$10,768,439	= g + h
q	Costs avoided	-$15,364,896	= n + o
r	QALYs saved	157	Table 4, row k
s	Cost of intervention over lifetime of birth cohort (1.5% discount)	$10,096,096	Calculated
t	Costs avoided (1.5% discount)	-$13,499,918	Calculated
u	QALYs saved (1.5% discount)	138	Calculated
v	**CE ($/QALY saved)**	**-$24,690**	= (s + t) / u

√ = Estimates from the literature

We also modified several major assumptions and recalculated the cost per QALY as follows:

- Assume the change in QoL associated with improved oral health is reduced from 0.01 to 0.005 (Table 4, row *l*): CE = -$24,359
- Assume the change in QoL associated with improved oral health is increased from 0.01 to 0.019 (Table 4, row *l*): CE = -$24,851
- Assume that the cost per filling is reduced from $92.75 to $83.10 (Table 5, row *j*): CE = -$17,132

[226] Dye B, Tan S, Smith V et al. Trends in oral health status: United States, 1988-1994 and 1999-2004. *National Center for Health Statistics*. 2007; 11(248): 1-104.

- Assume that the cost per filling is increased from $92.75 to $102.40 (Table 5, row *j*): CE = -$32,248

Dental Sealants – Summary

Applying a 1.5% discount rate, the clinically preventable burden (CPB) associated with applying dental sealants for the prevention of dental caries in children and youth with permanent teeth is estimated to be 138 quality-adjusted life years (QALYs) while the cost-effectiveness (CE) is estimated to result in cost savings of $24,690 per QALY (see Table 6).

Table 6: Dental Sealants for Children with Permanent Teeth in a Birth Cohort of 40,000
Summary

	Base Case	Range	
CPB (Potential QALYs Gained)			
Assume No Current Service			
1.5% Discount Rate	**138**	69	262
3% Discount Rate	121	61	231
0% Discount Rate	157	78	298
CE ($/QALY) **including** patient time costs			
1.5% Discount Rate	**-$24,690**	-$32,248	-$17,132
3% Discount Rate	-$19,774	-$27,326	-$12,222
0% Discount Rate	-$29,320	-$36,884	-$21,755
CE ($/QALY) **excluding** patient time costs			
1.5% Discount Rate	-$27,902	-$35,460	-$20,344
3% Discount Rate	-$24,922	-$32,474	-$14,370
0% Discount Rate	-$30,715	-$38,280	-$23,150

Screening for Asymptomatic Disease or Risk Factors

Screening for Breast Cancer

Canadian Task Force on Preventive Health Care Recommendations (2011)

For women aged 40–49 we recommend not routinely screening with mammography. (Weak recommendation; moderate quality evidence)

For women aged 50–69 years we recommend routinely screening with mammography every 2 to 3 years. (Weak recommendation; moderate quality evidence)

For women aged 70–74 we recommend routinely screening with mammography every 2 to 3 years. (Weak recommendation; low quality evidence) [227]

United States Preventive Services Task Force Recommendations (2016)

The USPSTF recommends biennial screening mammography for women aged 50 to 74 years. (B recommendation)[228]

Modelling the Clinically Preventable Burden

In this section, we will calculate the CPB associated with screening women ages 50 to 74 years of age for breast cancer every 2 to 3 years.

In modelling CPB, we made the following assumptions:

- Based on BC life tables for 2010 to 2012, a total of 3,938 deaths would be expected in females between the ages of 50-79 in a BC birth cohort of 40,000 (see Table 1). While routine screening occurs to age 74, we have assumed the protective effect of that routine screening would continue to age 79.
- Based on BC vital statistics data, there were 1,990 deaths in females between the ages of 45 and 64 in BC in 2012, with 215 (10.8%) of these deaths due to breast cancer (ICD-10 codes C50). There were also 3,566 deaths between the ages of 65 and 79 that year, with 230 (6.4%) of these deaths due to breast cancer.[229] This suggests that 288 of the 3,938 (7.3%) of the female deaths in the BC birth cohort between the ages of 50 and 79 would be due to breast cancer (see Table 1).

[227] Canadian Task Force on Preventive Health Care. *Screening for Breast Cancer*. 2011. Available at http://canadiantaskforce.ca/guidelines/2011-breast-cancer/. Accessed October 2013.
[228] U.S. Preventive Services Task Force. Screening for breast cancer: U.S. Preventive Services Task Force recommendation statement. *Annals of Internal Medicine*. 2016; 164(4): 279-97.
[229] British Columbia Vital Statistics Agency. *Selected Vital Statistics and Health Status Indicators: One Hundred and Forty-First Annual Report*. Apendix 2. 2012. British Columbia Ministry of Health. Available at https://www2.gov.bc.ca/assets/gov/birth-adoption-death-marriage-and-divorce/statistics-reports/annual-reports/2012/pdf/annual-report-2012.pdf. Accessed December 2017.

Table 1: Mortality Due to Breast Cancer Between the Ages of 50 and 79
in a British Columbia Birth Cohort of 40,000

Age Group	Mean Survival Rate		Individuals in Birth Cohort			Life Years Lived	Deaths in Birth Cohort		Deaths due to Breast Cancer		Life Years Lost Per Death	Life Years Lost Total
	Males	Females	Males	Females	Total		%	#	%	#		
45-49	0.977		19,546	19,546								
50-54	0.969		19,375	19,375		96,873	0.9%	171	10.8%	19	33.8	626
55-59	0.956		19,118	19,118		95,591	1.3%	256	10.8%	28	29.2	809
60-64	0.936		18,726	18,726		93,630	2.1%	392	10.8%	42	24.7	1,046
65-69	0.906		18,113	18,113		90,567	3.4%	613	6.4%	39	20.4	800
70-74	0.857		17,144	17,144		85,720	5.7%	969	6.4%	62	16.3	1,011
75-79	0.780		15,608	15,608		78,041	9.8%	1,536	6.4%	98	12.6	1,238
								3,938	**7.3%**	**288**	**19.2**	**5,530**

- Screening mammography in women ages 50-74 leads to a reduction in breast cancer mortality of 21% (RR 0.79, 95% CI of 0.68 – 0.90). This is based on 10 trials in which the attendance rates at first screening were approximately 85%.[230]
- For every death avoided, 204 women will have false positive results.[231] We have assumed a one-time QALY loss of 0.013 (4.7 days) after a false-positive mammography result.[232]
- For every death avoided, 26 women will have an unnecessary biopsy.[233]
- For every death avoided, 3 women will have an unnecessary lumpectomy or mastectomy (with a 3:1 ratio for lumpectomy vs. mastectomy).[234]
- Other assumptions used in assessing the clinically preventable burden are detailed in the Reference Document.

Based on these assumptions, the CPB associated with screening women ages 50 to 74 years of age for breast cancer every 2 to 3 years is 1,189 QALYs saved (Table 2, row *o*). The CPB of 1,189 represents the gap between no coverage and the 'best in the world' coverage estimated at 88%. The CPB of 486 QALYs saved (see Table 2, row *p*) represents the gap between the current coverage of 52% and the 'best in the world' coverage estimated at 88%.

[230] Fitzpatrick-Lewis D, Hodgson N, Ciliska D et al. *Breast Cancer Screening*. 2011. Available at http://canadiantaskforce.ca/wp-content/uploads/2012/09/Systematic-review.pdf?0136ff. Accessed October 2013.
[231] Ibid.
[232] Schousboe JT, Kerlikowske K, Loh A et al. Personalizing mammography by breast density and other risk factors for breast cancer: analysis of health benefits and cost-effectiveness. *Annals of Internal Medicine*. 2011; 155(1): 10-20.
[233] Fitzpatrick-Lewis D, Hodgson N, Ciliska D et al. *Breast Cancer Screening*. 2011. Available at http://canadiantaskforce.ca/wp-content/uploads/2012/09/Systematic-review.pdf?0136ff. Accessed October 2013.
[234] Independent UK Panel on Breast Cancer Screening. The benefits and harms of breast cancer screening: an independent review. *The Lancet*. 2012; 380: 1778-86.

Table 2. Calculation of Clinically Preventable Burden of Breast Cancer Screening Being Offered to a Birth Cohort of 40,000 Between the Ages of 50 to 74			
Row	**Variable**	**Base Case**	**Data Source**
	Estimated Current Status		
a	Estimated deaths due to breast cancer in birth cohort between ages 50-79	288	Table 1
b	Effectiveness of mammography screening in preventing mortality (based on 85% adherence in clinical trials)	21.0%	√
c	Effectiveness of mammography screening in preventing mortality (assuming 100% adherence in clinical trials)	24.7%	=b*1.1764
d	Frequency of screening in last 30 months	52%	Ref Doc
e	Potential adherence	88%	Ref Doc
f	Predicted deaths in the absence of screening	331	= a / (1 - d * c)
	Benefits of Screening		
g	Deaths avoided - 100% adherence	82	= f * c
h	Deaths avoided - 88% adherence	72	= g * e
i	Deaths avoided - 52% adherence	42	= g * d
j	Life expectancy at average age of breast cancer death	19.2	Table 1
k	QALYs saved with 88% adherence to screening	1,379	= h * j
	Harms Associated with Screening		
l	False positive results per death avoided	204	√
m	Reduced QALYs per false positive	0.013	√
n	Reduced QALYs associated with false positives	-191	= h * l * m
	Summary of Benefits and Harms		
o	Potential QALYs saved - Utilization increasing from 0% to 88%	1,189	= k + n
p	Potential QALYs saved - Utilization increasing from 52% to 88%	486	= o * (e-d)/e

√ = Estimates from the literature

We modified the following major assumptions and recalculated the CPB as follows:

- Assume the effectiveness of screening mammography in reducing deaths from breast cancer is reduced from 21% to 10% (Table 2, row *b*): CPB = 526.
- Assume the effectiveness of screening mammography in reducing deaths from breast cancer is increased from 21% to 32% (Table 2, row *b*): CPB = 1,963.

Modelling Cost-Effectiveness

In this section, we will calculate the CE associated with screening women ages 50 to 74 years of age for breast cancer every 2 to 3 years.

In estimating the CE of screening mammography, we made the following assumptions:

- **Costs of screening** - Information from the BC Cancer Agency Screening Mammography Program indicates a cost of $79.35 per screen in 2015/16.[235] There are a total of 462,381 life years lived in females ages 50-74 in a BC birth cohort of 40,000 (see Table 1). We assumed that, on average, women would participate in screening once every 30 months (i.e., every 2.5 years), resulting in 184,952 screens for the birth cohort assuming 100% adherence. At 88% adherence, the number of screens would be reduced to 162,758 (Table 3, row *a* & *b*).

[235] BC Cancer Agency. *Screening Mammography Program: 2016 Annual Report*. 2016. Available at http://www.bccancer.bc.ca/screening/Documents/SMP_Report-AnnualReport2016.pdf. Accessed August 2017.

- **Costs associated with overtreatment** – For every death avoided, 3 women will have an unnecessary lumpectomy or mastectomy (with a 75:25 ratio for lumpectomy vs. mastectomy) with a cost per lumpectomy of $5,152 and a mastectomy of $7,260 (see reference document) for a weighted cost of $5,679 (Table 2, row *k*).
- **Patient time and travel costs** - For patient time and travel costs, we assumed an estimated two hours of patient time required per screening visit of $57.56, 7.5 for a biopsy and 37.5 hours for a lumpectomy or mastectomy.
- Other costs and assumptions used in assessing cost-effectiveness are detailed in the Reference Document.
- Discount rate of 1.5%, varied from 0% to 3% in the sensitivity analysis.

Based on these assumptions, the CE associated with screening women ages 50 to 74 years of age for breast cancer every 2 to 3 years would be $19,720 / QALY (Table 3, row *u*).

Table 3. Summary of CE Estimate for Breast Cancer Screening
B.C. Birth Cohort of 40,000

Row	Variable	Base Case	Data Source
a	Screening visits with 100% Adherence	184,952	√
b	Screening visits with 88% Adherence	162,758	= a * Table 2, row e
c	Cost per screen	$79.35	Ref Doc
d	Value of patient time (per hour)	$29.69	Ref Doc
e	Screening costs	$12,914,856	= b * c
f	Patient time costs	$9,664,577	= (b * d) * 2
g	Deaths avoided	72	Table 2, row h
h	Costs avoided per death prevented	-$47,230	Ref Doc
i	Costs avoided due to deaths prevented	-$3,394,150	= g * h
j	Unnecessary lumpectomies / mastectomies for every death avoided	3	√
k	Costs per lumpectomy / mastectomy	$5,679	Ref Doc
l	Costs associated with unnecessary lumpectomies / mastectomies	$1,224,352	= g * j * k
m	Unnecessary biopsies per death avoided	26	√
n	Cost per unnecessary biopsy	$386	Ref Doc
o	Costs for unnecessary biopsies	$721,230	= n * f * o
p	Patient time and travel costs associated with unnecessary procedures	$656,098	= ((g * j * 7.5)+(g * m * 37.5)) * d
q	Net costs undiscounted	$21,786,962	= e + f + i + l + o + p
r	CPB undiscounted	1,189	Table 2, row o
s	Net costs 1.5% discount	$18,103,440	Calculated
t	CPB 1.5% discount	918	Calculated
u	CE ($/QALY saved)- 1.5% discount	$19,720	= s / t

√ = Estimates from the literature

We also modified the major assumption and recalculated the cost per QALY as follows:

- Assume the effectiveness of screening mammography in reducing deaths from breast cancer is reduced from 21% to 10% (Table 2, row *b*): $/QALY = $45,514.
- Assume the effectiveness of screening mammography in reducing deaths from breast cancer is increased from 21% to 32% (Table 2, row *b*): $/QALY = $11,659.

Summary

Applying a 1.5% discount rate, the clinically preventable burden (CPB) associated with screening women ages 50 to 74 years of age for breast cancer every 2 to 3 years is estimated to be 918 quality-adjusted life years (QALYs) while the cost-effectiveness (CE) is estimated to be $19,720 per QALY (see Table 4).

Table 4: Breast Cancer Screening Being Offered to a Birth Cohort of 40,000 Between the Ages of 50 to 74
Summary

	Base Case	Range	
CPB (Potential QALYs Gained)			
Assume No Current Service			
1.5% Discount Rate	**918**	406	1,516
3% Discount Rate	721	319	1,191
0% Discount Rate	1,189	526	1,963
Gap between B.C. Current (52%) and 'Best in the World' (88%)			
1.5% Discount Rate	376	166	620
3% Discount Rate	295	131	487
0% Discount Rate	486	215	803
CE ($/QALY) **including** patient time costs			
1.5% Discount Rate	**$19,720**	$11,659	$45,514
3% Discount Rate	$21,048	$12,444	$48,580
0% Discount Rate	$18,326	$10,835	$42,298
CE ($/QALY) **excluding** patient time costs			
1.5% Discount Rate	$10,378	$5,769	$25,132
3% Discount Rate	$11,077	$6,156	$26,825
0% Discount Rate	$9,645	$5,360	$23,356

Screening (Cytology-Based) for Cervical Cancer

Canadian Task Force on Preventive Health Care Recommendations (2013)

> *The following recommendations refer to cytologic screening, using either conventional or liquid-based methods, whether manual or computer-assisted.*
>
> *For women aged 20–24 years, we recommend not routinely screening for cervical cancer. (Weak recommendation; moderate-quality evidence)*
>
> *For women aged 25–29 years, we recommend routine screening for cervical cancer every 3 years. (Weak recommendation; moderate-quality evidence)*
>
> *For women aged 30–69 years, we recommend routine screening for cervical cancer every 3 years. (Strong recommendation; high-quality evidence)*
>
> *For women aged 70 years and older who have undergone adequate screening (i.e., 3 successive negative Pap test results in the previous 10 years), we recommend that routine screening may end. For women aged 70 years and older who have not undergone adequate screening, we recommend continued screening until 3 negative test results have been obtained. (Weak recommendation; low-quality evidence)*[236]

United States Preventive Services Task Force Recommendations (2017)

> *The USPSTF recommends screening for cervical cancer in women age 21 to 65 years with cytology (Pap smear) every 3 years or, for women age 30 to 65 years who want to lengthen the screening interval, screening with a combination of cytology and human papillomavirus (HPV) testing every 5 years.*[237]

Modelling the Clinically Preventable Burden

In this section, we will calculate the CPB associated with screening women ages 25 to 69 years of age for cervical cancer, using cytology screening, every 3 years.

In modelling CPB, we made the following assumptions:

- Based on BC life tables for 2010 to 2012, a total of 2,721 deaths would be expected in females between the ages of 25-74 in a BC birth cohort of 40,000 (see Table 1). While routine screening occurs to age 69, we have assumed the protective effect of that routine screening would continue to age 74.
- Based on BC vital statistics data, there were 357 deaths in females between the ages of 25 and 44 in BC in 2012, with 8 (2.2%) of these deaths due to cervical cancer (ICD-10 codes C53). There were also 1,990 deaths between the ages of 45 and 64 that year, with 20 (1.0%) of these deaths due to cervical cancer. Finally, there were 3,566 deaths between the ages of 65 and 79 that year, with 10 (1.0%) of these deaths due to cervical cancer.[238] This suggests that 18 of the 2,721 (0.7%) of the female deaths in the BC birth cohort between the ages of 25 and 74 would be due to cervical cancer (see Table 1).

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[236] Canadian Task Force on Preventive Health Care. Recommendations on screening for cervical cancer. *Canadian Medical Association Journal*. 2013; 185(1): 35-45.

[237] US Preventive Services Task Force. Draft Recommendation Statement *Cervical Cancer: Screening.* 2017. Available online at https://www.uspreventiveservicestaskforce.org/Page/Document/draft-recommendation-statement/cervical-cancer-screening2. Accessed December 2017.

[238] British Columbia Vital Statistics Agency. *Selected Vital Statistics and Health Status Indicators: One Hundred and Forty-First Annual Report*. Apendix 2. 2012. British Columbia Ministry of Health. Available at https://www2.gov.bc.ca/assets/gov/birth-adoption-death-marriage-and-divorce/statistics-reports/annual-reports/2012/pdf/annual-report-2012.pdf. Accessed December 2017.

Table 1: Mortality Due to Cervical Cancer Between the Ages of 25 and 74
in a British Columbia Birth Cohort of 40,000

Age Group	Mean Survival Rate		Individuals in Birth Cohort			Life Years Lived	Deaths in Birth Cohort		Deaths due to Cervical Cancer		Life Years Lost Per Death	Life Years Lost Total
	Males	Females	Males	Females	Total		%	#	%	#		
20-24	0.993		19,865									
25-29	0.992		19,833			99,163	0.2%	32	2.2%	0.7	57.8	41
30-34	0.990		19,795			98,975	0.2%	38	2.2%	0.8	52.9	45
35-39	0.987		19,741			98,706	0.3%	54	2.2%	1.2	48.1	58
40-44	0.983		19,662			98,311	0.4%	79	2.2%	1.8	43.2	76
45-49	0.977		19,546			97,730	0.6%	116	1.0%	1.2	38.5	45
50-54	0.969		19,375			96,873	0.9%	171	1.0%	1.7	33.8	58
55-59	0.956		19,118			95,591	1.3%	256	1.0%	2.6	29.2	75
60-64	0.936		18,726			93,630	2.1%	392	1.0%	3.9	24.7	97
65-69	0.906		18,113			90,567	3.4%	613	0.3%	1.6	20.4	32
70-74	0.857		17,144			85,720	5.7%	969	0.3%	2.5	16.3	40
								2,721	**0.7%**	**18.0**	**31.6**	**568**

- Cervical cancer screening in women ages 25-69 leads to a reduction in cervical cancer mortality of 35% (RR 0.65, 95% CI of 0.47 to 0.90).[239]
- Cervical cancer screening in women ages 25-69 leads to a reduction in cervical cancer incidence of 44% (RR 0.56, 95% CI of 0.42 to 0.75).[240]
- Potential harms associated with cervical cancer screening include anxiety caused by false positive screening results and pain, bleeding or discharge after an unnecessary biopsy or loop electrosurgical excision and an increase in preterm births caused by excisional treatment of CIN.[241]
- The false positive rate associated with cytology screening ranges from 3.2% to 6.5%.[242] We have used the midpoint for our base case (4.9%) and the range in our sensitivity analysis. A false-positive Pap smear result is associated with a disutility of 0.046 for a period of approximately 10 months (or a one-time QALY loss of 0.038).[243]
- Other assumptions used in assessing the clinically preventable burden are detailed in the Reference Document.

Based on these assumptions, the CPB associated with screening women ages 25 to 69 years of age for cervical cancer every 3 years is 1,471 QALYs saved (Table 2, row *v*). The CPB of 1,471 represents the gap between no coverage and the 'best in the world' coverage estimated at 88%. The CPB of 317 QALYs saved (see Table 2, row *w*) represents the gap between the current coverage of 69% and the 'best in the world' coverage estimated at 88%.

[239] Peirson L, Fitzpatrick-Lewis D, Ciliska D, et al. Screening for cervical cancer: A systematic review and meta-analysis. *Systematic Reviews*. 2013; 2(35).
[240] Ibid.
[241] Habbema D, Weinmann S, Arbyn M, et al. Harms of cervical cancer screening in the United States and the Netherlands. *International Journal of Cancer*. 2017; 140: 1215-22.
[242] Melnikow J, Henderson J, Burda B, et al. *Draft Evidence Review: Cervical Cancer Screening, U.S. Preventive Services Task Force. October 2017.* Table 6. Available online at https://www.uspreventiveservicestaskforce.org/Page/Document/draft-evidence-review/cervical-cancer-screening2. Accessed December 2017.
[243] Insinga R, Glass A, Myers E et al. Abnormal outcomes following cervical cancer screening: event duration and health utility loss. *Medical Decision Making*. 2007; 27(4): 414-22.

Table 2. Calculation of Clinically Preventable Burden for Cervical Cancer in Average Risk Women in a BC Birth Cohort of 40,000			
Row	**Variable**	**Base Case**	**Data Source**
	Estimated Current Status		
a	Total cervical cancer mortality in a birth cohort of 40,000 between the ages of 25 and 74	18.0	Table 1
b	Ratio of nonfatal cervical cancers per fatal cervical cancer	10.1	Ref Doc
c	Estimated nonfatal cervical cancers	181.4	= a * b
d	Effectiveness of screening in reducing mortality	35%	√
e	Effectiveness of screening in reducing incidence	44%	√
f	Current screening rate in BC	69%	Ref Doc
g	Potential screening rate	88%	Ref Doc
h	Predicted deaths in the absence of screening	23.7	= a / (1 - f * d)
i	Predicted nonfatal cervical cancers in absence of screening	260.5	= c / (1 - f * e)
	Benefits of Screening		
j	Deaths avoided - 100% adherence	8.3	= h * d
k	Deaths avoided - 88% adherence	7.3	= j * g
l	Deaths avoided - 69% adherence	5.7	= j * f
m	Nonfatal cancers avoided - 100% adherence	114.6	= i * e
n	Nonfatal cancers avoided - 88% adherence	100.9	= m * g
o	Nonfatal cancers avoided - 69% adherence	79.1	= m * f
p	LE at average age of cervical cancer death	31.6	Table 1
q	Life years lost per nonfatal cervical cancer	17	Ref Doc
r	QALYs saved with 88% adherence to screening	1,945	= (k * p) + (n * q)
	Harms Associated with Screening		
s	False-positive screening rate	4.9%	√
t	Reduced QALYs per false positive	0.038	√
u	Reduced QALYs associated with false positives	-475	= -(s * Table 3, row c) * t
	Summary of Benefits and Harms		
v	Potential QALY saved - Utilization increasing from 0% to 88%	1,471	= r + u
w	Potential QALY saved - Utilization increasing from 69% to 88%	317	= v * (g - f) / g

√ = Estimates from the literature

We also modified several major assumptions and recalculated the CPB as follows:

- Assume the effectiveness of screening in reducing cervical cancer deaths is reduced from 35% to 10% and the effectiveness of reducing cervical cancer incidence is reduced from 44% to 25% (Table 2, rows *d* & *e*): CPB = 399.
- Assume the effectiveness of screening in reducing cervical cancer deaths is increased from 35% to 53% and the effectiveness of reducing cervical cancer incidence is increased from 44% to 58% (Table 2, rows *d* & *e*): CPB = 2,567.
- Assume that the false-positive screening rate is reduced from 4.9% to 3.2% (Table 2, row *s*): CPB = 1,635.
- Assume that the false-positive screening rate is increased from 4.9% to 6.5% (Table 2, row *s*): CPB = 1,315.

Modelling Cost-Effectiveness

In this section, we will calculate the CE associated with screening women ages 25 to 69 years of age for cervical cancer every 3 years.

In estimating the CE of screening for cervical cancer, we made the following assumptions:

- We assumed a screening rate of once every 3 years starting at age 25. There are an estimated 869,546 life years lived by women between the ages of 25 and 69 in a BC birth cohort of 40,000, resulting in an estimated 255,067 screens (with 88% adherence) between the ages of 25 and 69 in this birth cohort. We have also assumed that 5% of screens would have a mildly abnormal Pap resulting in a rescreen.[244] Total screens in this cohort are therefore estimated at 267,820 (Table 3, row *d*).
- Based on the BC HPV FOCAL study, the colposcopy referral rate is 3.1% (with a 95% CI of 2.8% to 3.5%). The participation rate for these referrals is approximately 85%.[245] Women are typically recalled for multiple follow-ups if something is identified on the initial colposcopy. We have assumed an average of two colposcopies per accepted referral,[246] yielding a colposcopy rate of 5.3% (0.031 * 0.85 * 2).
- In 2007, the rate of detection of CIN2/3 lesions in BC was 5.9 per 1,000 screens (Table 3, row *o*).[247] These would typically be treated by a loop electrosurgical excision procedure (LEEP) as an ambulatory procedure in a colposcopy suite. Three Canadian studies estimated the cost per treatment for a precancerous lesion to be $965[248], $1,032[249] and $1,071[250] in 2005 or 2006 CAD. We updated these estimates to 2017 CAD and then used the average for the base case estimate and the extremes in the sensitivity analysis ($1,216 with a range from $1,137 to $1,295, in 2017 CAD).
- For patient time and travel costs, we estimated two hours of patient time would be required per screening visit and 7.5 hours per colposcopy or treatment for a precancerous lesion.
- Other costs and assumptions used in assessing cost-effectiveness are detailed in the Reference Document.
- Discount rate of 1.5%, varied from 0% to 3% in the sensitivity analysis.

Based on these assumptions, the CE associated with screening women ages 25 to 69 years of age for cervical cancer every 3 years would be $25,542 / QALY (Table 3, row *af*).

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[244] Dr. Andy Coldman, Vice President, Population Oncology, BC Cancer Agency. Personal communication, May 2014.

[245] BC Cancer Agency. *Cervical Cancer Screening Program 2012 Annual Report*. 2012. Available at http://www.screeningbc.ca/NR/rdonlyres/4545C16F-3F34-496C-ABF4-CB4B9BA04076/66569/CCSPAnnualReport2012PrintVersionLowRes.pdf. Accessed October, 2013.

[246] Dr. Andy Coldman, Vice President, Population Oncology, BC Cancer Agency. Personal communication, May 2014.

[247] Ibid.

[248] Kulasingam S, Rajan R, St Pierre Y et al. Human papillomavirus testing with Pap triage for cervical cancer prevention in Canada: a cost-effectiveness analysis. *BioMed Central Medicine*. 2009; 7(1): 69.

[249] Krahn M, McLauchlin M, Pham B et al. *Liquid-Based Techniques for Cervical Cancer Screening: Systematic Review and Cost-Effectiveness Analysis*. 2008. Available at https://www.cadth.ca/sites/default/files/pdf/333_LBC-Cervical-Cancer-Screenin_tr_e.pdf. Accessed August 2017.

[250] Brisson M, Van de Velde N, De Wals P et al. The potential cost-effectiveness of prophylactic human papillomavirus vaccines in Canada. *Vaccine*. 2007; 25(29): 5399-408.

Table 3. Summary of CE Estimate for Cervical Cancer Screening B.C. Birth Cohort of 40,000			
Row	**Variable**	**Base Case Ages 25-69**	**Data Source**
	Costs of Screening and Treatment		
a	Life years lived between age 25 and 69 in birth cohort	869,546	Table 1
b	Screening visits at 100% adherence	289,849	= a / 3
c	Screening visits at 88% adherence	255,067	= b * Table 2, row g
d	Screening visits with 5% rescreen rate	267,820	= c * 1.05
e	Cost per screening visit	$70	Ref Doc
f	Screening costs	$18,747,412	= e * d
g	Value of patient time (per hour)	$29.69	Ref Doc
h	Patient time per screening visit (in hours)	2	Ref Doc
i	Value of patient time - screening	$15,903,162	= d * h * g
j	Rate of colposcopies per screen	5.3%	√
k	Cost per colposcopy	$251	Ref Doc
l	Colposcopy costs	$3,562,812	= j * d * k
m	Patient time per colposcopy (in hours)	7.5	√
n	Value of patient time - colposcopy	$3,160,753	= d * j * m * g
o	Proportion of screens resulting in treatment for CIN2 or 3	0.59%	√
p	Treatment costs per CIN2/3	$1,216	Ref Doc
q	Treatment costs for CIN2/3	$1,921,449	= d * o * p
r	Patient time per treatment for CIN2/3 (in hours)	7.5	√
s	Value of patient time - treatment of CIN2/3	$351,857	= d * o * r * g
t	**Costs of screening and treatment**	**$43,647,445**	= f + i + l + n + q + s
	Costs Avoided		
u	Deaths prevented	7.3	Table 2, row k
v	Costs avoided per death prevented	-$46,603	Ref Doc
w	Costs avoided due to deaths prevented	-$339,908	= u * v
x	# of cervical cancers prevented	100.9	Table 2, row n
y	Costs avoided per cervical cancer prevented	-$36,021	Ref Doc
z	Costs avoided due to cervical cancers prevented	-$3,633,357	= x * y
aa	**Costs avoided**	**-$3,973,265**	= w + z
ab	Net costs	$39,674,180	= t + aa
ac	CPB undiscounted	1,471	Table 2, row v
ad	Net costs (1.5% discount)	$24,509,536	Calculated
ae	CPB (1.5% discount)	960	Calculated
af	**CE ($/QALY saved)**	**$25,542**	= ad / ae

√ = Estimates from the literature

We also modified several major assumptions and recalculated the cost per QALY as follows:

- Assume the effectiveness of screening in reducing cervical cancer deaths is reduced from 35% to 10% and the effectiveness of reducing cervical cancer incidence is reduced from 44% to 25% (Table 2, rows *d* & *e*): CE = $99,328.
- Assume the effectiveness of screening in reducing cervical cancer deaths is increased from 35% to 53% and the effectiveness of reducing cervical cancer incidence is increased from 44% to 58% (Table 2, rows *d* & *e*): CE = $13,818.
- Assume that the false-positive screening rate is reduced from 4.9% to 3.2% (Table 2, row *s*): CE = $22,968.

- Assume that the false-positive screening rate is increased from 4.9% to 6.5% (Table 2, row *s*): CE = $28,553.
- Assume the cost per screening visit is reduced from $70 to $33 (Table 3, row *e*): CE = $19,162.
- Assume the cost per screening visit is increased from $70 to $108 (Table 3, row *e*): CE = $32,094.
- Assume the cost per colposcopy is reduced from $251 to $176 (Table 3, row *k*): CE = $24,857.
- Assume the cost per colposcopy is increased from $251 to $392 (Table 3, row *k*): CE = $26,831.

Summary

Applying a 1.5% discount rate, the clinically preventable burden (CPB) associated with screening women ages 25 to 69 years of age for cervical cancer every 3 years is estimated to be 960 quality-adjusted life years (QALYs) while the cost-effectiveness (CE) is estimated to be $25,542 per QALY (see Table 4).

Table 4: Cervical Cancer Screening Being Offered to a Birth Cohort of 40,000 Women Between the Ages of 25 to 69

Summary

	Base Case	Range	
CPB (Potential QALYs Gained)			
Assume No Current Service			
1.5% Discount Rate	**960**	260	1,675
3% Discount Rate	657	178	1,147
0% Discount Rate	1,471	399	2,567
Gap between B.C. Current (69%) and 'Best in the World' (88%)			
1.5% Discount Rate	207	56	362
3% Discount Rate	142	38	248
0% Discount Rate	318	86	554
CE ($/QALY) **including** patient time costs			
1.5% Discount Rate	**$25,542**	$13,818	$99,328
3% Discount Rate	$28,928	$15,524	$113,289
0% Discount Rate	$26,980	$14,596	$104,919
CE ($/QALY) **excluding** patient time costs			
1.5% Discount Rate	$13,042	$6,658	$53,225
3% Discount Rate	$14,594	$7,314	$60,424
0% Discount Rate	$13,776	$7,033	$56,221

Screening (HPV-Based) for Cervical Cancer

United States Preventive Services Task Force Recommendations (2017)

> *The USPSTF recommends screening for cervical cancer in women age 21 to 65 years with cytology (Pap smear) every 3 years or, for women age 30 to 65 years who want to lengthen the screening interval, screening with a combination of cytology and human papillomavirus (HPV) testing every 5 years.*[251]

Modelling the Clinically Preventable Burden

In this section, we will calculate the CPB associated with incorporating HPV-based screening in females ages 30-65 in a BC birth cohort of 40,000.

In modelling CPB, we made the following assumptions:

- Based on BC life tables for 2010 to 2012, a total of 1,719 deaths would be expected in females between the ages of 30-69 in a BC birth cohort of 40,000 (see Table 1). While routine HPV-based screening occurs to age 65, we have assumed the protective effect of routine screening would continue to age 69.
- Based on BC vital statistics data, there were 357 deaths in females between the ages of 25 and 44 in BC in 2012, with 8 (2.2%) of these deaths due to cervical cancer (ICD-10 codes C53). There were also 1,990 deaths between the ages of 45 and 64 that year, with 20 (1.0%) of these deaths due to cervical cancer. Finally, there were 3,566 deaths between the ages of 65 and 79 that year, with 10 (1.0%) of these deaths due to cervical cancer.[252] This suggests that 14.8 of the 1,719 (0.9%) of the female deaths in the BC birth cohort between the ages of 30 and 69 would be due to cervical cancer (see Table 1).

Table 1: Mortality Due to Cervical Cancer Between the Ages of 30 and 69
in a British Columbia Birth Cohort of 40,000

Age Group	*Mean Survival Rate*		*Individuals in Birth Cohort*			*Life Years Lived*	*Deaths in Birth Cohort*		*Deaths due to* Cervical Cancer		*Life Years Lost* Per Death	
	Males	Females	Males	Females	Total		%	#	%	#		Total
25-29	0.992		19,833			99,163						
30-34	0.990		19,795			98,975	0.2%	38	2.2%	0.8	52.9	45
35-39	0.987		19,741			98,706	0.3%	54	2.2%	1.2	48.1	58
40-44	0.983		19,662			98,311	0.4%	79	2.2%	1.8	43.2	76
45-49	0.977		19,546			97,730	0.6%	116	1.0%	1.2	38.5	45
50-54	0.969		19,375			96,873	0.9%	171	1.0%	1.7	33.8	58
55-59	0.956		19,118			95,591	1.3%	256	1.0%	2.6	29.2	75
60-64	0.936		18,726			93,630	2.1%	392	1.0%	3.9	24.7	97
65-69	0.906		18,113			90,567	3.4%	613	0.3%	1.6	20.4	32
								1,719	**0.9%**	**14.8**	**32.9**	**487**

- HPV-based screening is associated with a 55% reduction in the incidence of cervical cancers (RR of 0.45, 95% CI of 0.25 to 0.81) in females ages 30 – 64, when

[251] US Preventive Services Task Force. Draft Recommendation Statement *Cervical Cancer: Screening.* 2017. Available online at https://www.uspreventiveservicestaskforce.org/Page/Document/draft-recommendation-statement/cervical-cancer-screening2. Accessed December 2017.

[252] British Columbia Vital Statistics Agency. *Selected Vital Statistics and Health Status Indicators: One Hundred and Forty-First Annual Report*. Apendix 2. 2012. British Columbia Ministry of Health. Available at https://www2.gov.bc.ca/assets/gov/birth-adoption-death-marriage-and-divorce/statistics-reports/annual-reports/2012/pdf/annual-report-2012.pdf. Accessed December 2017.

compared to cytology-based screening.[253] The effectiveness of HPV-based screening is observed primarily in the reduction in adenocarcinomas. We assumed that the effectiveness of HPV-based screening in reducing mortality from cervical cancers would be the same as the observed effectiveness in reducing the incidence of cervical cancers.

- The cumulative incidence of cervical cancer is lower at 5.5 years after a negative HPV test than 3.5 years after a negative cytology test, indicating that 5 year screening intervals with HPV testing are safer than 3 year screening intervals with cytology testing.[254]

In estimating the effect of the additional CPB associated with incorporating HPV-based we first re-ran the model for cytology-based screening above but modified the age range to 30-69 (from 25-74). The result is a modest reduction in QALYs saved, from 1,471 (based on ages 25-74) to 1,188 (based on ages 30-69) (see Table 2).

Table 2. Calculation of Clinically Preventable Burden for Cervical Cancer in Average Risk Women in a BC Birth Cohort of 40,000

Row	Variable	Base Case	Data Source
	Estimated Current Status		
a	**Total cervical cancer mortality in a birth cohort of 40,000 between the ages of 30 and 69**	14.8	Table 1
b	Ratio of nonfatal cervical cancers per fatal cervical cancer	10.1	Ref Doc
c	Estimated nonfatal cervical cancers	149.3	= a * b
d	Effectiveness of screening in reducing mortality	35%	√
e	Effectiveness of screening in reducing incidence	44%	√
f	Current screening rate in BC	69%	Ref Doc
g	Potential screening rate	88%	Ref Doc
h	Predicted deaths in the absence of screening	19.5	= a / (1 - f * d)
i	Predicted nonfatal cervical cancers in absence of screening	214.4	= c / (1 - f * e)
	Benefits of Screening		
j	Deaths avoided - 100% adherence	6.8	= h * d
k	Deaths avoided - 88% adherence	6.0	= j * g
l	Deaths avoided - 69% adherence	4.7	= j * f
m	Nonfatal cancers avoided - 100% adherence	94.3	= i * e
n	Nonfatal cancers avoided - 88% adherence	83.0	= m * g
o	Nonfatal cancers avoided - 69% adherence	65.1	= m * f
p	LE at average age of cervical cancer death	32.9	Table 1
q	Life years lost per nonfatal cervical cancer	17	Ref Doc
r	QALYs saved with 88% adherence to screening	1,609	= (k * p) + (n * q)
	Harms Associated with Screening		
s	False-positive screening rate	4.9%	√
t	Reduced QALYs per false positive	0.038	√
u	Reduced QALYs associated with false positives	-421	= -(s * Table 4, row c) * t
	Summary of Benefits and Harms		
v	Potential QALY saved - Utilization increasing from 0% to 88%	1,188	= r + u
w	Potential QALY saved - Utilization increasing from 69% to 88%	257	= v * (g - f) / g

√ = Estimates from the literature

[253] Ronco G, Dillner J, Elfström KM et al. Efficacy of HPV-based screening for prevention of invasive cervical cancer: follow-up of four European randomised controlled trials. *The Lancet*. 2014; 383(9916): 524-32.
[254] Ronco G, Dillner J, Elfström KM et al. Efficacy of HPV-based screening for prevention of invasive cervical cancer: follow-up of four European randomised controlled trials. *The Lancet*. 2014; 383(9916): 524-32.

We then adjusted the assumptions in this table to reflect HPV-based screening. This meant that the effectiveness of HPV-based screening improved by 55% compared to cytology-based screening (Table 3, row *j*) while the false-positive screening rate increased from 4.9% to 7.28% (Table 3, row *p*).[255]

The result is a gain of 975 QALYs saved, from 1,188 (see Table 2, row *v*) to 2,163 (Table 3, row *s*) associated with incorporating HPV-based screening in females ages 30-65 in a BC birth cohort of 40,000.

Table 3. Calculation of CPB for HPV-Based Cervical Cancer Screening in Average Risk Women in a BC Birth Cohort of 40,000

Row	Variable	Base Case	Data Source
	Estimated Current Status - Cytology-based Screening		
a	**Total cervical cancer mortality in a birth cohort of 40,000 between the ages of 30 and 69**	14.8	Table 1
b	Ratio of nonfatal cervical cancers per fatal cervical cancer	10.1	Ref Doc
c	Estimated nonfatal cervical cancers	149.3	= a * b
d	Effectiveness of screening in reducing mortality	35%	Table 2, row d
e	Effectiveness of screening in reducing incidence	44%	Table 2, row e
f	Current screening rate in BC	69%	Ref Doc
g	Potential screening rate	88%	Ref Doc
h	Predicted deaths in the absence of screening	19.5	Table 2, row h
i	Predicted nonfatal cervical cancers in absence of screening	214.4	Table 2, row i
	Benefits of HPV-based Screening		
j	Rate ratio comparing HPV- to cytology-based screening	55%	√
k	Deaths avoided - 88% adherence	9.3	= Table 2, row k + (Table 2, row k * j)
l	Nonfatal cancers avoided - 88% adherence	128.7	= Table 2, row n + (Table 2, row n * j)
m	LE at average age of cervical cancer death	32.9	Table 1
n	Life years lost per nonfatal cervical cancer	17	Ref Doc
o	QALYs saved with 88% adherence to screening	2,494	= (k * l) + (l * n)
	Harms Associated with Screening		
p	False-positive screening rate	7.28%	√
q	Reduced QALYs per false positive	0.038	√
r	Reduced QALYs associated with false positives	-331	= -(p * Table 5, row e) * q
	Summary of Benefits and Harms		
s	Potential QALY saved - Utilization increasing from 0% to 88%	2,163	= o + r

√ = Estimates from the literature

We also modified a major assumption and recalculated the CE as follows:

- Assume that the effectiveness of HPV-based screening compared to cytology-based screening is reduced from 55% to 19% (Table 3, rows *j*): CPB = 395.
- Assume that the effectiveness of HPV-based screening compared to cytology-based screening is reduced from 55% to 75% (Table 3, rows *j*): CPB = 1,296.

[255] Melnikow J, Henderson J, Burda B, et al. *Draft Evidence Review: Cervical Cancer Screening, U.S. Preventive Services Task Force. October 2017.* Table 6. Available online at https://www.uspreventiveservicestaskforce.org/Page/Document/draft-evidence-review/cervical-cancer-screening2. Accessed December 2017.

Modelling Cost-effectiveness

Note that in modelling cost-effectiveness we are trying to tease out the additional benefits and costs associated with HPV-based screening to generate a cost/QALY associated with moving from cytology-based screening every three years in women ages 30-69 to HPV-based screening every five years in women ages 30-65 in a BC birth cohort of 40,000.

In estimating the effect on CE associated with incorporating HPV-based screening, we first re-ran the model for cytology-based screening used in the previous section but modified the age range to 30-69 (from 25-74). The result is a reduction in net costs from $39,674,180 (based on ages 25-74) to $35,399,781 (based on ages 30-69) (see Table 4, row *ab*).

Table 4. Summary of Net Costs for Cervical Cancer Screening B.C. Birth Cohort of 40,000

Row	Variable	Base Case Ages 30-69	Data Source
	Costs of Screening and Treatment		
a	Life years lived between age 30 and 69 in birth cohort	770,383	Table 1
b	Screening visits at 100% adherence	256,794	= a / 3
c	Screening visits at 88% adherence	225,979	= b * Table 2, row g
d	Screening visits with 5% rescreen rate	237,278	= c * 1.05
e	Cost per screening visit	$70	Ref Doc
f	Screening costs	$16,609,457	= e * d
g	Value of patient time (per hour)	$29.69	Ref Doc
h	Patient time per screening visit (in hours)	2	Ref Doc
i	Value of patient time - screening	$14,089,566	= d * h * g
j	Rate of colposcopies per screen	5.3%	√
k	Cost per colposcopy	$251	Ref Doc
l	Colposcopy costs	$3,156,509	= j * d * k
m	Patient time per colposcopy (in hours)	7.5	√
n	Value of patient time - colposcopy	$2,800,301	= d * j * m * g
o	Proportion of screens resulting in treatment for CIN2 or 3	0.59%	√
p	Treatment costs per CIN2/3	$1,216	Ref Doc
q	Treatment costs for CIN2/3	$1,702,327	= d * o * p
r	Patient time per treatment for CIN2/3 (in hours)	7.5	√
s	Value of patient time - treatment of CIN2/3	$311,732	= d * o * r * g
t	**Costs of screening and treatment**	**$38,669,892**	= f + i + l + n + q + s
	Costs Avoided		
u	Deaths prevented	6.0	Table 2, row k
v	Costs avoided per death prevented	-$46,603	Ref Doc
w	Costs avoided due to deaths prevented	-$279,754	= u * v
x	# of cervical cancers prevented	83.0	Table 2, row n
y	Costs avoided per cervical cancer prevented	-$36,021	Ref Doc
z	Costs avoided due to cervical cancers prevented	-$2,990,356	= x * y
aa	**Costs avoided**	**-$3,270,110**	= w + z
ab	**Net costs**	**$35,399,781**	= t + aa

√ = Estimates from the literature

We then estimated the net costs of incorporating HPV-based screening in females ages 30-65 in a BC birth cohort of 40,000. In doing so, we made the following assumptions:

- **Number of HPV-based screens** – We assumed a screening rate of once every five years starting at age 30. Based on the initial results of the HPV FOCAL trial, 91.9% of tests are negative and the woman is recalled at 5 years. The 8.1% of women with

hr-HPV positive tests (Table 5, row *f*) are reflexed to cytology (Table 5, row *g*). Cytology results are negative for 64% of these women (Table 5, row *h*). Women with positive results are referred to colposcopy. Women who are hr-HPV positive but cytology negative are retested with HPV and cytology after 6-12 months. 43% of these women are both HPV and cytology negative and move into routine HPV-based screening at 5-year intervals. The 57% of women who are HPV and/or cytology positive are referred to colposcopy.[256] This approach results in 125,850 HPV-based screens (Table 5, row *l*) and 15,894 cytology-based screens (Table 5, row *m*) in females between the ages of 30 and 65 in a BC birth cohort of 40,000.

- Based on the BC HPV FOCAL study, the colposcopy referral rate associated with cytology-based screening is 3.1% (with a 95% CI of 2.8% to 3.5%) while the colposcopy referral rate associated with HPV-based screening is 5.9% (with a 95% CI of 5.5% to 6.3%).[257] The participation rate for these referrals is approximately 85%.[258] Women are typically recalled for multiple follow-ups if something is identified on the initial colposcopy. We have assumed an average of two colposcopies per accepted referral,[259] yielding a HPV-based colposcopy rate of 10.0% (0.059 * 0.85 * 2).
- In 2007, the rate of detection of CIN2/3 lesions in BC was 5.9 per 1,000 screens.[260] Based on the BC HPV FOCAL study, the detection rate of CIN2/3 lesions is increased by 50% with HPV-based screening, to 8.85 per 1,000 screens.[261] These lesions would typically be treated by a loop electrosurgical excision procedure (LEEP) as an ambulatory procedure in a colposcopy suite.
- For patient time and travel costs, we estimated two hours of patient time would be required per screening visit and 7.5 hours per colposcopy or treatment for a precancerous lesion.
- Other costs and assumptions used in assessing net costs are detailed in the Reference Document.

Based on these assumptions, the estimated net costs of incorporating HPV-based screening in females ages 30-65 in a BC birth cohort of 40,000 is $22,776,189 (see Table 5, row *ak*). This is $12,623,593 less than the estimated net costs associated with the current cytology-based screening (ref. Table 4, row *ab*) for females ages 30-69 in a BC birth cohort of 40,000.

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[256] Ogilvie G, Krajden M, Van Niekerk D et al. Primary cervical cancer screening with HPV testing compared with liquid-based cytology: results of round 1 of a randomised controlled trial–the HPV FOCAL Study. *British Journal of Cancer*. 2012; 107(12): 1917-24.

[257] Melnikow J, Henderson J, Burda B, et al. *Draft Evidence Review: Cervical Cancer Screening, U.S. Preventive Services Task Force. October 2017.* Table 6. Available online at https://www.uspreventiveservicestaskforce.org/Page/Document/draft-evidence-review/cervical-cancer-screening2. Accessed December 2017.

[258] BC Cancer Agency. *Cervical Cancer Screening Program 2012 Annual Report*. 2012. Available at http://www.screeningbc.ca/NR/rdonlyres/4545C16F-3F34-496C-ABF4-CB4B9BA04076/66569/CCSPAnnualReport2012PrintVersionLowRes.pdf. Accessed October, 2013.

[259] Dr. Andy Coldman, Vice President, Population Oncology, BC Cancer Agency. Personal communication, May 2014.

[260] Ibid.

[261] Melnikow J, Henderson J, Burda B, et al. *Draft Evidence Review: Cervical Cancer Screening, U.S. Preventive Services Task Force. October 2017.* Table 6. Available online at https://www.uspreventiveservicestaskforce.org/Page/Document/draft-evidence-review/cervical-cancer-screening2. Accessed December 2017.

Table 5. Summary of Net Cost for HPV-Based Cervical Cancer Screening			
Row Label	**Variable**	**Base Case**	**Data Source**
	Costs of Screening and Treatment		
a	Life years lived between age 30 and 65 in birth cohort	679,816	Table 1
b	Annual frequency of HPV-based screening	20%	√
c	Number of HPV-based screens - 100% adherence	135,963	= a * b
d	Adherence with HPV-based screening	88%	Table 3, row g
e	Number of HPV-based screens - 88% adherence	119,648	= c * d
f	Proportion of screens hrHPV-positive	8.1%	√
g	Number of reflex cytology screens	9,691	= e * f
h	Proportion of reflex cytology screens negative	64%	√
i	Number of reflex cytology screens negative	6,203	= g * h
j	Number of follow-up cytology screens	6,203	= i
k	Number of follow-up HPV screens	6,203	= i
l	HPV-based screening - number of HPV-based screens	125,850	= e + k
m	HPV-based screening - number of cytology-based screens	15,894	= g + j
n	Cost per HPV-based screen	$96	Ref Doc
o	Cost for HPV-based screening	$12,081,614	= l * n
p	Value of patient time (per hour)	$29.69	Ref Doc
q	Patient time per screening visit (in hours)	2	√
r	Value of patient time - screening	$8,416,767	= (l + m) * q * p
s	Rate of colposcopies per screen	10.0%	√
t	Cost per colposcopy	$251	Ref Doc
u	Colposcopy costs	$3,158,839	= l * s * t
v	Patient time per colposcopy (in hours)	7.5	√
w	Value of patient time - colposcopy	$2,664,253	= e * s * v * p
x	Proportion of screens resulting in treatment for CIN2 or 3	0.885%	√
y	Treatment costs per CIN2/3	$1,216	Ref Doc
z	Treatment costs for CIN2/3	$1,287,600	= e * x * y
aa	Patient time per treatment for CIN2/3 (in hours)	7.5	√
ab	Value of patient time - treatment of CIN2/3	$235,786	= e * x * aa * p
ac	**Costs of screening and treatment**	**$27,844,859**	= o + r + u + w + z + ab
	Costs Avoided		
ad	Deaths prevented	9.3	Table 3, row k
ae	Costs avoided per death prevented	-$46,603	Ref Doc
af	Costs avoided due to deaths prevented	-$433,618	= ad * ae
ag	# of cervical cancers prevented	128.7	Table 3, row l
ah	Costs avoided per cervical cancer prevented	-$36,021	Ref Doc
ai	Costs avoided due to cervical cancers prevented	-$4,635,053	= ag * ah
aj	**Costs avoided**	**-$5,068,671**	= af + ai
ak	**Net costs**	**$22,776,189**	**= af + aj**

√ = Estimates from the literature

After discounting costs and QALYs by 1.5%, the cost per QALY associated with cytology-based cervical cancer screening is $33,340 (see Table 6, row *i*) compared to the cost per QALY associated with HPV-based cervical cancer screening of $11,784 (see Table 6, row *l*). Implementing HPV-based cervical cancer screening in females ages 30-65 in a BC birth cohort of 40,000 is estimated to cost $21,556 ***less*** per QALY than the current cytology-based screening in this cohort (see Table 6, row *m*).

Table 6. Summary of CE Estimate for HPV-Based Cervical Cancer Screening B.C. Birth Cohort of 40,000			
Row	Variable	Base Case Ages 30-65	Data Source
	Undiscounted Cost / QALY		
a	Net costs for cytology-based cervical cancer screening	$35,399,781	Table 4, row ab
b	QALYs gained with cytology-based cervical cancer screening	1,188	Table 2, row v
c	Undiscounted cost / QALY	$29,796	= a / c
d	Net costs for HPV-based cervical cancer screening	$22,776,189	Table 5, row ak
e	QALYs gained with HPV-based cervical cancer screening	2,163	Table 3, row s
f	Undiscounted cost / QALY	$10,531	= d / e
	Discounted Cost / QALY - 1.5%		
g	Net costs for cytology-based cervical cancer screening	$26,636,256	Calculated
h	QALYs gained with cytology-based cervical cancer screening	799	Calculated
i	Discounted cost / QALY	$33,340	= g / h
j	Net costs for HPV-based cervical cancer screening	$17,137,744	Calculated
k	QALYs gained with HPV-based cervical cancer screening	1,454	Calculated
l	Discounted cost / QALY	$11,784	= j / k
m	Cost / QALY saved with incorporating HPV-based cervical cancer screening	-$21,556	= l - i

We also modified a major assumption and recalculated the CE as follows:

- Assume that the effectiveness of HPV-based screening compared to cytology-based screening is reduced from 55% to 19% (Table 3, rows *j*): CE = -$16,414.
- Assume that the effectiveness of HPV-based screening compared to cytology-based screening is reduced from 55% to 75% (Table 3, rows *j*): CE = -$23,377.

Summary

Applying a 1.5% discount rate, the clinically preventable burden (CPB) associated with incorporating HPV-based screening in females ages 30-65 is estimated to be 655 quality-adjusted life years (QALYs) while the cost-effectiveness (CE) is estimated to result in cost savings of $21,556 per QALY (see Table 7).

Table 7: HPV-based Cervical Cancer Screening Being Offered to a Birth Cohort of 40,000 Between the Ages of 30 and 65 Summary			
	Base Case	Range	
CPB (Potential QALYs gained in moving from cytology- to HPB-based screening)			
Gap between B.C. Current (0%) and 'Best in the World' (88%)			
1.5% Discount Rate	**655**	266	872
3% Discount Rate	459	186	611
0% Discount Rate	975	395	1,296
CE ($/QALY) **including** patient time costs			
1.5% Discount Rate	**-$21,556**	-$16,414	-$23,377
3% Discount Rate	-$23,624	-$17,989	-$25,620
0% Discount Rate	-$19,264	-$14,669	-$20,892
CE ($/QALY) **excluding** patient time costs			
1.5% Discount Rate	-$11,210	-$8,210	-$12,273
3% Discount Rate	-$12,286	-$8,998	-$13,450
0% Discount Rate	-$10,019	-$7,337	-$10,968

Screening for Colorectal Cancer

Canadian Task Force on Preventive Health Care Recommendations (2016)

We recommend screening adults aged 50 to 59 years for colorectal cancer with FOBT (gFOBT or FIT) every two years or flexible sigmoidoscopy every 10 years. (Weak recommendation; moderate-quality evidence)

We recommend screening adults aged 60 to 74 years for colorectal cancer with FOBT (gFOBT or FIT) every two years or flexible sigmoidoscopy every 10 years. (Strong recommendation; moderate-quality evidence) [262]

United States Preventive Services Task Force Recommendations (2016)

The USPSTF recommends screening for colorectal cancer starting at age 50 years and continuing until age 75 years. (A recommendation)[263]

Modelling the Clinically Preventable Burden

In this section, we will calculate the CPB associated with screening adults aged 50 to 74 years of age for colorectal cancer with a fecal occult blood test (with either a guaiac fecal occult blood test [gFOBT] or a fecal immunochemical test [FIT]) every two years or flexible sigmoidoscopy / colonoscopy every 10 years.

In modelling CPB, we made the following assumptions:

- Based on BC life tables for 2010 to 2012, a total of 9,340 deaths would be expected between the ages of 50-79 in a BC birth cohort of 40,000 (see Table 1). Routine screening occurs to age 74, and we have assumed the protective effect of routine screening continues to age 79.
- Based on BC vital statistics data, there were 5,117 deaths between the ages of 45 and 64 in BC in 2012, with 257 (5.0%) of these deaths due to CRC (ICD-10 codes C18-20). There were also 8,674 deaths between the ages of 65 and 79 that year, with 379 (4.4%) of these deaths due to CRC.[264] This suggests that 423 of the 9,340 (4.5%) of the deaths in the BC birth cohort between the ages of 50 and 79 would be due to CRC (see Table 1).

Table 1: Mortality Due to Colorectal Cancer Between the Ages of 50 and 79
in a British Columbia Birth Cohort of 40,000

Age Group	Mean Survival Rate		Individuals in Birth Cohort			Life Years Lived	Deaths in Birth Cohort		Deaths due to Colorectal Cancer		Life Years Lost Per Death	Life Years Lost Total
	Males	Females	Males	Females	Total		%	#	%	#		
45-49	0.963	0.977	19,263	19,546	38,809							
50-54	0.950	0.969	19,003	19,375	38,378	191,890	1.1%	431	5.0%	22	32.2	694
55-59	0.931	0.956	18,619	19,118	37,737	188,686	1.7%	641	5.0%	32	27.7	888
60-64	0.902	0.936	18,041	18,726	36,767	183,834	2.6%	970	5.0%	49	23.4	1,135
65-69	0.858	0.906	17,164	18,113	35,277	176,387	4.2%	1,489	4.4%	66	19.2	1,258
70-74	0.792	0.857	15,837	17,144	32,981	164,903	7.0%	2,297	4.4%	101	15.3	1,546
75-79	0.693	0.780	13,861	15,608	29,469	147,346	11.9%	3,511	4.4%	155	11.8	1,823
								9,340	**4.5%**	**423**	**17.4**	**7,344**

[262] Canadian Task Force on Preventive Health Care. Recommendations on screening for colorectal cancer in primary care. *Canadian Medical Association Journal*. 2016; 188(5): 340-8.
[263] US Preventive Services Task Force. Screening for colorectal cancer: US Preventive Services Task Force recommendation statement. *Journal of the American Medical Association*. 2016; 315(23): 2,564-75.
[264] British Columbia Vital Statistics Agency. *Selected Vital Statistics and Health Status Indicators: One Hundred and Forty-First Annual Report*. Apendix 2. 2012. British Columbia Ministry of Health. Available at https://www2.gov.bc.ca/assets/gov/birth-adoption-death-marriage-and-divorce/statistics-reports/annual-reports/2012/pdf/annual-report-2012.pdf. Accessed December 2017.

- The overall screening delivery rate for BC in 2012 is 49.6%, with an equal mix of fecal immunochemical testing (FIT) at 31.3% of the population ages 50-74 and sigmoidoscopy/colonoscopy at 31.1%. Across Canada, approximately 40% of those who have a FIT also have a sigmoidoscopy or colonoscopy.[265]
- Screening with gFOBT reduces the risk of mortality from CRC by 18% (RR of 0.82 with a 95% CI of 0.73 to 0.92) and the incidence of late stage CRC by 8% (RR of 0.92 with a 95% CI of 0.85 to 0.99). Screening with flexible sigmoidoscopy reduces the risk of mortality from CRC by 26% (RR of 0.74 with a 95% CI of 0.67 to 0.82) and the incidence of late stage CRC by 27% (RR of 0.73 with a 95% CI of 0.66 to 0.82).[266]
- Approximately 25% of CRCs are diagnosed as late stage cancers (stage III or IV). The life expectancy for an individual diagnosed with a late-stage CRC is approximately 30 months (2.5 years).[267] The average individual with CRC survives for 6.6 years (see Reference Document) so early detection is estimated to save 4.1 years (6.6 minus 2.5).
- Harms associated with screening for CRC include a false positive rate of 1.22% for gFOBT and between 5.55% and 12.89% for FIT. Harms following flexible sigmoidoscopy are rare but include intestinal perforation (0.001% of patients), minor bleeding (0.05% of patients), major bleeding (0.009% of patients) and death (0.015% of patients).[268]
- Other assumptions used in assessing the clinically preventable burden are detailed in the Reference Document.

Based on these assumptions, the CPB associated with screening adults aged 50 to 74 years of age for CRC with FOBT every two years or flexible sigmoidoscopy / colonoscopy every 10 years is 1,734 QALYs saved (Table 2, row *ah*). The CPB of 1,734 QALYs saved represents the gap between no coverage and the 'best in the world' coverage estimated at 76%. The CPB of 593 QALYs saved (see Table 2, row *ai*) represents the gap between the current coverage of 50% and the 'best in the world' coverage estimated at 76%.

[265] Singh H, Bernstein C, Samadder J et al. Screening rates for colorectal cancer in Canada: a cross-sectional study. *Canadian Medical Association Journal Open*. 2015; 3(2): E149-57.
[266] Canadian Task Force on Preventive Health Care. Recommendations on screening for colorectal cancer in primary care. *Canadian Medical Association Journal*. 2016; 188(5): 340-8.
[267] Siegel R, Miller K, Fedewa S, et al. Colorectal Cancer Statistics, 2017. *CA: A Cancer Journal for Clinicians*. 2017; 67(3): 177-93.
[268] Canadian Task Force on Preventive Health Care. Recommendations on screening for colorectal cancer in primary care. *Canadian Medical Association Journal*. 2016; 188(5): 340-8.

Table 2. Calculation of Clinically Preventable Burden (CPB) Estimate for Colorectal Cancer Screening in a BC Birth Cohort of 40,000			
Row Label	**Variable**	**Base Case**	**Data Source**
	Estimated Current Status		
a	Colorectal cancer deaths ages 55-79	423	Table 1
b	Predicted CRC deaths ages 55-79 in the absence of screening	475	=a / (1 - w * q)
c	Weighted life expectancy at death	17.4	Table 1
d	Life years lost due to CRC deaths	8,252	= b * c
e	Ratio of nonfatal CRC per fatal CRC	4.32	Ref Doc
f	Nonfatal CRCs	1,828	= a * e
g	Average age of CRC incidence	70.4	Ref Doc
h	Life years lost per CRC case	9.9	Ref Doc
i	Life years lost due to CRC incidence	18,099	= f * h
j	Years lived with CRC per case	6.6	Ref Doc
k	Total years lived with CRC	12,066	= f * j
l	QoL disutility for CRC survivors	0.061	Ref Doc
m	QALYs lost for cancer survivors	740	= k * l
n	**Total QALYs lost due to CRC**	**27,091**	= d + i + m
	Benefits if 100% Adherence with Screening		
o	Effectiveness in reducing the risk of mortality from CRC - gFOBT	18.0%	√
p	Effectiveness in reducing the risk of mortality from CRC - flexible sigmoidoscopy	26.0%	√
q	Weighted effectiveness	22.0%	= (o * u) + (p * v)
r	Effectiveness in reducing the incidence of late-stage CRC - gFOBT	8.0%	√
s	Effectiveness in reducing the incidence of late-stage CRC - flexible sigmoidoscopy	27.0%	√
t	Proportion of CRCs detected as late-stage (III or IV)	25.0%	√
u	Proportion of screening via gFOBT / FIT	50.0%	√
v	Proportion of screening via flexible sigmoidoscopy / colonoscopy	50.0%	√
w	Weighted proportion screened	50.0%	= (u + v) / 2
x	CRC deaths avoided via gFOBT / FIT	42.8	= (b * u) * o
y	CRC deaths avoided via flexible sigmoidoscopy / colonoscopy	61.8	= (b * v) * p
z	Proportion of CRC deaths avoided via screening	22.0%	= (x + y) / b
aa	Life years lost due to CRC deaths avoided	1,815	= d * z
ab	Late stage CRCs avoided via gFOBT / FIT	59.4	= (f * t) * u * p
ac	Late stage CRCs avoided via flexible sigmoidoscopy / colonoscopy	61.7	= (f * t) * v * s
ad	Life years saved per CRC due to earlier detection of CRC	4.1	√
ae	Life years saved due to earlier detection of CRC	497	= (ab + ac) * ad
af	QALYs lost for cancer survivors	-30	= -ae * l
ag	**Potential QALYs saved with 100% Utilization of Screening**	**2,282**	= aa + ae + af
ah	**Potential QALYs saved (CPB) - Utilization increasing from 0% to 76%**	**1,734**	= ag * 0.76
ai	Potential QALYs saved (CPB) - Utilization increasing from 50% to 76%	593	= ah - (ag * 0.50)

√ = Estimates from the literature

We modified several major assumptions and recalculated the CPB as follows:

- Assume the QoL disutility for CRC survivors is reduced from 0.061 to 0.039 (Table 2, row *l*): CPB = 1,742.
- Assume the QoL disutility for CRC survivors is increased from 0.061 to 0.090 (Table 2, row *l*): CPB = 1,723.
- Assume the effectiveness of gFOBT in reducing the risk of mortality from CRC is reduced from 18% to 8% (Table 2, row *o*), the effectiveness of flexible sigmoidoscopy / colonoscopy in reducing the risk of mortality from CRC is reduced from 26% to 18% (Table 2, row *p*), the effectiveness of gFOBT in reducing the

incidence of late-stage CRC is reduced from 8% to 1% (Table 2, row *r*) and the effectiveness of flexible sigmoidoscopy / colonoscopy in reducing the incidence of late-stage CRC is reduced from 27% to 18% (Table 2, row *s*): CPB = 1,017.

- Assume the effectiveness of gFOBT in reducing the risk of mortality from CRC is increased from 18% to 27% (Table 2, row *o*), the effectiveness of flexible sigmoidoscopy / colonoscopy in reducing the risk of mortality from CRC is increased from 26% to 33% (Table 2, row *p*), the effectiveness of gFOBT in reducing the incidence of late-stage CRC is increased from 8% to 15% (Table 2, row *r*) and the effectiveness of flexible sigmoidoscopy / colonoscopy in reducing the incidence of late-stage CRC is increased 27% to 34% (Table 2, row *s*): CPB = 2,418.

Modelling Cost-Effectiveness

In this section, we will calculate the CE associated with screening adults aged 50 to 74 years of age for colorectal cancer with FOBT (gFOBT or FIT) every two years or flexible sigmoidoscopy every 10 years.

In modelling the estimated CE of colorectal cancer screening, we made the following assumptions:

- **Costs of screening** – We assumed a biennial FIT test would cost $14.74. This is based on a $5.36 fee for sample collection (MSP Fee 92007 *Fecal immunochemical test - For sample collection only*) and a $9.38 fee for analysis (MSP Fee 92006 *Fecal immunochemical test - For analysis only*). A colonoscopy every 10 years would cost $593.40. This is based on the assumption that 16% of colonoscopies would involve the removal of polyps. Colonoscopy with polyp removal could cost $850.39 ($250 for facility fee, $347.55 for physician fee [MSP fee #S33374], $65.48 for anesthesia fee [MSP fee #01172] and $187.36 for laboratory fees). Colonoscopy without polyp removal could cost $544.45 ($250 for facility fee, $228.97 [MSP fee #S10731] for physician fee and $65.48 for anesthesia fee).
- **Patient time and travel costs** - For patient time and travel costs, we assumed that two hours of patient time would be required per FIT screening visit and that 7.5 hours of patient time would be required for a colonoscopy.
- **Costs of follow-up colonoscopies** - An average of 9.8% of FIT tests are positive, ranging from 5.3% to 14.2%.[269] Each positive FIT test would be followed by a colonoscopy. Approximately 40% of these colonoscopies would be positive for polyps. Individuals in whom a colonoscopy is positive for polyps would require a further follow-up colonoscopy.[270]
- Other costs and assumptions used in assessing cost-effectiveness are detailed in the Reference Document.
- Discount rate of 1.5%, varied from 0% to 3% in the sensitivity analysis.

Based on these assumptions, the estimated cost per QALY would be $47,265 (see Table 3, row *ah*).

[269] Lee JK, Liles EG, Bent S et al. Accuracy of fecal immunochemical tests for colorectal cancer: systematic review and meta-analysis. *Annals of Internal Medicine*. 2014; 160(3): 171.
[270] Dr. Andy Coldman, Vice President, Population Oncology, BC Cancer Agency. Personal communication, May, 2014.

Table 3. Summary of Cost Effectiveness (CE) Estimate for Colorectal Cancer Screening in BC			
Row Label	**Variable**	**Base Case**	**Data Source**
a	Life years lived between age 50-74 in the birth cohort	905,700	Table 1
b	Estimated total screens with 76% screening adherence	260,570	= e + f
c	Proportion receiving a biennial FIT screen	48.0%	√
d	Proportion receiving a colonoscopy every 10 years	47.7%	√
e	Number receiving a FIT screen	217,368	= (a * c) / 2
f	Number receiving a colonoscopy screen	43,202	= (a * d) / 10
g	Cost per screen - FIT	$14.74	√
h	Cost per screen - Colonoscopy (no polyps - 84%)	$544.45	√
i	Cost per screen - Colonoscopy (polyps - 16%)	$850.39	√
j	Weighted cost per screen - Colonoscopy	$593.40	= (h * 0.84) + (i * 0.16)
k	Cost of screening	$28,840,023	=(e*g) + (f*j)
l	Cost of 10-minute office visit	$34.85	Ref Doc
m	Value of patient time (per hour)	$29.69	Ref Doc
o	Proportion of office visit for screening	50.0%	Ref Doc
p	Value of patient time	$22,527,293	= ((e * 2)+(f * 7.5)) * m
q	Total cost of office visits	$4,540,430	= b * l * o
r	Proportion of FIT tests positive	9.8%	√
s	% of Follow-up colonoscopies with polyps	40.0%	√
t	Follow-up colonoscopies	21,302	= e * r
u	Further follow-up colonoscopies	8,521	= s * t
v	Weighted cost per follow-up colonoscopy	$666.83	= (h * 0.6) + (i * 0.4)
w	Cost of follow-up colonoscopies	$14,204,770	= t * v
x	Cost of further follow-up colonoscopies	$5,056,261	= u * j
y	Patient time costs associated with follow-up colonoscopies	$6,640,812	= ((t + u) * 7.5)) * m
z	**Total Costs of Screening and Follow-up**	**$81,809,590**	= k + p + q + w + x + y
aa	Deaths prevented	105	Table 2, row x + y
ab	Costs avoided per death prevented	-$49,197	Ref Doc
ac	**Costs avoided due to deaths prevented**	**-$5,146,491**	= aa * ab
ad	Net screening and patient costs (undiscounted)	$76,663,099	= ff + dd + aa
ae	QALYs saved (undiscounted)	1,734	Table 2, row ah
af	Net screening and patient costs (1.5% discount)	$63,701,669	Calculated
ag	QALYs saved (1.5% discount)	1,348	Calculated
ah	**CE ($/QALY saved)**	**$47,265**	= af/ag

√ = Estimates from the literature

We also modified several major assumptions and recalculated the cost per QALY as follows:

- Assume the effectiveness of gFOBT in reducing the risk of mortality from CRC is reduced from 18% to 8% (Table 2, row *o*), the effectiveness of flexible sigmoidoscopy / colonoscopy in reducing the risk of mortality from CRC is reduced from 26% to 18% (Table 2, row *p*), the effectiveness of gFOBT in reducing the incidence of late-stage CRC is reduced from 8% to 1% (Table 2, row *r*) and the effectiveness of flexible sigmoidoscopy / colonoscopy in reducing the incidence of late-stage CRC is reduced from 27% to 18% (Table 2, row *s*): CE = $82,979.
- Assume the effectiveness of gFOBT in reducing the risk of mortality from CRC is increased from 18% to 27% (Table 2, row *o*), the effectiveness of flexible sigmoidoscopy / colonoscopy in reducing the risk of mortality from CRC is increased from 26% to 33% (Table 2, row *p*), the effectiveness of gFOBT in reducing the

incidence of late-stage CRC is increased from 8% to 15% (Table 2, row *r*) and the effectiveness of flexible sigmoidoscopy / colonoscopy in reducing the incidence of late-stage CRC is increased 27% to 34% (Table 2, row *s*): CE = $32,923.

- Assume that the proportion of FIT tests that are positive is decreased from 9.8% to 5.3% (Table 3, row *r*): CE = $39,932.
- Assume that the proportion of FIT tests that are positive is increased from 9.8% to 14.2% (Table 3, row *r*): CE = $54,434.

Summary

Applying a 1.5% discount rate, the clinically preventable burden (CPB) associated with screening adults aged 50 to 74 years of age for colorectal cancer is estimated to be 1,348 quality-adjusted life years (QALYs) while the cost-effectiveness (CE) is estimated to be $47,265 per QALY (see Table 4).

Table 4: Colorectal Cancer Screening Being Offered to a Birth Cohort of 40,000 Between the Ages of 50 and 74

Summary

	Base Case	Range	
CPB (Potential QALYs Gained)			
Assume No Current Service			
1.5% Discount Rate	**1,348**	790	1,879
3% Discount Rate	1,065	624	1,484
0% Discount Rate	1,734	1,017	2,418
Gap between B.C. Current (50%) and 'Best in the World' (76%)			
1.5% Discount Rate	461	270	643
3% Discount Rate	364	213	508
0% Discount Rate	593	348	827
CE ($/QALY) **including** patient time costs			
1.5% Discount Rate	**$47,265**	$32,923	$82,979
3% Discount Rate	$50,162	$34,942	$88,066
0% Discount Rate	$44,213	$30,798	$77,622
CE ($/QALY) **excluding** patient time costs			
1.5% Discount Rate	$29,282	$20,027	$52,309
3% Discount Rate	$31,077	$21,254	$55,515
0% Discount Rate	$27,391	$18,734	$48,931

Screening for Lung Cancer

Canadian Task Force on Preventive Health Care (2016)

> *We recommend screening for lung cancer among adults 55 to 74 years of age with at least a 30 pack-year smoking history, who smoke or quit smoking less than 15 years ago, with low-dose computed tomography (CT) every year up to three consecutive years. Screening should only be done in health care settings with access to expertise in early diagnosis and treatment of lung cancer. (Weak recommendation, low-quality evidence.)*
>
> *We recommend not screening all other adults, regardless of age, smoking history or other risk factors, for lung cancer with low-dose CT. (Strong recommendation, very low quality evidence.)*
>
> *We recommend that chest radiography, with or without sputum cytology, not be used to screen for lung cancer. (Strong recommendation, low-quality evidence.)* [271]

United States Preventive Services Task Force Recommendations (2014)

> *The USPSTF recommends annual screening for lung cancer with low-dose computed tomography in adults aged 55 to 80 years who have a 30 pack-year smoking history and currently smoke or have quit within the past 15 years. Screening should be discontinued once a person has not smoked for 15 years or develops a health problem that substantially limits life expectancy or the ability or willingness to have curative lung surgery. (Grade B recommendation)* [272]

The relevant BC population includes all adults aged 55 to 74 years who have a 30 pack-year smoking history and currently smoke or have quit within the past 15 years. To estimate the relevant BC population, we used data from the 2012 Canadian Community Health Survey (CCHS) to determine the proportion of the population by age group who were current daily smokers, former daily (now occasional) smokers and former daily (now non-) smokers (variable SMKDSTY, type of smoker).[273] This information was combined with data on the number of years smoked (variable SMKDYCS), years since stopped smoking daily (variable SMK_G09C), number of cigarettes smoked/day for daily smokers (variable SMK_204) and number of cigarettes smoked/day for former daily smokers (variable SMK_208) to calculate the proportion of smokers or former smokers who meet the criteria of a 30 pack-year smoking history and currently smoke or have quit within the past 15 years.

The data suggest that approximately 90,900 individuals between the ages of 55 to 74 meet the criteria for lung cancer screening in BC, or 8.7% of this population (see Table 1).

[271] Canadian Task Force on Preventive Health Care. Recommendations on screening for lung cancer. *Canadian Medical Association Journal*. 2016: 1-8.
[272] Moyer VA. Screening for lung cancer: US Preventive Services Task Force recommendation statement. *Annals of Internal Medicine*. 2014; 160(5): 330-8.
[273] Statistics Canada. Canadian Community Health Survey (CCHS), 2012 Public Use Microdata file (Catalogue number 82M0013X2013001). 2013: All computations, use and interpretation of these data are entirely that of H. Krueger & Associates Inc.

Table 1: Proportion of Population Eligible for Lung Cancer (LC) Screening
British Columbia, 2013
by Age Group, Based on CCHS Data 2012

	Age Group (years)				
	55 to 59	60 to 64	65 to 69	70 to 74	**55 to 74**
BC Population 2013	335,332	293,907	244,139	175,627	**1,049,005**
Current Daily Smokers					
Proportion of the Population in BC who are CD Smokers	14.44%	10.04%	6.84%	5.78%	
Proportion of CD Smokers who Meet Criteria	48.64%	48.96%	54.80%	48.34%	
Number of CD Smokers Eligible for LC Screening	23,560	14,452	9,154	4,910	**52,076**
Former Daily (Now Occasional) Smokers					
Proportion of the Population in BC who are FD(NO) Smokers	0.43%	0.33%	0.38%	0.00%	
Proportion of FD(NO) Smokers who Meet Criteria	53.10%	89.86%	18.40%	0.00%	
Number of FD(NO) Smokers Eligible for LC Screening	760	859	172	0	**1,791**
Former Daily (Now Non-) Smokers					
Proportion of the Population in BC who are FD(NN) Smokers	6.44%	5.00%	6.00%	3.57%	
Proportion of FD(NN) Smokers who Meet Criteria	50.9%	67.7%	81.5%	66.0%	
Number of FD(NN) Smokers Eligible for LC Screening	11,002	9,957	11,939	4,140	**37,038**
BC Population Eligible for LC Screening, by Age Group	**35,323**	**25,268**	**21,264**	**9,050**	**90,905**
Proportion of the BC Population Eligible for LC Screening, by Age Group	**10.5%**	**8.6%**	**8.7%**	**5.2%**	**8.7%**

CD=current daily; FD(NO) = former (now occasional); FD(NN) = former daily (now non-)

Note that this estimate is lower than the Canadian average based on the Cancer Risk Management Model (CRMM). In a cost-effectiveness analysis using the CRMM, Goffin and colleagues estimated that 32% of 55-59 year-olds would be eligible for screening, decreasing to 30% for 60-64, 23% for 65-69 and 15% for 70-74.[274]

Modelling the Clinically Preventable Burden

In this section, we will calculate the CPB associated with screening for lung cancer in adults aged 55 to 74 years who have a 30 pack-year smoking history and currently smoke or have quit within the past 15 years, in a BC birth cohort of 40,000.

In modelling CPB, we made the following assumptions:

- Based on BC life tables for 2010 to 2012, a total of 8,909 deaths would be expected between the ages of 55-79 in a BC birth cohort of 40,000 (see Table 2). Routine screening occurs to age 74, but we have assumed the protective effect of routine screening continues to age 79.
- Based on BC vital statistics data, there were 5,117 deaths between the ages of 45 and 64 in BC in 2012, with 544 (10.6%) of these deaths due to lung cancer (ICD-10 codes C34). There were also 8,674 deaths between the ages of 65 and 79 that year, with 1,102 (12.7%) of these deaths due to lung cancer.[275] This suggests that 1,098 of the 8,909 (12.3%) of the deaths in the BC birth cohort between the ages of 55 and 79 would be due to lung cancer (see Table 2).

[274] Goffin JR, Flanagan WM, Miller AB et al. Cost-effectiveness of lung cancer screening in Canada. *JAMA Oncology*. 2015; 1(6): 807-13.
[275] British Columbia Vital Statistics Agency. *Selected Vital Statistics and Health Status Indicators: One Hundred and Forty-First Annual Report*. Apendix 2. 2012. British Columbia Ministry of Health. Available at https://www2.gov.bc.ca/assets/gov/birth-adoption-death-marriage-and-divorce/statistics-reports/annual-reports/2012/pdf/annual-report-2012.pdf. Accessed December 2017.

Table 2: Mortality Due to Lung Cancer Between the Ages of 55 and 79
in a British Columbia Birth Cohort of 40,000

Age Group	*Mean Survival Rate*		*Individuals in Birth Cohort*			*Life Years Lived*	*Deaths in Birth Cohort*		Deaths due to Lung Cancer		*Life Years Lost* Per Death	Total
	Males	Females	Males	Females	Total		%	#	%	#		
50-54	0.950	0.969	19,003	19,375	38,378	191,890						
55-59	0.931	0.956	18,619	19,118	37,737	188,686	1.7%	641	10.6%	68	27.7	1,882
60-64	0.902	0.936	18,041	18,726	36,767	183,834	2.6%	970	10.6%	103	23.4	2,407
65-69	0.858	0.906	17,164	18,113	35,277	176,387	4.2%	1,489	12.7%	189	19.2	3,632
70-74	0.792	0.857	15,837	17,144	32,981	164,903	7.0%	2,297	12.7%	292	15.3	4,463
75-79	0.693	0.780	13,861	15,608	29,469	147,346	11.9%	3,511	12.7%	446	11.8	5,262
								8,909	**12.3%**	**1,098**	**16.1**	**17,645**

- In the National Lung Cancer Screening Trial (NLST), 53,454 persons at high risk of lung cancer were randomly assigned to undergo three annual screenings (see Table 4, row *j*) with low-dose computed tomography (LDCT group) or single-view posteroanterior chest radiography (X-ray group). Mortality from lung cancer was reduced by 19.6% (RR of 0.804, 95% CI of 0.700 to 0.923) in the CT group (see Table 4, row *w*) compared to the X-ray group. Mortality from any cause was reduced by 6.1% (RR of 0.939, 95% CI of 0.884 to 0.998). Based on a nodule cut-off size of 4mm (to be identified as a positive screen), 24.2% of all screens in the CT group were positive (see Table 4, row *m*). Of these positive screens, 96.4% were false positives (see Table 4, row *o*).[276]
- Three smaller, low quality RCTs have found no significant reduction in either lung cancer or all-cause mortality associated with screening with LDCT versus usual care (RR of 1.42, 95% CI of 0.91 to 2.22).[277]
- Compared with usual care, screening with LDCT detects lung cancers at an earlier stage. With LDCT, 66% of lung cancers at detected at Stage I or II, versus 40% with usual care (see Table 3).[278,279]

Table 3: Stage of Lung Cancers: Screening with LDCT vs. Usual Care

	Usual Care Group		LDCT Group	
Stage	#	%	#	%
I or II	21	40.4%	83	65.9%
III or IV	31	59.6%	43	34.1%
Total	**52**	**100.0%**	**126**	**100.0%**

Source: Canadian Task Force on Preventive Health Care. Screening for Lung Cancer: Systematic Review and Meta-analysis. 2015.

[276] National Lung Screening Trial Research Team. Reduced lung-cancer mortality with low-dose computed tomographic screening. *New England Journal of Medicine*. 2011; 365(5): 395-409.
[277] Canadian Task Force on Preventive Health Care. *Screening for Lung Cancer: Systematic Review and Meta-analysis*. 2015. Available at http://canadiantaskforce.ca/files/lung-cancer-screening-systematic-reviewfinal-2.pdf. Accessed March 2016.
[278] Ibid.
[279] Field J, Duffy S, Baldwin D et al. UK Lung Cancer RCT Pilot Screening Trial: baseline findings from the screening arm provide evidence for the potential implementation of lung cancer screening. *Thorax*. 2016; 71: 161-70.

- To date, the uptake of lung cancer screening has been less than optimal, with just 6.0% of the eligible US population being screened in 2015 (see *Reference Document* for more details).[280] For modelling purposes we have assumed that screening rates of 60% (see Table 4, row *k*) would eventually be achieved, with sensitivity analysis using a range from 50-70%. The 60% is approximately half-way between current screening rates in BC for breast cancer (52%) and cervical cancer (69%) (see *Reference Document*).
- Screening with LDCT is also associated with a number of harms, including deaths following invasive follow-up testing, over diagnosis, major complications, false positive results and invasive procedures as a consequence of the false positive results.[281]
- **Death from follow-up testing** refers to "mortality that is the direct consequence of an invasive follow-up procedure (e.g., video-assisted thoracoscopic surgery, fine-needle aspiration biopsy or fine-needle aspiration cytology, thoracotomy, bronchoscopy, mediastinoscopy, surgical resection) initiated as a result of screening."[282] Based upon a review of seven studies, the CTFPHC found that 20 of 1,502 (1.33%) patients died as a result of follow-up testing after screening with LDCT (see Table 4, row *s*).
- "**Overdiagnosis** refers to the detection of a lung cancer that will not otherwise cause symptoms throughout the person's lifetime or result in death."[283] Based upon a review of four studies, the CTFPHC found an overdiagnosis rate of between 11.0% and 25.8%. The rate in the NLST was 11.0% (95% CI of 3.2% to 18.2%).
- **Major complications** are defined as "requiring hospitalization or medical intervention (e.g., hemothorax and pneumothorax requiring tube placement, lung collapse, severe pain, cardiac arrhythmias and thromboembolic complications) that are the direct result of an invasive procedure (e.g., video-assisted thoracoscopic surgery, fine-needle aspiration biopsy or fine-needle aspiration cytology, thoracotomy, bronchoscopy, mediastinoscopy, surgical resection) initiated as a result of screening."[284] Based upon a review of four studies, the CTFPHC found that 92 of 1,336 (1.33%) patients had major complications as a result of follow-up testing after screening with LDCT.
- "A **false positive** refers to a screening test result that indicates the presence of lung cancer, when in fact no lung malignancy exists."[285] Based upon a review of seven studies, the CTFPHC found that 8,290 of 42,774 (19.4%) individuals who underwent screening with LDCT received at least one false positive result.
- Minor (e.g., fine-needle aspiration biopsy or fine-needle aspiration cytology, thoracic or lymph node biopsy, bronchoscopy) and major (e.g., video-assisted thoracoscopic surgery, thoracotomy, surgical resection) **invasive procedures initiated as a result of false positive screening tests**. Based on a review of

[280] Huo J, Shen C, Volk R et al. Use of CT and chest radiography for lung cancer screening before and after publication of screening guidelines: intended and unintended uptake. *Journal of American Medical Association Internal Medicine*. 2017; 177(3): 439-41.
[281] Canadian Task Force on Preventive Health Care. *Screening for Lung Cancer: Systematic Review and Meta-analysis*. 2015. Available at http://canadiantaskforce.ca/files/lung-cancer-screening-systematic-reviewfinal-2.pdf. Accessed March 2016.
[282] Ibid.
[283] Ibid.
[284] Ibid.
[285] Ibid.

seven studies, the CTFPHC found that 0.72% (95% CI of 0.33% to 1.11%) of individuals with benign conditions underwent minor invasive procedures. Based on a further review of 17 studies, the CTFPHC found that 0.50% (95% CI of 0.37% to 0.63%) of individuals with benign conditions underwent major invasive procedures. [286]

- We have assumed a disutility of 0.05 associated with a false positive screen (see Table 4, row *q*).[287,288]
- Note that the NLTS (which the CTFPHC and our model follow) used a nodule cut-off size of 4mm (to be identified as a positive screen). Significant analysis has since been completed to assess the pros and cons of moving to a larger nodule cut-off size as well as developing more advanced algorithms to fine-tune screening frequency.
- Gierada and colleagues re-examined the NLST results based on results associated with different size nodules.[289] Moving the nodule cut-off size from 4mm to 5mm resulted in a 1.0% increase in missed or delayed lung cancer diagnosis but a 15.8% reduction in false positive results. With a cut-off of 8mm, there would have been a 10.5% increase in missed or delayed lung cancer diagnosis but a 65.8% reduction in false positive results.
- Henschke et al. tested the effect of moving the nodule cut-off size to between 6mm and 9mm on false positive results and potential delays in detecting lung cancers.[290] When alternative cut-offs of 6, 7, 8 and 9mm were used, the overall proportion of positive results declined to 10.2%, 7.1%, 5.1% and 4.8%. The use of these alternative cut-offs would have reduced the work-up load by 36%, 56%, 68% and 75% respectively. Concomitantly, a lung cancer diagnosis would have been delayed by at most 9 months in 0%, 5.0%, 5.9%, and 6.7% of cases of cancer.
- The Pan-Canadian Early Detection of Lung Cancer Study (PAN-CAN) developed a more sophisticated approach to ascertaining the probability of lung cancer in pulmonary nodules detected on first screening CT, based on a combination of nodule size, age, sex, family history of lung cancer, emphysema location, type and count of the nodule and spiculation.[291] Based on this approach, 80% of first screens placed patients in Category I (<1.5% lung cancer risk over the next 5.5 years), 12% in Category II (1.5% - <6% risk), 6% in Category 3 (6% - <30% risk) and 2% in Category IV (≥ 30% risk).[292]

[286] Canadian Task Force on Preventive Health Care. *Screening for Lung Cancer: Systematic Review and Meta-analysis*. 2015. Available at http://canadiantaskforce.ca/files/lung-cancer-screening-systematic-reviewfinal-2.pdf. Accessed March 2016.
[287] Black WC, Gareen IF, Soneji SS et al. Cost-effectiveness of CT screening in the National Lung Screening Trial. *New England Journal of Medicine*. 2014; 371(19): 1793-802.
[288] Gareen IF, Duan F, Greco EM, et al. Impact of lung cancer screening results on participant health-related quality of life and state anxiety in the National Lung Screening Trial. *Cancer*. 2014; November 1: 3401-09.
[289] Gierada DS, Pinsky P, Nath H et al. Projected outcomes using different nodule sizes to define a positive CT lung cancer screening examination. *Journal of the National Cancer Institute*. 2014; 106(11): dju284.
[290] Henschke CI, Yip R, Yankelevitz DF et al. Definition of a positive test result in computed tomography screening for lung cancer: a cohort study. *Annals of Internal Medicine*. 2013; 158(4): 246-52.
[291] McWilliams A, Tammemagi MC, Mayo JR et al. Probability of cancer in pulmonary nodules detected on first screening CT. *New England Journal of Medicine*. 2013; 369(10): 910-9.
[292] Tammemagi MC and Lam S. Screening for lung cancer using low dose computed tomography. *BMJ* 2014; 348: g2253-63.

- The PAN-CAN lung cancer risk model has been validated in at least two studies.[293,294] The results suggest that nodule size is still the most important predictor of lung cancer risk, with nodule spiculation, age and family history of lung cancer also being important predictive variables.
- The developers of the PAN-CAN lung cancer risk model suggest that patients in Category I require biennial screening, those in Category II require annual screening, those in Category III require rescreening in three months with annual screening thereafter if no growth in nodule size and those in Category IV should be referred for a definitive diagnosis.[295]
- A recent retrospective analysis of the NLST data suggests that annual screening might not be needed in individuals who have no abnormality identified on their initial screen and that a screening interval of at least two years could be considered on these individuals.[296,297]

Based on the above assumptions drawn from the NLST and the CTFPHC, the CPB is 1,745 quality-adjusted life years saved (see Table 4, row *z*). The CPB of 1,745 represents the gap between the existing coverage (no coverage) and 60%.

Table 4. Calculation of Clinically Preventable Burden (CPB) Estimate for Lung Cancer Screening in a Birth Cohort of 40,000

Row Label	Variable	Base Case	Data Source
a	Age 55-59: # of individuals alive in cohort	37,737	Table 2
b	Age 55-59: % of individuals eligible for screening	10.5%	Table 1
c	Age 60-64: # of individuals alive in cohort	36,767	Table 2
d	Age 60-64: % of individuals eligible for screening	8.6%	Table 1
e	Age 65-69: # of individuals alive in cohort	35,277	Table 2
f	Age 65-69: % of individuals eligible for screening	8.7%	Table 1
g	Age 70-74: # of individuals alive in cohort	32,981	Table 2
h	Age 70-74: % of individuals eligible for screening	5.2%	Table 1
i	# of individuals eligible for screening	2,977	= ((a * b)+ (c * d) + (e * f) + (g * h))/4
j	Average # of screens per eligible individual	3	√
k	Adherence with offers to receive screening	60.0%	√
l	Total # of screens in cohort	5,359	= i * j * k
m	Proportion of screens positive	24.2%	√
n	# of positive screens	1,297	= l * m
o	Proportion of screens false positive	96.4%	√
p	# of false positive screens	1,250	= n * o
q	QALYs lost per false positive test	0.05	√
r	QALYs lost due to false positive test	63	= p * q
s	Rate of death due to follow-up testing after screening	1.33%	√
t	'Unnecessary' deaths due to follow-up testing after screening	17	= p * s
u	Lung cancer deaths ages 55-79	1,098	Table 2
v	Remaining life expectancy at death from lung cancer (in years)	16.08	Table 2
w	Effectiveness of screening in reducing LC deaths	19.6%	√
x	LC deaths avoided due to LC screening	129	= u * w * k
y	Net deaths avoided due to LC screening	112	= x - t
z	Potential QALYs saved (CPB) - Utilization increasing from 0% to 60%	1,745	= (y * v)- r

√ = Estimates from the literature

[293] Winkler Wille MM, van Riel SJ, Saghir Z et al. Predictive Accuracy of the PanCan Lung Cancer Risk Prediction Model-External Validation based on CT from the Danish Lung Cancer Screening Trial. *European Radiology*. 2015; 25(10): 3093-9.

[294] Al-Ameri A, Malhotra P, Thygesen H et al. Risk of malignancy in pulmonary nodules: a validation study of four prediction models. *Lung Cancer*. 2015; 89(1): 27-30.

[295] Tammemagi MC and Lam S. Screening for lung cancer using low dose computed tomography. *BMJ* 2014; 348: g2253-63.

[296] Patz EF, Greco E, Gatsonis C et al. Lung cancer incidence and mortality in National Lung Screening Trial participants who underwent low-dose CT prevalence screening: a retrospective cohort analysis of a randomised, multicentre, diagnostic screening trial. *The Lancet Oncology*. 2016: Published online March 18, 2016.

[297] Field JK and Duffy SW. Lung cancer CT screening: is annual screening necessary? *The Lancet Oncology*. 2016: Published online March 18, 2016.

We also modified a number of major assumptions and recalculated the CPB as follows:

- Assume the estimated effectiveness of lung cancer screening in reducing deaths due to lung cancers is reduced from 19.6% to 7.7% (Table 4, row *w*): CPB = 485.
- Assume the estimated effectiveness of lung cancer screening in reducing deaths due to lung cancers is increased from 19.6% to 30.0% (Table 4, row *w*): CPB = 2,846.
- Assume the adherence rate is reduced from 60% to 50% (Table 4, row *k*): CPB = 1,454.
- Assume the adherence rate is increased from 60% to 70% (Table 4, row *k*): CPB = 2,036.

Modelling Cost-Effectiveness

In this section, we will calculate the CE associated with screening for lung cancer in adults aged 55 to 74 years who have a 30 pack-year smoking history and currently smoke or have quit within the past 15 years, in a BC birth cohort of 40,000.

In modelling CE, we made the following assumptions:

- **Assessment of patient risk** – There are an expected 37,737 individuals in a BC birth cohort of 40,000 who are expected to survive to age 55 (see Table 2). Each of the 37,737 survivors would undergo a one-time screen by their primary care practitioner to determine if they were eligible for lung cancer screening. We assumed that 85% of individuals would agree to this screening and varied this in the sensitivity analysis from 75% to 95% (see Table 6, row *c*).
- **Costs of screening** - We assumed an annual LDCT screening exam would cost $198 (2017 CAD) (see Table 6, row *i*).[298]
- **Physician visits** - LDCT screening results in an additional 14 physician visits per 100 persons screened (see Table 6, row *j*).[299]
- Positive findings on the screening CT result in the **ensuing follow-up procedures** (Table 5 rows *c* to *k*):[300]
    - Follow-up chest CT – 49.8%
    - Follow-up chest radiograph – 14.4%
    - Follow-up PET/CT scan – 8.3%
    - Percutaneous biopsy – 1.8%
    - Bronchoscopy without biopsy – 1.8%
    - Bronchoscopy with biopsy – 1.8%
    - Mediastinoscopy – 0.7%
    - Thoracoscopy – 1.3%
    - Thoracotomy – 2.9%

    By including all ensuing procedures following a positive screening CT result, we also include those procedures attributable to all identified harms, including deaths following invasive follow-up testing, overdiagnosis, major complications, false positive results and invasive procedures as a consequence of the false positive results.

[298] Cressman S, Lam S, Tammemagi MC et al. Resource Utilization and Costs during the Initial Years of Lung Cancer Screening with Computed Tomography in Canada. *Journal of Thoracic Oncology*. 2014; 9(10): 1449-58.
[299] Ibid.
[300] Goulart BH, Bensink ME, Mummy DG et al. Lung cancer screening with low-dose computed tomography: costs, national expenditures, and cost-effectiveness. *Journal of the National Comprehensive Cancer Network*. 2012; 10(2): 267-75.

- The **unit cost** of the ensuing follow-up procedures is as follows (Table 5, rows *u* to *ac*):[301]
    - Follow-up chest radiograph – $67
    - Follow-up chest CT – $164
    - Follow-up PET/CT scan – $1,399
    - Percutaneous biopsy – CT-guided = $1,083, US-guided = $682
    - Bronchoscopy without biopsy – $747
    - Bronchoscopy with biopsy – $804
    - Mediastinoscopy – $976
    - Thoracoscopy – $16,814
    - Thoracotomy – $18,689
- **Patient time and travel costs for follow-up procedures** – We assumed 2 hours of patient time for a follow-up chest radiograph or chest CT, and 7.5 hours of patient time for a PET/CT scan, percutaneous biopsy or bronchoscopy. For a mediastinoscopy or a thoracoscopy we assumed a hospital stay of 3 days plus 4 weeks recovery (see Table 5, rows *ae* to *am*).

Table 5. Calculation of Costs Associated with Follow-up Procedures

Row Label	Variable	Base Case	Data Source
a	Number of positive screens	1,297	Table 4, row n
b	Number of false positive screens	1,250	Table 4, row p
	Proportion of positive screens undergoing investigation		
c	Follow-up chest radiograph	14.4%	√
d	Follow-up chest CT	49.8%	√
e	Follow-up PET/CT scan	8.3%	√
f	Percutaneous biopsy	1.8%	√
g	Bronchoscopy without biopsy	1.8%	√
h	Bronchoscopy with biopsy	1.8%	√
i	Mediastinoscopy	0.7%	√
j	Thoracoscopy	1.3%	√
k	Thoracotomy	2.9%	√
	Number of procedures following a positive screen		
l	Follow-up chest CT	187	= a * c
m	Follow-up chest radiograph	646	= a * d
n	Follow-up PET/CT scan	108	= a * e
o	Percutaneous biopsy	23	= a * f
p	Bronchoscopy without biopsy	23	= a * g
q	Bronchoscopy with biopsy	23	= a * h
r	Mediastinoscopy	9	= a * i
s	Thoracoscopy	16	= a * j
t	Thoracotomy	36	= a * k
	Unit cost of procedures following a positive screen		
u	Follow-up chest radiograph	$67	√
v	Follow-up chest CT	$164	√
w	Follow-up PET/CT scan	$1,399	√
x	Percutaneous biopsy	$883	√
y	Bronchoscopy without biopsy	$747	√
z	Bronchoscopy with biopsy	$804	√
aa	Mediastinoscopy	$976	√
ab	Thoracoscopy	$16,814	√
ac	Thoracotomy	$18,689	√
ad	Follow-up costs of positive screens	**$1,283,108**	= l*u + m*v + n*w + o*x + p*y + q*z + r*aa + s*ab + t*ac
	Estimated patient time (in hours) per follow-up procedure		
ae	Follow-up chest CT	2.0	Assumed
af	Follow-up chest radiograph	2.0	Assumed
ag	Follow-up PET/CT scan	7.5	Assumed
ah	Percutaneous biopsy	7.5	Assumed
ai	Bronchoscopy without biopsy	7.5	Assumed
aj	Bronchoscopy with biopsy	7.5	Assumed
ak	Mediastinoscopy	7.5	Assumed
al	Thoracoscopy	172.5	Assumed
am	Thoracotomy	172.5	Assumed
an	Hours of patient time associated with positive screens	12,101	= l*ae + m*af + n*ag + o*ah + p*ai + q*aj + r*ak + s*al + t*am
ao	Value of patient time per hour	$29.69	√
ap	Total cost of patient time for follow-up procedures	**$359,290**	= ao * ap
aq	**Cost of follow-up procedures**	**$1,642,398**	= ad + ap

[301] Cressman S, Lam S, Tammemagi MC et al. Resource Utilization and Costs during the Initial Years of Lung Cancer Screening with Computed Tomography in Canada. *Journal of Thoracic Oncology*. 2014; 9(10): 1449-58.

- **Costs avoided due to early detection of lung cancers** – As noted in Table 3, screening with LDCT results in the earlier detection of lung cancers, thus potentially reducing the cost of treatment. Research by Cressman et al. suggests that the mean per person cost of treating stage I & II lung cancer is $34,267 (95% CI of $32,426 - $35,902).[302] This increases to $49,115 (95% CI of $44,451 - $53,645) for stage III & IV lung cancers. These costs include the diagnostic work-up, treatment and 2 years of follow-up. Based on the stage distribution noted in Table 3, the weighted cost would be $43,119 for the usual care group and $37,288 for the CT group, resulting in costs avoided of $5,831 per lung cancer associated with LDCT screening (see Table 6, row *n*).
- Other costs and assumptions used in assessing cost-effectiveness are detailed in the Reference Document.
- Discount rate of 1.5%, varied from 0% to 3% in the sensitivity analysis.

Based on these assumptions, the estimated cost per QALY would be $2,204 (see Table 6, row u).

Table 6. Summary of Cost Effectiveness (CE) Estimate for Lung Cancer Screening

Row Label	Variable	Base Case	Data Source
	Assessment of patient risk		
a	Proportion of cohort alive at age 55	94.3%	√
b	Total number of primary care provider screens (100% adherence)	37,737	= a * 40,000
c	Adherence with screening	85%	Assumed
d	Cost of 10-minute office visit	$34.85	Ref Doc
e	Value of patient time and travel for office visit	$59.38	Ref Doc
f	Portion of 10-minute office visit for screen	50%	Assumed
g	Cost of primary care provider screening	$1,511,290	=(b*c) * ((d+e) * f)
	Screening for Lung Cancer		
h	Potential screens with 60% adherence	5,359	=Table 4, row l
i	Cost per screen	$198	√
j	Additional physician visits per screening exam	0.14	√
k	Cost of screening	$1,131,712	=(i*h) + ((h*j) * (d+e))
l	Costs Asspociated with Follow-up Procedures	$1,642,398	=Table 5, row aq
m	Total Costs of Screening and Follow-up	$4,285,400	= g + k + l
	Costs Avoided		
n	Treatment costs avoided with earlier detection, per cancer	-$5,831	√
o	Number of incident lung cancers detected earlier	112	= Table 4, row y
p	Treatment costs avoided with earlier detection	-$655,691	= n * o
q	Net screening and patient costs (undiscounted)	$3,629,710	= m + p
r	QALYs saved (undiscounted)	1,745	Table 4, row z
s	Net screening and patient costs (1.5% discount)	$3,140,279	Calculated
t	QALYs saved (1.5% discount)	1,402	Calculated
u	**CE ($/QALY saved)**	$2,240	= s / t

√ = Estimates from the literature

[302] Cressman S, Lam S, Tammemagi MC et al. Resource Utilization and Costs during the Initial Years of Lung Cancer Screening with Computed Tomography in Canada. *Journal of Thoracic Oncology*. 2014; 9(10): 1449-58.

We also modified a number of major assumptions and recalculated the cost per QALY as follows:

- Assume the estimated effectiveness of lung cancer screening in reducing deaths due to lung cancers is reduced from 19.6% to 7.7% (Table 4, row *w*): CE = $9,026.
- Assume the estimated effectiveness of lung cancer screening in reducing deaths due to lung cancers is increased from 19.6% to 30.0% (Table 4, row *w*): CE = $1,228.
- Assume the adherence rate is reduced from 60% to 50% (Table 4, row *k*): CE = $2,425.
- Assume the adherence rate is increased from 60% to 70% (Table 4, row *k*): CE = $2,107.
- Assume the adherence rate with the assessment of patient risk is reduced from 85% to 75% (Table 6, row *c*): CE = $2,131.
- Assume the adherence rate with the assessment of patient risk is increased from 85% to 95% (Table 6, row *c*): CE = $2,349.
- Assume that the portion of a 10-minute office visit for the assessment of patient risk is reduced from 50% to 33% (Table 6, row *f*): CE = $1,924.
- Assume that the portion of a 10-minute office visit for the assessment of patient risk is increased from 50% to 67% (Table 6, row *f*): CE = $2,555.

Summary

Applying a 1.5% discount rate, the clinically preventable burden (CPB) associated with screening for lung cancer in adults aged 55 to 74 years who have a 30 pack-year smoking history and currently smoke or have quit within the past 15 years is estimated to be 1,402 quality-adjusted life years (QALYs) while the cost-effectiveness (CE) is estimated to be $2,240 per QALY (see Table 7).

Table 7: Lung Cancer Screening Being Offered to a Birth Cohort of 40,000 Between the Ages of 55 and 74

Summary

	Base Case	Range	
CPB (Potential QALYs Gained)			
Gap between B.C. Current (0%) and 'Best in the World' (60%)			
1.5% Discount Rate	**1,402**	390	2,287
3% Discount Rate	1,303	362	2,125
0% Discount Rate	1,745	485	2,846
CE ($/QALY) **including** patient time costs			
1.5% Discount Rate	**$2,240**	$1,228	$9,206
3% Discount Rate	$2,296	$1,261	$9,239
0% Discount Rate	$2,080	$1,135	$8,419
CE ($/QALY) **excluding** patient time costs			
1.5% Discount Rate	$1,408	$718	$6,035
3% Discount Rate	$1,445	$739	$6,180
0% Discount Rate	$1,303	$658	$5,625

Hypertension Screening and Treatment

United States Preventive Services Task Force Recommendations (2015)

The USPSTF recommends screening for high blood pressure in adults age 18 years and older. (A recommendation).

The USPSTF recommends obtaining measurements outside of the clinical setting for diagnostic confirmation before starting treatment.[303]

Canadian Task Force on Preventive Health Care Recommendations (2012)

We recommend blood pressure measurement at all appropriate primary care visits… (in) adults aged 18 years and older without previously diagnosed hypertension for the purpose of screening for hypertension . (Strong recommendation; moderate quality evidence)

We recommend that blood pressure be measured according to the current techniques described in the Canadian Hypertension Education Program (CHEP) recommendations for office and out-of-office (ambulatory) blood pressure measurement). (Strong recommendation; moderate quality evidence)

For people who are found to have an elevated blood pressure during screening, the CHEP criteria for assessment and diagnosis of hypertension should be applied to determine whether the patient meets diagnostic criteria for hypertension. (Strong recommendation; moderate quality evidence)[304]

Modelling the Clinically Preventable Burden

In this section, we will calculate the CPB associated with screening for and treatment of hypertension in adults aged 18 and older in a BC birth cohort of 40,000.

In modelling CPB, we made the following assumptions:

- Based on BC life tables for 2010 to 2012, there are a total of 2,436,832 life years lived and 15,233 deaths between the ages of 18 and 84 in a BC birth cohort of 40,000 (see Table 1).
- Based on BC vital statistics data, 59 of 993 (5.9%) deaths in 25-44 year olds in 2011 were due to **cardiovascular disease** (ICD-10 codes I00-I51). In 45-64 year olds, 601 of 5,076 (11.8%) deaths were due to cardiovascular disease. In 65-84 year olds, 2,248 of 13,481 (16.7%) deaths were due to cardiovascular disease.[305]
- Congestive heart failure deaths (ICD-10 codes I50) are a subset of cardiovascular disease (ICD-10 codes I50). In 2011, 23 of the 5,076 (0.45%) deaths in 45-64 year olds was due to CHF. In 65-79 year olds, 88 of 8,600 (1.02%) deaths were due to

[303] Siu A on behalf of the U.S. Preventive Services Task Force. Screening for high blood pressure in adults: U.S. Preventive Services Task Force Recommendation Statement. *Annals of Internal Medicine*. 2015; 163(10): 778-86.
[304] Canadian Task Force on Preventive Health Care. *Recommendations on screening for high blood pressure in Canadian Adults*. 2012. Available at http://canadiantaskforce.ca/wp-content/uploads/2012/10/CTFPHC-hypertension-recommendations-final-reformat.pdf?0136ff. Accessed November 2013.
[305] British Columbia Vital Statistics Agency. *Selected Vital Statistics and Health Status Indicators: One Hundred and Fortieth Annual Report*. 2011. British Columbia Ministry of Health. Available at http://www2.gov.bc.ca/assets/gov/birth-adoption-death-marriage-and-divorce/statistics-reports/annual-reports/2011/pdf/ann2011.pdf. Accessed January 2017.

CHF. In the population ages 80 and older, 596 of 16,612 (3.59%) deaths were due to CHF. [306]

- Based on BC vital statistics data, 31 of 993 (3.1%) deaths in 25-44 year olds in 2011 were due to **cerebrovascular disease** (ICD-10 codes I60-I69). In 45-64 year olds, 191 of 5,076 (3.8%) deaths were due to cerebrovascular disease. In 65-84 year olds, 905 of 13,481 (6.7%) deaths were due to cerebrovascular disease.[307]
- This data was used to estimate that approximately 2,092 (13.7%) of the 15,233 deaths in the birth cohort would be due to cardiovascular disease (excluding deaths due to CHF), 266 (1.74%) due to CHF and 929 (6.1%) due to cerebrovascular disease (see Table 1)

Table 1: Deaths and Years of Life Lived and Lost Between the Ages of 18 and 84
in a British Columbia Birth Cohort of 40,000

						Deaths due to									*Life Years Lost*			
Age Group	*Mean Survival Rate*	*Individuals in Birth Cohort*	*Life Years Lived*	*Deaths in Birth Cohort* %	*Deaths in Birth Cohort* #	Cardiovascular Disease %	Cardiovascular Disease #	Congestive Heart Failure %	Congestive Heart Failure #	Cardiovascular Disease (excl CHF) %	Cardiovascular Disease (excl CHF) #	Cerebrovascular Disease %	Cerebrovascular Disease #	Life Expectancy	All Deaths	Cardio	CHF	Cerebro
18-19	0.994	39,744	79,488	0.1%	40	5.9%	2	0.0%	0	5.9%	2	3.1%	1	63.7	2,548	150	0	79
20-24	0.992	39,682	198,408	0.2%	62	5.9%	4	0.0%	0	5.9%	4	3.1%	2	60.8	3,794	224	0	118
25-29	0.989	39,570	197,850	0.3%	112	5.9%	7	0.0%	0	5.9%	7	3.1%	3	56.0	6,250	369	0	194
30-34	0.986	39,458	197,290	0.3%	112	5.9%	7	0.0%	0	5.9%	7	3.1%	3	51.1	5,723	338	0	177
35-39	0.983	39,310	196,550	0.4%	148	5.9%	9	0.0%	0	5.9%	9	3.1%	5	46.3	6,852	404	0	212
40-44	0.978	39,105	195,526	0.5%	205	5.9%	12	0.0%	0	5.9%	12	3.1%	6	41.5	8,499	501	0	263
45-49	0.970	38,814	194,070	0.8%	291	11.8%	34	0.45%	1	11.4%	33	3.8%	11	36.8	10,716	1,216	48	407
50-54	0.960	38,390	191,948	1.1%	424	11.8%	50	0.45%	2	11.4%	48	3.8%	16	32.2	13,666	1,551	61	519
55-59	0.944	37,757	188,786	1.7%	632	11.8%	75	0.45%	3	11.4%	72	3.8%	24	27.7	17,517	1,988	79	666
60-64	0.920	36,800	183,998	2.6%	958	11.8%	113	0.45%	4	11.4%	109	3.8%	36	23.4	22,408	2,543	101	851
65-69	0.883	35,332	176,658	4.2%	1,468	16.7%	245	1.02%	15	15.7%	230	6.7%	98	19.2	28,186	4,420	287	1,888
70-74	0.827	33,072	165,362	6.8%	2,259	16.7%	377	1.02%	23	15.7%	354	6.7%	151	15.3	34,566	5,420	353	2,316
75-79	0.741	29,628	148,142	11.6%	3,444	16.7%	575	1.02%	35	15.7%	540	6.7%	231	11.8	40,639	6,372	415	2,723
80-84	0.614	24,551	122,756	20.7%	5,077	16.7%	848	3.59%	182	13.1%	666	6.7%	340	8.7	44,172	5,791	1,586	2,959
Total			**2,436,832**		**15,233**	**15.5%**	**2,358**	**1.74%**	**266**	**13.7%**	**2,092**	**6.1%**	**929**		**245,536**	**31,288**	**2,930**	**13,374**

- An estimated 38.5% (Table 2, row *l*) of cerebrovascular deaths, 24.6% (Table 2, row *j*) of cardiovascular deaths and 33.0% (Table 2, row *k*) of CHF deaths are attributable to hypertension.[308]
- In a meta-analysis of 147 randomized trials, Law and colleagues found that lowering blood pressure by 10/5 mm Hg (the equivalent of taking one drug at a standard dose) resulted in a 22% (95% CI of 17% to 27%) (Table 2, rows *q* & *r*) reduction in cardiovascular events and a 41% (95% CI of 33% to 48%) (Table 2, row *s*) reduction in cerebrovascular events.[309]
- Other assumptions used in assessing the clinically preventable burden are detailed in the Reference Document.

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[306] British Columbia Vital Statistics Agency. *Selected Vital Statistics and Health Status Indicators: One Hundred and Fortieth Annual Report*. 2011. British Columbia Ministry of Health. Available at http://www2.gov.bc.ca/assets/gov/birth-adoption-death-marriage-and-divorce/statistics-reports/annual-reports/2011/pdf/ann2011.pdf. Accessed January 2017.

[307] Ibid.

[308] Maciosek M, Edwards N, Nelson W, et al. *Hypertension Screening: Technical Report Prepared for the National Commission on Prevention Priorities.* HealthPartners Research Foundation and Partnership for Prevention. 2008. Available online at http://prevent.org/data/files/initiatives/hypertension_screening_and_treatment.pdf. Accessed February 2018.

[309] Law M, Morris J, Wald N. Use of blood pressure lowering drugs in the prevention of cardiovascular disease: meta-analysis of 147 randomised trials in the context of expectations from prospective epidemiological studies. *British Medical Journal*. 2009; 338: 1665f.

Based on these assumptions, the CPB associated with screening for and treatment of hypertension in adults aged 18 and older is 11,587 QALYs saved (Table 2, row *az*). The CPB of 11,587 QALYs saved represents the gap between no coverage and the 'best in the world' coverage estimated at 73%.

We also modified several major assumptions and recalculated the CPB as follows:

- Assume that the proportion of the population with hypertension receiving drug treatment is decreased from 73% to 68% (Table 2, row *p*): CPB =10,523.
- Assume that the proportion of the population with hypertension receiving drug treatment is increased from 73% to 78% (Table 2, row *p*): CPB =12,707.
- Assume that the effectiveness of drug treatment in reducing cardiovascular disease events is decreased from 22% to 17% (Table 2, rows *q & r*) and the effectiveness of drug treatment in reducing cerebrovascular disease events is decreased from 41% to 33% (Table 2, row *s*): CPB =8,199.
- Assume that the effectiveness of drug treatment in reducing cardiovascular disease events is increased from 22% to 29% (Table 2, rows *q & r*) and the effectiveness of drug treatment in reducing cerebrovascular disease events is increased from 41% to 48% (Table 2, row *s*): CPB =15,792.
- Assume that the disutility associated with living with a nonfatal cerebrovascular event is reduced from 0.264 to 0.177 (Table 2, row *al*): CPB =11,019.
- Assume that the disutility associated with living with a nonfatal cerebrovascular event is increased from 0.264 to 0.350 (Table 2, row *al*): CPB 12,146.
- Assume that the disutility associated with taking pills for cardiovascular prevention is reduced from 0.0032 to 0.0 (Table 2, row *ax*): CPB =13,128.
- Assume that the disutility associated with taking pills for cardiovascular prevention is increased from 0.0032 to 0.0044 (Table 2, row *ax*): CPB =11,009.

Table 2: Summary of Clinically Preventable Burden Estimate for Hypertension in a Birth Cohort of 40,000 (B.C.)			
Row	**Variable**	**Base Case**	**Data Source**
	Estimated Current Status - Mortality		
a	Total CHD (excluding CHF) mortality in the birth cohort	2,092	Table 1
b	Total CHF mortality in the birth cohort	266	Table 1
c	Total stroke mortality in the birth cohort	929	Table 1
d	Life years lost per CHD death	15.0	Table 1
e	Life years lost per CHF death	11.0	Table 1
f	Life years lost per stroke death	14.4	Table 1
g	Total life years lost due to CHD death	31,288	= a * d
h	Total life years lost due to CHF death	2,930	= b * e
i	Total life years lost due to stroke death	13,374	= c * f
j	% CHD mortality attributable to hypertension	24.6%	√
k	% CHF mortality attributable to hypertension	33.0%	√
l	% stroke mortality attributable to hypertension	38.5%	√
m	Total CHD mortality in the birth cohort attributable to hypertension	515	= a * j
n	Total CHF mortality in the birth cohort attributable to hypertension	88	= b * k
o	Total stroke mortality in the birth cohort attributable to hypertension	358	= c * l
p	% with hypertension receiving drug treatment	73%	Ref Doc
q	Effectiveness of drug treatment on CHD deaths	22%	√
r	Effectiveness of drug treatment on CHF deaths	22%	√
s	Effectiveness of drug treatment on stroke deaths	41%	√
	Estimates in the Absence of Screening / Treatment		
	Mortality attributable to hypertension		
t	Predicted hypertension-attributable CHD deaths in absence of screening	613	= m / (1 - (p * q))
u	Predicted hypertension-attributable CHF deaths in absence of screening	104	= n / (1 - (p * r))
v	Predicted hypertension-attributable stroke deaths in absence of screening	511	= o / (1 - (p * s))
w	Predicted hypertension-attributable CHD life years lost in absence of screening	9,169	= t * d
x	Predicted hypertension-attributable CHF life years lost in absence of screening	1,152	= u * e
y	Predicted hypertension-attributable stroke life years lost in absence of screening	7,348	= v * f
	Life years lost due to total deaths	**17,670**	= w + x + y
	Morbidity attributable to hypertension		
z	Ratio of nonfatal cardiovascular events per fatal event	5.09	See Ref Doc
aa	# of nonfatal cardiovascular events	3,652	= (t + u) * z
ab	Average age of individual with a cardiovascular event	68.0	See Ref Doc
ac	Life years lived with a nonfatal cardiovascular event	12.1	See Ref Doc
ad	Life years lost due to a nonfatal cardiovascular event	6.3	See Ref Doc
ae	QoL reduction living with a nonfatal cardiovascular event (for 1 month)	0.125	See Ref Doc
af	**QALYs lost due to nonfatal cardiovascular events**	**23,047**	= aa * (ad + (ae / 12))
ag	Ratio of nonfatal cerebrovascular events per fatal event	4.58	See Ref Doc
ah	# of nonfatal cerebrovascular events	2,339	v * ag
ai	Average age of individual with a cerebrovascular event	72.8	See Ref Doc
aj	Life years lived with a nonfatal cerebrovascular event	9.3	See Ref Doc
ak	Life years lost due to a nonfatal cerebrovascular event	5.5	See Ref Doc
al	QoL reduction living with a nonfatal cerebrovascular event	0.264	See Ref Doc
am	**QALYs lost due to nonfatal cerebrovascular events**	**18,608**	= ah * (ak + (aj * al))
	***Benefits* if 73% of individuals with hypertension are on drug treatment**		
ao	Number of CHD deaths prevented	98	= t * p * q
ap	Number of CHF deaths prevented	17	=u * p * r
aq	Number of stroke deaths prevented	153	=v * p * s
ar	Number of life years saved from CHD death prevented	1,473	= w * p * q
as	Number of life years saved from CHF death prevented	185	=x * p * r
at	Number of life years saved from stroke death prevented	2,199	=y * p * s
au	Total years of live saved from deaths prevented	**3,857**	= ar + as + at
av	QALY saved from prevented nonfatal cardiovascular disease events	**3,701**	= af * p * q
aw	QALY saved from prevented nonfatal cerebrovascular disease events	**5,569**	= am * p * s
	***Harms* if 73% of individuals with hypertension are on drug treatment**		
ax	Disutility per year associated with taking pills for cardiovascular prevention	-0.0032	See Ref Doc
ay	**Disutility associated with taking pills for cardiovascular prevention**	**-1,541**	=p * Table 4, row b * ax
az	**Potential QALYs gained, screening and intervention from 0% to 73%**	**11,587**	=au + av + aw + ay

√ = Estimates from the literature

Modelling Cost-Effectiveness

In this section, we will calculate the CE associated with screening for and treatment of hypertension in adults aged 18 and older in a BC birth cohort of 40,000.

In modelling CE, we made the following assumptions:

- The proportion of the population with diagnosed hypertension is based on data provided by the BC Ministry of Health, Chronic Disease Management for fiscal 2002/03 (Table 3).[310]

Table 3: Years Lived with Hypertension in a Birth Cohort of 40,000

Age Group	% Hypertensive	*Life Years Lived*	*Life Years Lived with hypertension*
18-19	0.7%	79,488	544
20-24	1.5%	198,408	2,921
25-29	2.6%	197,850	5,166
30-34	4.0%	197,290	7,821
35-39	6.3%	196,550	12,359
40-44	10.7%	195,526	20,869
45-49	17.4%	194,070	33,803
50-54	26.3%	191,948	50,529
55-59	35.4%	188,786	66,816
60-64	43.9%	183,998	80,713
65-69	52.1%	176,658	92,077
70-74	59.6%	165,362	98,560
75-79	68.2%	148,142	101,101
80-84	75.3%	122,756	92,490
Total		**2,436,832**	**665,769**
	% of years lived with hypertension		27.3%

- **Costs of laboratory tests** - The costs per diagnostic test (Table 4, rows *h* to *o*) are based on information from the BC Medical Services Plan 2016/17 payment analysis.[311]
- **Average annual cost of antihypertensive medication** – Calculated based on an estimated average cost per day of treatment for antihypertensive medication in Canada of $0.53 (Table 4, row *p*).[312]
- Other costs and assumptions used in assessing cost-effectiveness are detailed in the Reference Document.
- Discount rate of 1.5%, varied from 0% to 3% in the sensitivity analysis.

Based on these assumptions, the CE associated with universal screening for and treatment of hypertension in adults aged 18 and older is $15,254 / QALY (Table 4, row *av*).

[310] BC Ministry of Health. *Chronic Disease Management - Reports and Research.* Available online at http://www.health.gov.bc.ca/library/publications/year/2003/cdm/cdm_cases_age_02-03.pdf. Accessed February 2018.
[311] Medical Services Plan. *MSP Fee-For-Service Payment Analysis: 2012/13 to 2016/17.* Available at https://www2.gov.bc.ca/assets/gov/health/practitioner-pro/medical-services-plan/ffs_complete.pdf. Accessed February 2018.
[312] Centre for Health Services and Policy Research. *The Canadian Rx Atlas: Third Edition*. 2013. Available at http://www.chspr.ubc.ca/sites/default/files/file_upload/publications/2013/RxAtlas/canadianrxatlas2013.pdf. Accessed February 2018.

Table 4: Summary of Cost-effectiveness Estimate for Hypertension in a Birth Cohort of 40,000 (B.C.)			
Row	**Variable**	**Base Case**	**Data Source**
a	Years of life in target population age range	2,436,832	Table 1
b	Years of life lived with hypertension in target population age range	665,769	Table 3
c	Portion of years eligible for screening	1,771,063	= a - b
	Costs of screening, lab monitoring and antihypertensive therapy		
d	Cost of patient time and travel for office visit	$59.38	Ref Doc
e	Cost of office visit	$34.85	Ref Doc
f	Portion of 10 minute office visit used for screen	50%	Ref Doc
g	Portion of 10 minute office visit used for monitoring	50%	Ref Doc
h	12-lead ECG	$24.05	√
i	Urinalysis	$7.42	√
j	Blood glucose	$1.25	√
k	Hematocrit	$3.22	√
l	Serum potassium	$1.04	√
m	Creatinine	$1.52	√
n	Calcium	$1.11	√
o	Lipid profile	$6.87	√
p	Total costs for monitoring tests	$46.48	= h + i + j + k + l + m + n + o
q	Average annual cost of antihypertensive, given current market share and adherence	$193.45	√
r	Average number of recommended hypertension **screening** tests per person year without diagnosis of hypertension	0.5	Ref Doc
t	Average number of recommended hypertension **monitoring** tests per person year of treatment	2.0	Assumed
u	Adherence with screening	79%	Ref Doc
v	Adherence with treatment	73%	Ref Doc
w	Lifetime screening costs	$32,960,236	= (c * u * r) * ((d + e) * f)
x	Lifetime non-screening monitoring costs	$90,976,462	= (b * v * t) * (p + ((d + e) * g))
y	Lifetime anti-hypertensive therapy costs	$94,018,893	= b* q * v
	Estimated costs avoided due to intervention		
z	Acute care costs avoided per avoided cardiovascular death	$15,536	Ref Doc
aa	Acute care costs avoided per avoided cerebrovascular death	$9,583	Ref Doc
ab	Costs avoided due to deaths avoided	**$1,725,327**	= Table 2, row ao + (Table 2, row ap * z) + (Table 2, row aq * aa)
ac	First year costs avoided per nonfatal cardiovascular event avoided	$33,934	Ref Doc
ad	First year costs avoided per nonfatal cerebrovascular event avoided	$21,139	Ref Doc
ae	# of **cardiovascular** events avoided	587	= Table 2, row aa * Table 2, row p * Table 2, row q
af	First-year acute care costs avoided / event	$33,934	Ref Doc
ag	Post-first-year annual costs avoided per nonfatal cardiovascular events avoided	$2,278	Ref Doc
ah	Number of years for which the costs are avoided	12.1	Ref Doc
ai	Total costs avoided for nonfatal cardiovascular events avoided	$36,071,383	= ae * (af + (ag * ah))
aj	# of **cerebrovascular** events avoided	700	= Table 2, row ah * Table 2, row p * Table 2, row s
ak	First-year acute care costs avoided / event	$21,139	Ref Doc
al	Post-first-year annual costs avoided per nonfatal cerebrovascular events avoided	$6,246	Ref Doc
am	Number of years for which the costs are avoided	9.3	Ref Doc
an	Post-first-year costs avoided for nonfatal cerebrovascular events avoided	$55,453,391	= aj * (ak + (al * am))
ao	**Costs avoided due to intervention**	**$93,250,100**	=ab + ai + an
	Cost-effectiveness Calculation		
ap	Cost of intervention over lifetime of birth cohort	$217,955,592	= w + x + y
aq	Costs avoided due to intervention over lifetime of birth cohort	$93,250,100	ao
ar	QALYs saved	11,587	= Table 2, row az
as	Cost of intervention over lifetime of birth cohort (1.5% discount)	$140,544,975	Calculated
at	Costs avoided due to intervention over lifetime of birth cohort (1.5% discount)	$48,541,462	Calculated
au	QALYs saved (1.5% discount)	6,032	Calculated
av	**CE ($/QALY saved)**	$15,254	= (as - at) / au

√ = Estimates from the literature

We also modified several major assumptions and recalculated the CE as follows:

- Assume that the proportion of the population with hypertension receiving drug treatment is decreased from 73% to 68% (Table 2, row *p*): CE = $17,584.
- Assume that the proportion of the population with hypertension receiving drug treatment is increased from 73% to 78% (Table 2, row *p*): CE = $13,219.
- Assume that the effectiveness of drug treatment in reducing cardiovascular disease events is decreased from 22% to 17% (Table 2, rows *q & r*) and the effectiveness of drug treatment in reducing cerebrovascular disease events is decreased from 41% to 33% (Table 2, row *s*): CE = $24,485.
- Assume that the effectiveness of drug treatment in reducing cardiovascular disease events is increased from 22% to 29% (Table 2, rows *q & r*) and the effectiveness of drug treatment in reducing cerebrovascular disease events is increased from 41% to 48% (Table 2, row *s*): CE = $9,314.
- Assume that the disutility associated with living with a nonfatal cerebrovascular event is reduced from 0.264 to 0.177 (Table 2, row *al*): CE = $16,036.
- Assume that the disutility associated with living with a nonfatal cerebrovascular event is increased from 0.264 to 0.350 (Table 2, row *al*): CE = $14,549.
- Assume that the disutility associated with taking pills for cardiovascular prevention is reduced from 0.0032 to 0.0 (Table 2, row *ax*): CE = $13,461.
- Assume that the disutility associated with taking pills for cardiovascular prevention is increased from 0.0032 to 0.0044 (Table 2, row *ax*): CE = $16,051.
- Assume that the portion of a 10-minute office visit for screening and/or monitoring is reduced from 50% to 33% (Table 4, rows *f & g*): CE = $12,388.
- Assume that the portion of a 10-minute office visit for screening and/or monitoring is increased from 50% to 67% (Table 4, rows *f & g*): CE = $18,114.

Summary

Applying a 1.5% discount rate, the clinically preventable burden (CPB) associated with universal screening for and treatment of hypertension in adults aged 18 and older is estimated to be 6,032 quality-adjusted life years (QALYs) while the cost-effectiveness (CE) is estimated to be $15,254 per QALY (see Table 5).

Table 5: Screening and Treatment for Hypertension Being Offered to a Birth Cohort of 40,000 Starting at Age 18

Summary

	Base Case	Range	
CPB (Potential QALYs Gained)			
Gap between no current service 'Best in the World' of 73%			
1.5% Discount Rate	**6,032**	4,268	8,220
3% Discount Rate	3,088	2,185	4,208
0% Discount Rate	11,587	8,199	15,792
CE ($/QALY) **including** patient time costs			
1.5% Discount Rate	**$15,254**	$9,314	$24,485
3% Discount Rate	$22,850	$14,890	$35,244
0% Discount Rate	$10,760	$6,019	$18,139
CE ($/QALY) **excluding** patient time costs			
1.5% Discount Rate	$9,945	$5,421	$16,987
3% Discount Rate	$15,814	$9,727	$25,281
0% Discount Rate	$6,476	$2,876	$12,086

Screening for Cardiovascular Disease Risk and Treatment with Statins

United States Preventive Services Task Force Recommendations (2016)

> *The USPSTF recommends initiating use of low- to moderate-dose statins in adults aged 40 to 75 years without a history of CVD who have 1 or more CVD risk factors (dyslipidemia, diabetes, hypertension, or smoking) and a calculated 10-year CVD event risk of 10% or greater. (B recommendation)*
>
> *Identification of dyslipidemia and calculation of 10-year CVD event risk requires universal lipids screening in adults aged 40-74 years.*
>
> *The USPSTF recommends using the ACC/AHA Pooled Cohort Equations to calculate the 10-year risk of CVD events. The calculator derived from these equations takes into account age, sex, race, cholesterol levels, blood pressure level, antihypertension treatment, presence of diabetes, and smoking status as risk factors.* [313]

The CTFPHC has not completed a recent update due to the review completed by the Canadian Cardiovascular Society (CCS) in 2016.[314] A number of the CCS recommendations, particularly those associated with screening and primary prevention, are highlighted below.

Canadian Cardiovascular Society (2016)

> ***Screening***
> *We recommend that a CV risk assessment be completed every 5 years for men and women aged 40 to 75 years using the modified FRS (Framingham Heart Study Risk Score) or CLEM (Cardiovascular Life Expectancy Model) to guide therapy to reduce major CV events. A risk assessment might also be completed whenever a patient's expected risk status changes. (Strong Recommendation; High Quality Evidence).*
>
> ***Primary Prevention***
> *We recommend management that does not include statin therapy for individuals at low risk (modified FRS < 10%) to decrease the risk of CVD events. (Strong Recommendation; High-Quality Evidence).*
>
> *We recommend management that includes statin therapy for individuals at high risk (modified FRS ≥ 20%) to decrease the risk of CVD events. (Strong Recommendation; High-Quality Evidence).*
>
> *We recommend management that includes statin therapy for individuals at IR (intermediate risk: modified FRS 10%-19%) with LDL-C ≥ 3.5 mmol/L to decrease the risk of CVD events. Statin therapy should also be considered for IR persons with LDL-C < 3.5 mmol/L but with apoB ≥ 1.2 g/L or non-HDL-C ≥ 4.3 mmol/L or in men 50 years of age and older and women 60 years of age and older with ≥ 1 CV risk factor. (Strong Recommendation; High-Quality Evidence).* [315]

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[313] Bibbins-Domingo K, Grossman D, Curry S et al. Statin use for the primary prevention of cardiovascular disease in adults: US Preventive Services Task Force recommendation statement. *Journal of the American Medical Association*. 2016; 316(19): 1997-2007.

[314] Dr. Richard Birtwhistle, Member, Canadian Task Force on Preventive Health Care. Personal communication, January 25, 2017.

[315] Anderson T, Gregiore J, Pearson G et al. 2016 Canadian Cardiovascular Society guidelines for the management of dyslipidemia for the prevention of cardiovascular disease in then adult. *Canadian Journal of Cardiology.* 2016; 32: 1263-82.

Modelling the Clinically Preventable Burden

In this section, we will calculate the CPB and CE associated with universal screening for and initiating use of low- to moderate-dose statins in adults aged 40 to 75 years without a history of CVD, who have 1 or more CVD risk factors, and a calculated 10-year CVD event risk of 10% or greater.

In estimating CPB, we made the following assumptions:

- Based on BC life tables for 2010 to 2012, there are a total of 1,296,348 life years lived and 6,238 deaths between the ages of 40 and 74 in a BC birth cohort of 40,000 (see Table 1).

Table 1: Deaths and Years of Life Lived and Lost Between the Ages of 40 and 74
in a British Columbia Birth Cohort of 40,000

Age Group	*Mean Survival Rate*	*Individuals in Birth Cohort*	*Life Years Lived*	*Deaths in Birth Cohort*		*Deaths due to* Cardiovascular Disease		*Deaths due to* Cerebrovascular Disease		Life Expectancy	*Life Years Lost* All Deaths	Cardio	Cerebro
				%	#	%	#	%	#				
35-39	0.983	39,310											
40-44	0.978	39,105	195,526	0.5%	205	5.9%	12	3.1%	6	41.5	8,499	501	263
45-49	0.970	38,814	194,070	0.8%	291	11.8%	34	3.8%	11	36.8	10,716	1,265	407
50-54	0.960	38,390	191,948	1.1%	424	11.8%	50	3.8%	16	32.2	13,666	1,613	519
55-59	0.944	37,757	188,786	1.7%	632	11.8%	75	3.8%	24	27.7	17,517	2,067	666
60-64	0.920	36,800	183,998	2.6%	958	11.8%	113	3.8%	36	23.4	22,408	2,644	851
65-69	0.883	35,332	176,658	4.2%	1,468	16.7%	245	6.7%	98	19.2	28,186	4,707	1,888
70-74	0.827	33,072	165,362	6.8%	2,259	16.7%	377	6.7%	151	15.3	34,566	5,772	2,316
Total			**1,296,348**		**6,238**	**14.5%**	**907**	**5.5%**	**344**		**135,558**	**18,569**	**6,911**

- Based on BC vital statistics data, 59 of 993 (5.9%) deaths in 25-44 year olds in 2011 were due to cardiovascular disease (ICD-10 codes I00-I51) and 31 of 993 (3.1%) deaths were due to cerebrovascular disease (ICD-10 codes I60-I69). In 45-64 year olds, 601 of 5,076 (11.8%) deaths were due to cardiovascular disease, and 191 of 5,076 (3.8%) deaths were due to cerebrovascular disease. In 65-84 year olds, 2,248 of 13,481 (16.7%) deaths were due to cardiovascular disease while 905 of 13,481 (6.7%) deaths were due to cerebrovascular disease.[316] This data was used to estimate that approximately 907 (14.5%) of the 6,238 deaths in the birth cohort would be due to cardiovascular disease and 344 (5.5%) due to cerebrovascular disease (see Table 1 and Table 3, rows *f, g, h* & *i*).
- We are not aware of any information which indicates the proportion of adults aged 40 to 74 years in BC who have had a cardiovascular risk assessment within the past five years. Nor are we aware of BC-specific data on the proportion of adults at intermediate or higher risk of CVD who are taking statins over the longer term for primary prevention purposes. Research suggests that 54.8% of Canadians between the ages of 40 and 79 are at low risk (defined as a mean 10-year risk of a CVD event of less than 10%), 14.4% are at intermediate risk (mean 10-year risk of a CVD event of 10%-19%) and 30.9% are at high risk (mean 10-year risk of a CVD event of ≥20%)[317] (see Table 2 below and Table 3, row *b*).

[316] British Columbia Vital Statistics Agency. *Selected Vital Statistics and Health Status Indicators: One Hundred and Fortieth Annual Report*. 2011. British Columbia Ministry of Health. Available at http://www2.gov.bc.ca/assets/gov/birth-adoption-death-marriage-and-divorce/statistics-reports/annual-reports/2011/pdf/ann2011.pdf. Accessed January 2017.

[317] Hennessy D, Tanuseputro P, Tuna M et al. Population health impact of statin treatment in Canada. *Health Reports*. 2016; 27(1): 20-8.

Table 2: Estimated Number of Canadian Adults Ages 40-79 By CVD Risk Status, 2007 to 2011							
Age Group	Population	Estimated # by CVD Risk Status			Estimated % by CVD Risk Status		
		Low	Int.	High	Low	Int.	High
20-39	8,983,467	8,893,999	4,335	85,133	99.0%	0.05%	0.95%
40-59	9,863,690	7,231,730	1,014,437	1,617,523	73.3%	10.3%	16.4%
60-79	5,186,843	1,011,071	1,148,828	3,026,944	19.5%	22.1%	58.4%
Total	**24,034,000**	**17,136,800**	**2,167,600**	**4,729,600**	**71.3%**	**9.0%**	**19.7%**
40-79	15,050,533	8,242,801	2,163,265	4,644,467	54.8%	14.4%	30.9%

- In a systematic review for the USPSTF, Chou et al included 19 randomized control trials (RCTs) with 71,344 participants with a mean age between 51 and 66 years and an average of 4.1 years of follow-up. They conclude that statin therapy is associated with a decreased risk of the following: [318]
  - All-cause mortality (RR, 0.86 [95% CI, 0.80 to 0.93]) (Table 3, row *y*)
  - Cardiovascular mortality (RR, 0.69 [95% CI, 0.54 to 0.88])
  - Myocardial infarction (RR, 0.64 [95% CI, 0.57 to 0.71]) (Table 3, row *ab*)
  - Stroke (RR, 0.71 [95% CI, 0.62 to 0.82]) (Table 3, row *ae*)
- Based on the review for the USPSTF, statin therapy (when compared with a placebo) is not associated with an increased risk of withdrawal due to adverse events, serious adverse events, any cancer, fatal cancer, myalgias or elevated aminotransferase levels, rhabdomyolysis or myopathy, renal dysfunction, cognitive harms or new-onset diabetes following initiation of statin therapy.[319]
- The review for the USPSTF by Chou et al has been criticized on several fronts. Redberg and Katz note that the review did not exclude studies that included patients taking statins for secondary prevention.[320] A 2010 review by Ray and colleagues, which included only studies of patients receiving statins for primary prevention, did not find a benefit of statin use and all-cause mortality (RR, 0.91; 95% CI of 0.83 to 1.01).[321] In addition, Redberg and Katz note that the most commonly reported side effect of muscle weakness and pain is not included in the review by Chou et al. Clinical trials suggest that statin myopathy occurs in 1-5% of patients while it may range as high as 20-30% based on observations in clinical practice.[322,323]
- In a 2016 review of the available evidence on the safety of statin therapy, Collins and colleagues note that "(t)he only serious adverse events that have been shown to be caused by long-term statin therapy - i.e., adverse effects of the statin, are myopathy

[318] Chou R, Dana T, Blazina I et al. Statins for prevention of cardiovascular disease in adults: evidence report and systematic review for the US Preventive Services Task Force. *Journal of the American Medical Association*. 2016; 316(19): 2008-24.
[319] Ibid.
[320] Redberg R and Katz M. Statins for primary prevention: the debate is intense, but the data are weak. *Journal of the American Medical Association*. 2016; 316(19): 1979-81.
[321] Ray K, Seshasai S, Erqou S et al. Statins and all-cause mortality in high-risk primary prevention: a meta-analysis of 11 randomized controlled trials involving 65 229 participants. *Archives of Internal Medicine*. 2010; 170(12): 1024-31.
[322] Magni P, Macchi C, Morlotti B et al. Risk identification and possible countermeasures for muscle adverse effects during statin therapy. *European Journal of Internal Medicine*. 2015; 26(2): 82-8.
[323] Thompson P. What to believe and do about statin-associated adverse effects. *Journal of the American Medical Association*. 2016; 316(19): 1969-70.

(defined as muscle pain or weakness combined with large increases in blood concentrations of creatine kinase), new-onset diabetes mellitus, and, probably, haemorrhagic stroke. Typically, treatment of 10 000 patients for 5 years with an effective regimen (e.g., atorvastatin 40 mg daily) would cause about 5 cases of myopathy (one of which might progress, if the statin therapy is not stopped, to the more severe condition of rhabdomyolysis), 50–100 new cases of diabetes, and 5–10 haemorrhagic strokes. However, any adverse impact of these side-effects on major vascular events has already been taken into account in the estimates of the absolute benefits. Statin therapy may cause symptomatic adverse events (e.g., muscle pain or weakness) in up to about 50–100 patients (i.e., 0.5–1.0% absolute harm) per 10 000 treated for 5 years. However, placebo-controlled randomised trials have shown definitively that almost all of the symptomatic adverse events that are attributed to statin therapy in routine practice are not actually caused by it (i.e., they represent misattribution)….It is, therefore, of concern that exaggerated claims about side-effect rates with statin therapy may be responsible for its under-use among individuals at increased risk of cardiovascular events. For, whereas the rare cases of myopathy and any muscle-related symptoms that are attributed to statin therapy generally resolve rapidly when treatment is stopped, the heart attacks or strokes that may occur if statin therapy is stopped unnecessarily can be devastating."[324]

- The controversy over side-effects continues, especially regarding muscle problems, as evidenced by the series of letters in the March 18, 2017 issue of *The Lancet* responding to the Collins et al review. In our sensitivity analysis, we have included an assumption that 5%[325,326] of patients taking statins would develop muscle problems and that their QoL would be reduced by 53%[327] during the estimated 3 months it would take for the statin withdrawal and rechallenge process[328,329] to determine that the muscle problem is associated with the use of statins.
- Other assumptions used in assessing the clinically preventable burden are detailed in the Reference Document.

Based on these assumptions, the CPB associated with universal CVD risk-factor screening and initiating use of low- to moderate-dose statins in adults aged 40 to 74 years without a history of CVD who have 1 or more CVD risk factors and a calculated 10-year CVD event risk of 10% or greater is 9,370 QALYs (see Table 3, row *ap*). This is based on the assumption of moving from no statin use in this intermediate or high risk cohort, to 30% of this cohort initiating and sustaining statin use.

[324] Collins R, Reith C, Emberson J et al. Interpretation of the evidence for the efficacy and safety of statin therapy. *The Lancet*. 2016; 388(10059): 2532-61.
[325] Parker B, Capizzi J, Grimaldi A et al. The effect of statins on skeletal muscle function. *Circulation*. 2013; 127(1): 96-103.
[326] Ganga H, Slim H and Thompson P. A systematic review of statin-induced muscle problems in clinical trials. *American Heart Journal*. 2014; 168(1): 6-15.
[327] Cham S, Evans M, Denenberg J et al. Statin-associated muscle-related adverse effects: a case series of 354 patients. *Pharmacotherapy: The Journal of Human Pharmacology and Drug Therapy*. 2010; 30(6): 541-53.
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[329] Ahmad Z. Statin intolerance. *American Journal of Cardiology*. 2014; 113(10): 1765-71.

Table 3: CPB of Universal Screening for and Initiating Use of Statins in Adults Aged 40 to 74 Years with an Intermediate or High Risk of CVD in a Birth Cohort of 40,000			
Label	**Variable**	**Base Case**	**Data Source**
	Estimated current status		
a	# of life years lived between the ages of 40-74 in birth cohort	1,296,348	Table 1
b	% of life years at intermediate or high risk	45.2%	Table 2
c	# of life years at intermediate or high risk	586,371	= (a * b)
d	% of life years at intermediate or high risk on statins	30.0%	See Ref Doc
e	# of life years at intermediate or high risk on statins	175,911	= (c * d)
f	Total deaths in birth cohort between the ages of 40-74	6,238	Table 1
g	Cardiovascular deaths in birth cohort between the ages of 40-74	907	Table 1
h	Cerebrovascular deaths in birth cohort between the ages of 40-74	344	Table 1
i	**Life years lost due to total deaths**	**135,558**	Table 1
j	Life years lost per death	21.7	= (i / f)
k	# of nonfatal cardiovascular events per fatal event	5.09	See Ref Doc
l	# of nonfatal cardiovascular events	4,615	= (g * k)
m	Average age of individual with a cardiovascular event	68.0	See Ref Doc
n	Life years lived with a nonfatal cardiovascular event	12.1	See Ref Doc
o	Life years lost due to a nonfatal cardiovascular event	6.3	See Ref Doc
p	QoL reduction living with a nonfatal cardiovascular event (for 1 month)	0.125	See Ref Doc
q	**QALYs lost due to nonfatal cardiovascular events**	**29,120**	= (l * o) + (l * p/12)
r	Ratio of nonfatal cerebrovascular events per fatal event	4.58	See Ref Doc
s	# of nonfatal cerebrovascular events	1,574	= (r * h)
t	Average age of individual with a cerebrovascular event	72.8	See Ref Doc
u	Life years lived with a nonfatal cerebrovascular event	9.3	See Ref Doc
v	Life years lost due to a nonfatal cerebrovascular event	5.5	See Ref Doc
w	QoL reduction living with a nonfatal cerebrovascular event	0.264	See Ref Doc
x	**QALYs lost due to nonfatal cerebrovascular events**	**12,525**	= (s * v) + (s * u * w)
	Benefits **if 30% of intermediate or high risk individuals were on statins**		
y	% reduction in all cause mortality associated with statin use	14%	√
z	Deaths avoided with statin usage	262	= (f * d * y)
aa	**QALYs gained due to a reduction in all cause mortality**	**5,693**	= (z * j)
ab	% reduction in cardiovascular events associated with statin use	36%	√
ac	Cardiovascular events avoided with 30% statin usage	498	= (l * d *ab)
ad	**QALYs gained due to a reduction in nonfatal cardiovascular events associated with statin use**	**3,145**	= (q * d * ab)
ae	% reduction in cerebrovascular events associated with statin use	29%	√
af	Cerebrovascular events avoided with 30% statin usage	137	= (s * d * ae)
ag	**QALYs gained due to a reduction in nonfatal cerebrovascular events associated with statin use**	**1,090**	= (af * t * u)
ah	**Total QALYs gained if 30% of intermediate or high risk individuals were on statins**	**9,928**	= (aa + ad + ag)
	Harms if 30% of intermediate or high risk individuals were on statins		
ai	Disutility per year associated with taking pills for cardiovascular prevention	-0.0032	See Ref Doc
aj	**Disutility associated with taking pills for cardiovascular prevention**	**-558**	= (e * ai)
ak	Proportion of individuals taking statins who experience muscle problems	0.0%	√
al	Length of time for muscle problems to be indentified and resolved (in years)	0.25	√
am	Disutilty per year associated with muscle problems	-0.53	√
an	**Disutility associated with muscle problems**	**0**	Table 1 * b * ak * al * am
ao	**QALYs lost if 30% of intermediate or high risk individuals were on statins**	**-558**	= (aj + an)
ap	**Potential QALYs gained, Screening & Intervention from 0% to 30%**	**9,370**	= (ah + ao)

√ = Estimates from the literature

For our sensitivity analysis, we modified a number of major assumptions and recalculated the CPB as follows:

- Assume that the QoL reduction associated with a stroke is reduced from 0.264 to 0.177 (Table 3, row w): CPB = 9,259.

- Assume that the QoL reduction associated with a stroke is increased from 0.264 to 0.350 (Table 3, row *w*): CPB = 9,480.
- Assume that decreased risk of all-cause mortality associated with statin therapy is reduced from 14% to 7% (Table 3, row *y*), the decreased risk of a myocardial infarction is reduced from 36% to 29% (Table 3, row *ab*) and the decreased risk of stroke is reduced from 29% to 18% (Table 3, row *ae*): CPB = 5,499.
- Assume that decreased risk of all-cause mortality associated with statin therapy is increased from 14% to 20% (Table 3, row *y*), the decreased risk of a myocardial infarction is increased from 36% to 43% (Table 3, row *ab*) and the decreased risk of stroke is increased from 29% to 38% (Table 3, row *ae*): CPB = 12,760.
- Assume that the disutility per year associated with taking pills for cardiovascular prevention is reduced from -0.0032 to 0.0 (Table 3, row *ai*): CPB = 9,928.
- Assume that the disutility per year associated with taking pills for cardiovascular prevention is increased from -0.0032 to -0.0044 (Table 3, row *ai*): CPB = 9,161.
- Assume that the percent of life years at intermediate risk on statins is reduced from 30% to 25% (Table 3, row *d*): CPB = 7,809.
- Assume that the percent of life years at intermediate risk on statins is increased from 30% to 40% (Table 3, row *d*): CPB = 12,494.
- Assume that statin use is associated with muscle problems in 5% of users (Table 3, row *ak*): CPB = 9,259.

Modelling Cost-Effectiveness

In this section, we will calculate the CE associated with universal screening for and initiating use of low- to moderate-dose statins in adults aged 40 to 74 years without a history of CVD, who have 1 or more CVD risk factors, and a calculated 10-year CVD event risk of 10% or greater.

In estimating CE, we made the following assumptions:

Cost of Screening for CVD Risk

- The USPSTF recommends using the ACC/AHA Pooled Cohort Equations to calculate the 10-year risk of CVD events.[330]
- The *2013 ACC/AHA Guideline on the Assessment of Cardiovascular Risk* indicate that "it is reasonable to …estimate 10-year ASCVD risk every 4-6 years in adults 40-79 years of age who are free from ASCVD."[331]
- The ACC-AHA-ASCVD score, however, overestimates the 10-year ASCVD risk. The USPSTF recognizes this. "The reasons for this possible overestimation are still unclear. The Pooled Cohort Equations were derived from prospective cohorts of volunteers from studies conducted in the 1990s and may not be generalizable to a

[330] Bibbins-Domingo K, Grossman D, Curry S et al. Statin use for the primary prevention of cardiovascular disease in adults: US Preventive Services Task Force recommendation statement. *Journal of the American Medical Association*. 2016; 316(19): 1997-2007.

[331] Goff D, Lloyd-Jones D, Bennett G et al. 2013 ACC/AHA guideline on the assessment of cardiovascular risk: a report of the American College of Cardiology/American Heart Association Task Force on practice guidelines. *Circulation*. 2014; 135(2): S49-S74.

more contemporary and diverse patient population seen in current clinical practice."[332]

- Cook and Ridker, using the Women's Health Study, found that the ACC-AHA-ASCVD score overestimated the actual 10-year ASCVD risk in women by 43% to 90% in women, depending on their baseline risk.[333] DeFilippis and colleagues compared the performance of five risk assessment tools in a community-based, sex-balanced, multiethnic cohort. The ACC-AHA-ASCVD score overestimated the 10-year ASCVD risk by 78%. They found that the best risk assessment tool was the Reynolds Risk Score.[334] Rana and co-authors used a large contemporary, multi-ethnic population to assess the ACC-AHA-ASCVD score. They found that the ACC-AHA-ASCVD score substantially overestimated the actual 5-year ASCVD risk and that this overestimation was similar in both males and females and in four major ethnic groups (black, Asian/Pacific Islander, Hispanic and white).[335] In a commentary, Nissen notes that "the extent of miscalibration is substantial…. This is not a trivial problem…. Overestimation by the guideline risk equations would likely add millions of Americans to the roles of patients for whom statins are recommended."[336]
- The USPSTF notes that "because the Pooled Cohort Equations lack precision, the risk estimation tool should be used as a starting point to discuss with patients their desire for lifelong statin therapy."[337]
- For screening purposes, we have assumed that 54.8% of the BC population ages 40-75 is at a low risk for CVD (Table 4, row *b*), 14.4% is at an intermediate risk (Table 4, row *d*) and 30.9% is at a high risk (Table 4, row *f*) (see also Table 2).
- We have assumed that the CVD screening would take place once every five years and modified this to once every two years in the sensitivity analysis (Table 4, row *h*).
- Completion of a risk assessment includes a clinician visit and a full lipid profile (total cholesterol [TC]; high density lipoprotein cholesterol [HDL-C]; low-density lipoprotein cholesterol [LDL-C], non-HDL-C; and triglycerides [TG]). The full lipid profile costs $21.31 (Table 4, row *p*).[338]
- We assumed that a 10-minute office visit would be required for the initial screening. If the results indicate a low risk of CVD, then the follow-up would consist of a phone call to the patient. If the results indicate an intermediate or high risk of CVD, then a follow-up visit would be required to discuss the results and the possibility of taking statins (Table 4, row *l*).

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[332] Bibbins-Domingo K, Grossman D, Curry S et al. Statin use for the primary prevention of cardiovascular disease in adults: US Preventive Services Task Force recommendation statement. *Journal of the American Medical Association*. 2016; 316(19): 1997-2007.

[333] Cook NR and Ridker PM. Further insight into the cardiovascular risk calculator: the roles of statins, revascularizations, and underascertainment in the Women's Health Study. *Journal of the American Medical Association Internal Medicine*. 2014; 174(12): 1964-71.

[334] DeFilippis A, Young R, Carrubba C et al. An analysis of calibration and discrimination among multiple cardiovascular risk scores in a modern multiethnic cohort. *Annals of Internal Medicine*. 2015; 162(4): 266-75.

[335] Rana J, Tabada G, Solomon M et al. Accuracy of the atherosclerotic cardiovascular risk equation in a large contemporary, multiethnic population. *Journal of the American College of Cardiology*. 2016; 67(18): 2118-30.

[336] Nissen SE. Prevention guidelines: bad process, bad outcome. *Journal of the American Medical Association Internal Medicine*. 2014; 174(12): 1972-3.

[337] Bibbins-Domingo K, Grossman D, Curry S et al. Statin use for the primary prevention of cardiovascular disease in adults: US Preventive Services Task Force recommendation statement. *Journal of the American Medical Association*. 2016; 316(19): 1997-2007.

[338] Ministry of Health. *Cardiovascular Disease – Primary Prevention* 2014. Available at http://www2.gov.bc.ca/assets/gov/health/practitioner-pro/bc-guidelines/cvd.pdf. Accessed January 2017.

Costs of the Intervention

- Adherence with statin therapy in the real world is relatively poor. Benner and colleagues found that early and frequent follow-up by physicians (including cholesterol retesting) improves long-term adherence by approximately 45% (OR 1.45; 95% CI of 1.34 – 1.55).[339]
- Brookhart et al., in a study based on BC data, found that a return to adherence after a period of nonadherence was associated with a return visit to the physician who initially prescribed the statin and a retest of cholesterol. "Our results suggest that continuity of care combined with increased follow-up and cholesterol testing could promote long-term adherence."[340]
- Pandya and colleagues estimated one additional physician visit per year for individuals in a disease-free state taking statins (i.e., for primary prevention).[341]
- The BC Guidelines for the primary prevention of cardiovascular disease suggest a follow-up physician visit 4-6 months after the initiation of statin which includes the measuring of lipid levels with a non-HDL-C or an apolipoprotein B (apoB) test, to assess patient adherence to statin therapy and any response to statin therapy, with further follow-ups as clinically indicated. The cost of a non-HDL-C test is $12.20 while that of an apoB test is $16.60.[342] For modelling purposes, we used the midpoint cost of these two tests (Table 4, row *ab*).
- For modelling purposes, we have assumed that 30% of intermediate and high risk patients would adhere to long-term statin therapy and modified this from 25% to 40% in the sensitivity analysis (Table 3, row *d*). We further assumed, based on expert input, that one annual follow-up office visit per year (Table 4, row *y*) is required for patients on statin therapy, that 100% of this office visit (Table 4, row *z*) is allocated to discussing the statin therapy and that a follow-up lipid test (non-HDL-C or apoB) would be required once every five years (Table 4, row *aa*).
- The BC Reference Drug Pricing program fully covers the costs of two statins, atorvastatin and rosuvastatin.[343] The cost of 10mg rosuvastatin, taken by the majority of patients, is $95 plus four dispensing fees of $10 each, for an annual cost of $135 (Table 4, row *w*). The cost of 80mg atorvastatin is $206 plus four dispensing fees of $10 each, for an annual cost of $246. We have used this higher cost in the sensitivity analysis.

Costs Avoided due to the Intervention

- For modelling purposes, we assumed that the acute care costs avoided per death avoided would be $13,929 (Table 4, row *ah*). This is based on the mix of cardiovascular and cerebrovascular deaths in the cohort (73% and 27%, respectively)

[339] Benner J, Tierce J, Ballantyne C et al. Follow-up lipid tests and physician visits are associated with improved adherence to statin therapy. *PharmacoEconomics*. 2004; 22(3): 13-23.
[340] Brookhart M, Patrick A, Schneeweiss S et al. Physician follow-up and provider continuity are associated with long-term medication adherence: a study of the dynamics of statin use. *Archives of Internal Medicine*. 2007; 167(8): 847-52.
[341] Pandya A, Sy S, Cho S et al. Cost-effectiveness of 10-year risk thresholds for initiation of statin therapy for primary prevention of cardiovascular disease. *Journal of the American Medical Association*. 2015; 314(2): 142-50.
[342] Ministry of Health. *Cardiovascular Disease – Primary Prevention* 2014. Available at http://www2.gov.bc.ca/assets/gov/health/practitioner-pro/bc-guidelines/cvd.pdf. Accessed January 2017.
[343] See BC *Reference Drug Program*. Available online at http://www2.gov.bc.ca/gov/content/health/practitioner-professional-resources/pharmacare/prescribers/reference-drug-program. Accessed March 2017.

(see Table 1) and the estimated cost of the acute care phase associated with a fatal myocardial infarction ($15,536) and a fatal stroke ($9,583).

- Other costs and assumptions used in assessing cost-effectiveness are detailed in the Reference Document.
- Discount rate of 1.5%, varied from 0% to 3% in the sensitivity analysis.

Based on these assumptions, the CE associated with universal screening for and initiating use of low- to moderate-dose statins in adults aged 40 to 74 years without a history of CVD, who have 1 or more CVD risk factors, and a calculated 10-year CVD event risk of 10% or greater is $3,223 / QALY (Table 4, row *ay*).

Table 4: CE of Universal Screening for and Initiating Use of Statins in Adults Aged 40 to 74 Years with an Intermediate or High Risk of CVD in a Birth Cohort of 40,000			
Row Label	**Variable**	**Base Case**	**Data Source**
a	# of life years lived between the ages of 40-74 in birth cohort	1,296,348	Table 1
b	% of life years at low risk	54.8%	Table 2
c	# of life years at low risk	709,977	= (a * b)
d	% of life years at intermediate risk	14.4%	Table 2
e	# of life years at intermediate risk	186,329	= (a * d)
f	% of life years at high risk	30.9%	Table 2
g	# of life years at high risk	400,042	= (a * f)
h	Annual frequency of screening	0.20	√
i	Adherence with offers to receive screening	48%	See Ref Doc
j	Total # of screens in birth cohort	124,449	= (a * h * i)
	Estimated cost of screening		
k	Number of office visits associated with screening - low risk	1.0	Expert Opinion
l	Number of office visits associated with screening - medium or high risk	2.0	Expert Opinion
m	Cost of 10-minute office visit	$34.85	See Ref Doc
n	Cost of a follow-up phone call	$15.00	See Ref Doc
o	Cost to measure cholesterol	$21.31	√
p	Health care costs of screening - low risk	$4,850,111	= (j * b) * k * (m + n + o)
q	Health care costs of screening - intermediate and high risk	$5,123,096	= ((d + f) * j * l)*(m + (o/2))
r	Patient time required / office visit (hours)	2.0	√
s	Value of patient time (per hour)	$29.69	√
t	Value of patient time and travel for screening	$7,389,806	= (j * r * s)
	Estimated cost of intervention		
u	Adherence with long-term statin therapy in intermediate and high risk cohort	30%	Table 3, row d
v	Years on statin therapy	175,911	= (e + g) * u
w	Cost of statin therapy / year	$135	√
x	Cost of statin therapy	$23,748,009	= (v * w)
y	# of follow-up office visits per year re: statin therapy	1.0	Expert Opinion
z	Portion of 10-minute office visit for follow-up re: statin therapy	100%	Expert Opinion
aa	# of lab tests (non-HDL-C or apoB) per year re: statin therapy	0.2	Expert Opinion
ab	Cost per lab test	$14.40	√
ac	Follow-up costs	$6,637,129	= (v * y * z * m) + (v * aa * ab)
ad	Value of patient time and travel for intervention	$10,445,606	= (v * y * s * r)
	Estimated costs avoided due to intervention		
ae	# of deaths avoided	262.0	Table 3, row z
af	# of nonfatal cardiovascular events avoided	498.4	Table 3, row ac
ag	# of nonfatal cerebrovascular events avoided	136.9	Table 3, row af
ah	Acute care costs avoided per avoided death	-$13,929	See Ref Doc
ai	First year costs avoided per nonfatal cardiovascular event avoided	-$33,934	See Ref Doc
aj	First year costs avoided per nonfatal cerebrovascular event avoided	-$21,139	See Ref Doc
ak	First-year acute care costs avoided	-$23,455,536	= (ae * ah) + (af * ai) + (ag * aj)
al	Post-first-year annual costs avoided for nonfatal cardiovascular events avoided	-$2,278	See Ref Doc
am	Number of years for which the costs are avoided	12.1	See Ref Doc
an	Post-first-year costs avoided for nonfatal cardiovascular events avoided	-$13,736,935	= (af * am * al)
ao	Post-first-year annual costs avoided for nonfatal cerebrovascular events avoided	-$6,246	See Ref Doc
ap	Number of years for which the costs are avoided	9.3	See Ref Doc
aq	Post-first-year costs avoided for nonfatal cerebrovascular events avoided	-$7,954,795	= (ag * ap * ao)
ar	Costs avoided due to intervention	-$45,147,265	= ak + an + aq
	CE Calculation		
as	Cost of intervention over lifetime of birth cohort	$58,193,757	= p + q + t + x + ac + ad
at	Costs avoided due to intervention over lifetime of birth cohort	-$45,147,265	= ar
au	QALYs saved	9,370	Table 3, row ap
av	Cost of intervention over lifetime of birth cohort (1.5% discount)	$45,893,093	Calculated
aw	Costs avoided due to intervention over lifetime of birth cohort (1.5% discount)	-$28,135,568	Calculated
ax	QALYs saved (1.5% discount)	5,510	Calculated
ay	**CE ($/QALY saved)**	**$3,223**	= (av + aw) / ax

√ = Estimates from the literature

For our sensitivity analysis, we modified a number of major assumptions and recalculated the CE as follows:

- Assume that the QoL reduction associated with a stroke is reduced from 0.264 to 0.177 (Table 3, row *w*): CE = $3,261.
- Assume that the QoL reduction associated with a stroke is increased from 0.264 to 0.350 (Table 3, row *w*): CE = $3,186.
- Assume that decreased risk of all-cause mortality associated with statin therapy is reduced from 14% to 7% (Table 3, row *y*), the decreased risk of a myocardial infarction is reduced from 36% to 29% (Table 3, row *ab*) and the decreased risk of stroke is reduced from 29% to 18% (Table 3, row *ae*): CE = $7,849.
- Assume that decreased risk of all-cause mortality associated with statin therapy is increased from 14% to 20% (Table 3, row *y*), the decreased risk of a myocardial infarction is increased from 36% to 43% (Table 3, row *ab*) and the decreased risk of stroke is increased from 29% to 38% (Table 3, row *ae*): CE = $1,458.
- Assume that the disutility per year associated with taking pills for cardiovascular prevention is reduced from -0.0032 to 0.0 (Table 3, row *ai*): CE = $2,996.
- Assume that the disutility per year associated with taking pills for cardiovascular prevention is increased from -0.0032 to -0.0044 (Table 3, row *ai*): CE = $3,317.
- Assume that the percent of life years at intermediate risk on statins is reduced from 30% to 25% (Table 3, row *d*): CE = $3,720.
- Assume that the percent of life years at intermediate risk on statins is increased from 30% to 40% (Table 3, row *d*): CE = $2,601.
- Assume that statin use is associated with muscle problems in 5% of users (Table 3, row *ak*): CE = $3,272.
- Assume that the annual frequency of screening is increased from once every five years to once every two years (Table 4, row *i*): CE = $6,950.
- Assume that the cost of statin therapy in increased from $135 per year to $246 per year (Table 4, row *w*): CE = $6,017.
- Assume that the first-year costs avoided following a nonfatal cerebrovascular are decreased from $21,139 to $16,642 (Table 4, row *aj*) and the post-first-year annual costs avoided decreased from $6,246 to $4,930 (Table 4, row *ao*): CE = $3,471.
- Assume that the first-year costs avoided following a nonfatal cerebrovascular are increased from $21,139 to $25,635 (Table 4, row *aj*) and the post-first-year annual costs avoided increased from $6,246 to $7,562 (Table 4, row *ao*): CE = $2,974.

Summary

Applying a 1.5% discount rate, the clinically preventable burden (CPB) associated with universal screening for and initiating use of low- to moderate-dose statins in adults aged 40 to 74 years without a history of CVD, who have 1 or more CVD risk factors, and a calculated 10-year CVD event risk of 10% or greater is estimated to be 5,510 quality-adjusted life years (QALYs) while the cost-effectiveness (CE) is estimated to be $3,223 per QALY (see Table 5).

Table 5: Universal Screening for and Initiating Use of Statins in Adults aged 40 to 74 years with an Intermediate or High Risk of CVD in a Birth Cohort of 40,000

Summary

	Base Case	Range	
CPB (Potential QALYs Gained)			
Gap between No Service and 'Best in the World' (30%)			
1.5% Discount Rate	5,510	3,204	7,531
3% Discount Rate	3,144	1,800	4,322
0% Discount Rate	***9,370***	5,499	12,760
CE ($/QALY) **including** patient time costs			
1.5% Discount Rate	***$3,223***	$1,458	$7,849
3% Discount Rate	$6,222	$3,567	$13,376
0% Discount Rate	$1,392	$169	$4,537
CE ($/QALY) **excluding** patient time costs			
1.5% Discount Rate	$1,174	-$409	$3,459
3% Discount Rate	$2,634	$958	$7,109
0% Discount Rate	-$511	-$1,229	$1,293

Screening for Type 2 Diabetes Mellitus

Canadian Task Force on Preventive Health Care (2012)

The CTFPHC suggests a two-phase approach to screening.[344] First, it recommends screening all adults ages 18 and older using a validated risk calculator such as FINDRISC (Finnish Diabetes Risk Score) or CANRISK (Canadian Diabetes Risk Assessment Questionnaire). This first level of screening should be completed once every 3-5 years. Those with a FINDRISC score of 15 to 20 are considered to be at high risk of diabetes (an individual's risk of developing type 2 diabetes within 10 years is between 33% and 49%) and those with a score greater than 21 are at very high risk (an individual's risk of developing diabetes within 10 years is 50% or higher). The second phase of screening involves either an A1C, fasting glucose or oral glucose tolerance test. The CTFPHC recommends the use of the A1C test given its "convenience for patients." Individuals at high risk are to be screened every 3-5 years while individuals at very high risk are to be screened every year. The CTFPHC considers these recommendations to be "weak" based on "low-quality evidence".[345]

United States Preventive Services Task Force Recommendations (2015)

The USPSTF recommends screening for abnormal blood glucose in all adults ages 40 to 70 who are overweight or obese as part of a cardiovascular risk assessment. This recommendation receives a "B" grade from the USPSTF.[346]

Modelling the Clinically Preventable Burden

In this section, we model the CPB associated with the two-phase approach to screening for type 2 diabetes, recommended by the CTFPHC, in a British Columbia birth cohort of 40,000.

In modelling CPB, we made the following assumptions:

- 35% of the population aged 40 or older would have a FINDRISC score of 15-19 (high risk) and 10% would have a score of 20+ (very high risk) (see Table 1 and 2 below).[347]

- Detailed information on the prevalence of diagnosed diabetes in Canada in 2008/09 by age group and sex is provided by the CTFPHC. Overall, rates for Canadian females and males were 6.4% and 7.2%, respectively.[348] Rates of diagnosed diabetes in British Columbia in 2007/08 were 6.0% for females and 6.9% for males.[349] This data was not stratified by age. In estimating the age and sex specific prevalence rates for diagnosed diabetes in BC, we adjusted the Canadian age and sex specific rates downwards by the difference between the Canadian and British Columbian rates (see Figure 1).

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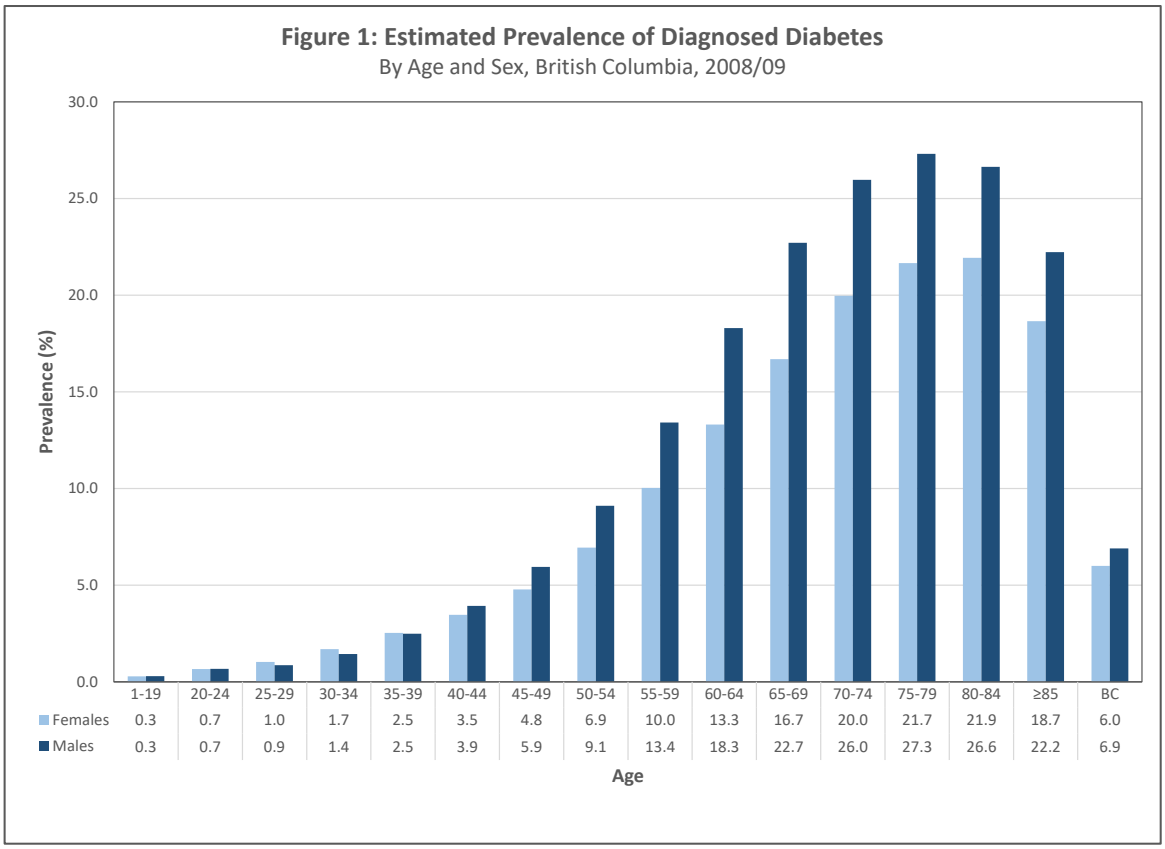
[344] Canadian Task Force on Preventive Health Care. Recommendations on screening for type 2 diabetes in adults. *Canadian Medical Association Journal*. 2012; 184(15): 1687-96.
[345] Ibid.
[346] Siu A. Screening for Abnormal Blood Glucose and Type 2 Diabetes Mellitus: U.S. Preventive Services Task Force Recommendation Statement. *Annals of Internal Medicine.* 2015; 163(11): 861-8.
[347] Makrilakis K, Liatis S, Grammatikou S et al. Validation of the Finnish diabetes risk score (FINDRISC) questionnaire for screening for undiagnosed type 2 diabetes, dysglycaemia and the metabolic syndrome in Greece. *Diabetes & Metabolism*. 2011; 37(2): 144-51.
[348] Canadian Task Force on Preventive Health Care. Recommendations on screening for type 2 diabetes in adults. *Canadian Medical Association Journal*. 2012; 184(15): 1687-96.
[349] Provincial Health Services Authority. *Summary Report on Health for British Columbia from Regional, Longitudinal and Gender Perspectives*. 2010. Available at http://www.phsa.ca/population-public-health-site/Documents/BCHealth_Indicators_Report.pdf. Accessed February 2015.



- Estimates of the proportion of diabetes cases that are undiagnosed by age group and sex are as follows: [350]

Age Group	Males	Females
40-49	44%	24%
50-59	21%	15%
60-69	17%	16%
70-79	19%	14%
80+	16%	14%

- A total of 798,605 years would be lived by males from age 40 - 89 in a BC birth cohort of 40,000 (see Table 1). The equivalent number for females would be 857,481 (see Table 2). Among males, 279,512 of these years would be spent at high risk for type 2 diabetes, and 79,861 would be spent at very high risk. Among females, 300,118 would be spent at high risk and 85,748 at very high risk.

[350] Wilson SE, Rosella LC, Lipscombe LL et al. The effectiveness and efficiency of diabetes screening in Ontario, Canada: a population-based cohort study. *BMC Public Health*. 2010; 10(1): 506.

Table 1: Prevalence and Increased Risk for Type 2 Diabetes in a *Male* Birth Cohort of 20,000

Age Group	Mean Survival Rate	Individuals in Birth Cohort	Years of Life in Birth Cohort	Estimated FINDRISC Status		Prevalence of Diabetes				Years of Life with Diabetes	
						Diagnosed		Undiagnosed			
				High	Very High	%	#	%	#	Diagnosed	Undiagnosed
40-44	0.972	19,442	97,211	34,024	9,721	3.9%	764	1.7%	336	3,820	1,681
45-49	0.963	19,263	96,314	33,710	9,631	5.9%	1,145	2.6%	504	5,723	2,518
50-54	0.950	19,003	95,017	33,256	9,502	9.1%	1,730	1.9%	363	8,651	1,817
55-59	0.931	18,619	93,095	32,583	9,310	13.4%	2,498	2.8%	525	12,490	2,623
60-64	0.902	18,041	90,204	31,571	9,020	18.3%	3,302	3.1%	561	16,511	2,807
65-69	0.858	17,164	85,820	30,037	8,582	22.7%	3,898	3.9%	663	19,492	3,314
70-74	0.792	15,837	79,183	27,714	7,918	26.0%	4,113	4.9%	781	20,564	3,907
75-79	0.693	13,861	69,305	24,257	6,931	27.3%	3,786	5.2%	719	18,929	3,596
80-84	0.553	11,053	55,266	19,343	5,527	24.4%	2,697	3.9%	432	13,485	2,158
85-89	0.372	7,438	37,190	13,017	3,719	24.4%	1,815	3.9%	290	9,074	1,452
Total Ages 40 - 89			**798,605**	**279,512**	**79,861**					**128,739**	**25,872**

Table 2: Prevalence and Increased Risk for Type 2 Diabetes in a *Female* Birth Cohort of 20,000

Age Group	Mean Survival Rate	Individuals in Birth Cohort	Years of Life in Birth Cohort	Estimated FINDRISC Status		Prevalence of Diabetes				Years of Life with Diabetes	
						Diagnosed		Undiagnosed			
				High	Very High	%	#	%	#	Diagnosed	Undiagnosed
40-44	0.984	19,672	98,358	34,425	9,836	3.5%	682	0.8%	164	3,412	819
45-49	0.978	19,560	97,800	34,230	9,780	4.8%	935	1.1%	224	4,676	1,122
50-54	0.970	19,395	96,977	33,942	9,698	6.9%	1,346	1.0%	202	6,728	1,009
55-59	0.957	19,150	95,748	33,512	9,575	10.0%	1,921	1.5%	288	9,605	1,441
60-64	0.939	18,774	93,872	32,855	9,387	13.3%	2,499	2.1%	400	12,497	1,999
65-69	0.909	18,190	90,948	31,832	9,095	16.7%	3,035	2.7%	486	15,177	2,428
70-74	0.863	17,265	86,325	30,214	8,633	20.0%	3,448	2.8%	483	17,238	2,413
75-79	0.790	15,799	78,995	27,648	7,900	21.7%	3,421	3.0%	479	17,107	2,395
80-84	0.676	13,517	67,587	23,655	6,759	20.3%	2,744	2.8%	384	13,720	1,921
85-89	0.509	10,174	50,871	17,805	5,087	20.3%	2,065	2.8%	289	10,327	1,446
Total Ages 40-89			**857,481**	**300,118**	**85,748**					**110,486**	**16,994**

- Screening of the entire target population every 3-5 years starting at age 40 is associated with the following benefits over a 50 year period:[351]
  - ✓ 5.2 (range of 2.7 - 7.5) myocardial infarction events prevented per 1,000 people screened (Table 3, row *d*).
  - ✓ 8.0 (range of 6.2 - 9.5) microvascular events (foot amputations/ulcers, end-stage renal disease or blindness) prevented per 1,000 people screened (Table 3, row *h*).
  - ✓ 3.2 (range of 1.0 - 5.8) premature deaths prevented per 1,000 people screened (Table 3, row *l*).
- We have assumed that each event would be prevented, on average, half way through the 50 year follow-up period.
- A myocardial infarction reduces a person's quality of life by 12.6% for a period of one month or a 0.0105 reduction in QoL (Table 3, row *f*).

[351] Kahn R, Alperin P, Eddy D et al. Age at initiation and frequency of screening to detect type 2 diabetes: a cost-effectiveness analysis. *Lancet*. 2010; 375(9723): 1365-74.

- End-stage renal disease (ESRD) reduces a person's quality of life by 20%, foot amputation by 10.5% and blindness by 16%.[352] For microvascular events prevented, we assumed an overall quality of life reduction of 15.8% based on a 40:33:27 distribution for incidence of ESRD, foot amputation or blindness (Table 3, row *j*).[353]

- Other assumptions used in assessing the clinically preventable burden are detailed in the Reference Document.

Based on these assumptions, the CPB associated with screening for type 2 diabetes is 3,494 QALYs (Table 3, row *p*).

Table 3: CPB of Screening for Type 2 Diabetes in a Birth Cohort of 40,000

Row Label	Variable	Base Case	Data Source
a	Individuals in birth cohort at age 40	39,114	Tables 1 and 2
b	Adherence with screening	80%	Ref Doc
c	Individuals screened	31,291	= a * b
	Benefits Associated with Screening		
d	Myocardial infarction events prevented / 1,000 people screened	5.2	√
e	Myocardial infarction events prevented	163	= (c / 1,000) * d
f	Quality of life adjustment per myocardial event	0.0105	Ref Doc
g	QALYs gained	1.7	= e * f
h	Microvascular events prevented / 1,000 people screened	8.0	√
i	Microvascular events prevented	250	= (c / 1,000) * h
j	Quality of life adjustment	15.8%	√
k	QALYs gained	989	= i * 25 * j
l	Premature deaths averted / 1,000 people screened	3.2	√
m	Premature deaths averted	100	= (c / 1,000) * m
n	Life-years gained / death averted	25	√
o	Life-years gained	2,503	= m * n
p	**Potential QALYs gained, Screening increasing from 0% to 80%**	**3,494**	= g + k + o

√ = Estimates from the literature

We also modified a major assumption and recalculated the CPB as follows:

- Assume the number of myocardial infarction events prevented per 1,000 people screened is reduced from 5.2 to 2.7 (Table 3, row *d*), the number of microvascular events prevented per 1,000 people screened is reduced from 8.0 to 6.2 (Table 3, row *h*) and the number of premature deaths prevented per 1,000 people screened is reduced from 3.2 to 1.0 (Table 3, row *l*): CPB = 1,549 QALYs.

- Assume the number of myocardial infarction events prevented per 1,000 people screened is increased from 5.2 to 7.5 (Table 3, row *d*), the number of microvascular events prevented per 1,000 people screened is increased from 8.0 to 9.5 (Table 3, row *h*) and the number of premature deaths prevented per 1,000 people screened is increased from 3.2 to 5.8 (Table 3, row *l*): CPB = 5,714 QALYs.

[352] Kahn R, Alperin P, Eddy D et al. Age at initiation and frequency of screening to detect type 2 diabetes: a cost-effectiveness analysis. *Lancet*. 2010; 375(9723): 1365-74.
[353] Deshpande AD, Harris-Hayes M and Schootman M. Epidemiology of diabetes and diabetes-related complications. *Physical Therapy*. 2008; 88(11): 1254-64.

Modelling Cost-Effectiveness

In this section, we model the CE associated with the two-phase approach to screening for type 2 diabetes, recommended by the CTFPHC, in a British Columbia birth cohort of 40,000.

In modelling CE, we made the following assumptions:

- Laboratory screening tests - The cost of an A1C test (MSP fee item 91745) in BC is $6.09 (Table 4, row *l*).[354]
- The typical event (i.e., first year) cost for an acute myocardial infarction is $33,934, with annual costs thereafter of $1,193 (see Reference Document).
- The annual costs for blindness are $2,330 (see Reference Document).
- The annual costs for end-stage renal disease are $86,278 (see Reference Document).
- The typical event cost for a lower extremity amputation is $33,642 with annual costs thereafter of $1,396 (see Reference Document).
- We have assumed that each event and the resulting costs would be prevented, on average, half way through the 50 year follow-up period.
- Screening detects diabetes, on average, 5.3 years earlier than no screening.[355]
- Average costs avoided per acute myocardial infarction event would therefore be $6,323 ($1,193 * 5.3) (Table 4, row *t*).
- For microvascular events prevented, we assumed a 40:33:27 distribution for ESRD, foot amputation or blindness.[356] Average costs avoided per microvascular event would therefore be $188,685 (Table 4, row *w*).
- Other costs and assumptions used in assessing cost-effectiveness are detailed in the Reference Document.
- Discount rate of 1.5%, varied from 0% to 3% in the sensitivity analysis.

Based on these assumptions, the CE associated with screening for type 2 diabetes is -$3,121 per QALY (Table 4, row *ee*).

[354] BC Ministry of Health. MSP Fee-For-Service Payment Analysis. 2012/2013 - 2016/2017. Available online at https://www2.gov.bc.ca/assets/gov/health/practitioner-pro/medical-services-plan/ffs_complete.pdf. Accessed January 2018.

[355] Kahn R, Alperin P, Eddy D et al. Age at initiation and frequency of screening to detect type 2 diabetes: a cost-effectiveness analysis. *Lancet*. 2010; 375(9723): 1365-74.

[356] Deshpande AD, Harris-Hayes M and Schootman M. Epidemiology of diabetes and diabetes-related complications. *Physical Therapy*. 2008; 88(11): 1254-64.

Table 4: CE of Screening for Type 2 Diabetes in a Birth Cohort of 40,000			
Row Label	**Variable**	**Base Case**	**Data Source**
a	Individuals in birth cohort at age 40	39,114	Table 3, row a
b	Life years at increased risk for diabetes	1,656,086	Tables 1 and 2
c	Life years at high risk for diabetes	579,630	Tables 1 and 2
d	Life years at very high risk for diabetes	165,609	Tables 1 and 2
	Costs of intervention		
e	Frequency of screening with FINDRISC/CANRISK (every x years)	4	√
f	Total number of screens with FINDRISC/CANRISK (100% adherence)	414,022	= b / e
g	Adherence with screening	80%	Ref Doc
h	Cost of 10-minute office visit	$34.85	Ref Doc
i	Value of patient time and travel for office visit	$59.38	Ref Doc
j	Portion of 10-minute office visit for screen	50%	Ref Doc
k	Cost of screening with FINDRISC/CANRISK	$15,605,298	= (f * g) * (h + i) * j
l	Lab cost of A1C test	$6.09	√
m	Value of patient time and travel for lab test	$29.69	Ref Doc
n	Frequency of lab testing for high risk patients (every x years)	4	√
o	# of lab tests high risk patients	115,926	= (c / n) * g
p	Frequency of lab testing for very high risk patients (every x years)	1	√
q	# of lab tests for very high risk patients	132,487	= d * p * g
r	Cost of lab testing	$20,592,187	= ((o + q) * (l + m))+((o + q) * (h + i) * j)
	Cost avoided		
s	Myocardial infarction events prevented	163	Table 3, row e
t	Cost avoided per event avoided	$6,323	√
u	Total costs avoided	$1,028,837	= s * t
v	Microvascular events prevented	250	Table 3, row i
w	Cost avoided per event avoided	$188,685	√
x	Total costs avoided	$47,233,248	= v * w
	CE calculation		
y	Cost of intervention over lifetime of birth cohort	$36,197,486	= k + r
z	Costs avoided	$48,262,085	= u + x
aa	QALYs saved	3,494	Table 3, row p
bb	Cost of intervention over lifetime of birth cohort (1.5% discount)	$25,566,103	Calculated
cc	Costs avoided (1.5% discount)	$31,908,799	Calculated
dd	QALYs saved (1.5% discount)	2,032	Calculated
ee	**CE ($/QALY saved)**	**-$3,121**	= (bb - cc) / dd

√ = Estimates from the literature

We also modified several major assumptions and recalculated the cost per QALY as follows:

- Assume the number of myocardial infarction events prevented per 1,000 people screened is reduced from 5.2 to 2.7 (Table 3, row *d*), the number of microvascular events prevented per 1,000 people screened is reduced from 8.0 to 6.2 (Table 3, row *h*) and the number of premature deaths prevented per 1,000 people screened is reduced from 3.2 to 1.0 (Table 3, row *l*): CE = $1,121
- Assume the number of myocardial infarction events prevented per 1,000 people screened is increased from 5.2 to 7.5 (Table 3, row *d*), the number of microvascular events prevented per 1,000 people screened is increased from 8.0 to 9.5 (Table 3, row *h*) and the number of premature deaths prevented per 1,000 people screened is increased from 3.2 to 5.8 (Table 3, row *l*): CE = -$3,761
- Assume the frequency of screening with FINDRISC is increased from every 4 years to every 3 years (Table 4, row *e*): CE = -$1,313
- Assume the frequency of screening with FINDRISC is decreased from every 4 years to every 5 years (Table 4, row *e*): CE = -$4,206

- Assume that the portion of a 10-minute office visit for the assessment of patient risk is reduced from 50% to 33% (Table 4, row *j*): CE = -$6,348
- Assume that the portion of a 10-minute office visit for the assessment of patient risk is increased from 50% to 67% (Table 4, row *j*): CE = $106

Summary

Applying a 1.5% discount rate, the clinically preventable burden (CPB) associated with screening for type 2 diabetes is estimated to be 2,032 quality-adjusted life years (QALYs) while the cost-effectiveness (CE) is estimated to result in cost savings of $3,121 per QALY (see Table 5).

Table 5: Screening for Type 2 Diabetes in a Birth Cohort of 40,000

Summary

	Base Case	Range	
CPB (Potential QALYs Gained)			
Gap between No Service and 'Best in the World' (80%)			
1.5% Discount Rate	**2,032**	901	3,324
3% Discount Rate	1,162	515	1,901
0% Discount Rate	3,494	1,459	5,714
CE ($/QALY) **including** patient time costs			
1.5% Discount Rate	**-$3,121**	-$6,348	$1,121
3% Discount Rate	-$1,879	-$5,990	$5,067
0% Discount Rate	-$3,453	-$6,111	-$608
CE ($/QALY) **excluding** patient time costs			
1.5% Discount Rate	-$11,666	-$12,859	-$18,145
3% Discount Rate	-$12,764	-$14,285	-$19,477
0% Discount Rate	-$10,490	-$11,473	-$16,475

Screening for Depression in the General Adult Population

Canadian Task Force on Preventive Health Care (2013)[357]

> *Recommendations on screening for depression in primary care settings are provided for people 18 years of age or older who present at a primary care setting with no apparent symptoms of depression. These recommendations do not apply to people with known depression, with a history of depression or who are receiving treatment for depression.*
>
> *For adults at average risk of depression,[358] we recommend not routinely screening for depression. (Weak recommendation; very-low-quality evidence)*
>
> *For adults in subgroups of the population who may be at increased risk of depression,[359] we recommend not routinely screening for depression.[360] (Weak recommendation; very-low-quality evidence)*

Note that the 2013 recommendations from the CTFPHC are different than their 2005 recommendations. In 2005, the CTFPHC recommended the following:

> *There is fair evidence to recommend screening adults in the general population for depression in primary care settings that have integrated programs for feedback to patients and access to case management or mental health care (grade B recommendation).*
>
> *This is insufficient evidence to recommend for or against screening adults in the general; population for depression in primary care settings where effective follow-up and treatment are not available (grade I recommendation).* [361]

United States Preventive Services Task Force Recommendations (2016)

> *The USPSTF recommends screening for depression in the general adult population, including pregnant and postpartum women. Screening should be implemented with adequate systems in place to ensure accurate diagnosis, effective treatment, and appropriate follow-up. (B recommendation)* [362]

Modelling the Clinically Preventable Burden

In this section, we will calculate the CPB associated with screening non-pregnant adults ages 18 and older for depression when staff-assisted depression care supports are in place to assure accurate diagnosis, effective treatment, and follow-up in a BC birth cohort of 40,000.

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[357] Canadian Task Force on Preventive Health Care. Recommendations on screening for depression in adults. *Canadian Medical Association Journal*. 2013; 185(9): 775-82.

[358] The average-risk population includes all individuals 18 years of age or older with no apparent symptoms of depression who are not considered to be at increased risk.

[359] Subgroups of the population who may be at increased risk of depression include people with a family history of depression, traumatic experiences as a child, recent traumatic life events, chronic health problems, substance misuse, perinatal and postpartum status, or Aboriginal origin.

[360] Clinicians should be alert to the possibility of depression, especially in patients with characteristics that may increase the risk of depression, and should look for it when there are clinical clues, such as insomnia, low mood, anhedonia and suicidal thoughts.

[361] MacMillan HL, Patterson CJ and Wathen CN. Screening for depression in primary care: recommendation statement from the Canadian Task Force on Preventive Health Care. *Canadian Medical Association Journal*. 2005; 172(1): 33-5.

[362] Siu AL and the US Preventive Services Task Force (USPSTF). Screening for depression in adults: US Preventive Services Task Force recommendation statement. *JAMA*. 2016; 315(4): 380-7.

In modelling CPB, we made the following assumptions:

- In BC in 2012, 4.6% of the population aged ≥15 had a major depressive episode (MDE) within the previous 12 months (4.0% for males and 5.2% for females). The lifetime risk for an MDE is 11.6% (9.3% for males and 13.9% for females).[363]
- The average duration of a first episode of a MDE is 71.0 weeks (1.37 years) for males and 75.9 weeks (1.46 years) for females (see Table 1).[364]

Table 1: Length of First Major Depression Episode
British Columbia in 2012 by Sex

		Males				***Females***		
Episode duration (as reported)	Episode duration (in weeks)	Number	Percent	Cumulative percent	Episode duration (in weeks)	Number	Percent	Cumulative percent
2 weeks	2.0	8	6.1%	6.1%	2.0	10	4.0%	4.0%
3 weeks	3.0	5	3.8%	9.9%	3.0	4	1.6%	5.6%
1 month	4.3	11	8.4%	18.3%	4.3	33	13.1%	18.7%
2 months	8.7	9	6.9%	25.2%	8.7	19	7.6%	26.3%
3 months	13.0	16	12.2%	37.4%	13.0	17	6.8%	33.1%
4 months	17.3	5	3.8%	41.2%	17.3	7	2.8%	35.9%
5 months	21.7	1	0.8%	42.0%	21.7	9	3.6%	39.4%
6 months	26.0	15	11.5%	53.4%	26.0	31	12.4%	51.8%
7 months	30.3	1	0.8%	54.2%	30.3	0	0.0%	51.8%
8 months	34.7	4	3.1%	57.3%	34.7	5	2.0%	53.8%
9 months	39.0	2	1.5%	58.8%	39.0	4	1.6%	55.4%
10 months	43.3	3	2.3%	61.1%	43.3	2	0.8%	56.2%
11 months	47.7	0	0.0%	61.1%	47.7	2	0.8%	57.0%
1 year	52.0	17	13.0%	74.0%	52.0	40	15.9%	72.9%
2 years*	156.0	25	19.1%	93.1%	156.0	48	19.1%	92.0%
5 years*	364.0	9	6.9%	100.0%	364.0	20	8.0%	100.0%
Total	**71.0**	**131**			**75.9**	**251**		

** Reponses were categorized as ranges: 2-4 years and 5 or more years. Assume a duration of 3 years for the first category and 7 years for the second.*

- Depression is a highly recurrent disorder.[365] On average, half of individuals experiencing at least one MDE during their lifetime will experience between 5-9 recurrent episodes during their lifetime.[366,367,368] For modelling purposes, we assumed that 50% of individuals experiencing an initial MDE would experience 7 recurrent episodes during their lifetime.
- The above information was used to generate the expected number of life years lived with depression by males and females in a BC birth cohort of 40,000. For males, an estimated 0.95% of life years lived between the age of 18 and death would be with

[363] Statistics Canada. Canadian Community Health Survey (CCHS), 2012 Public Use Microdata file (Catalogue number 82M0013X2013001). 2013: All computations, use and interpretation of these data are entirely that of H. Krueger & Associates Inc.
[364] Patten SB. A major depression prognosis calculator based on episode duration. *Clinical Practice and Epidemiology in Mental Health*. 2006; 2(1): 13-20.
[365] Burcusa SL and Iacono WG. Risk for recurrence in depression. *Clinical Psychology Review*. 2007; 27(8): 959-85.
[366] Kessler RC, Zhao S, Blazer DG et al. Prevalence, correlates, and course of minor depression and major depression in the National Comorbidity Survey. *Journal of Affective Disorders*. 1997; 45(1): 19-30.
[367] Kessler RC and Walters EE. Epidemiology of DSM-III-R major depression and minor depression among adolescents and young adults in the national comorbidity survey. *Depression and Anxiety*. 1998; 7(1): 3-14.
[368] Colman I, Naicker K, Zeng Y et al. Predictors of long-term prognosis of depression. *Canadian Medical Association Journal*. 2011; 183(17): 1969-76.

diagnosed depression (see Tables 2). For females, an estimated 1.33% of life years lived between the age of 18 and death would be with diagnosed depression (see Tables 3).

Table 2: Years of Life Lived with Depression
in a British Columbia Male Birth Cohort of 20,000

Males

Age Group	Mean Survival Rate	Individuals in Birth Cohort	Estimated First MDE	Estimated Subsequent MDE	Years of Life with Depression in Birth Cohort	Years of Life in Birth Cohort	% of Life Years with Depression
18-19	0.993	19,862	58.6	205.2	376.8	39,724	0.95%
20-24	0.991	19,821	146.3	512.0	940.0	99,106	0.95%
25-29	0.987	19,742	145.7	510.0	936.2	98,709	0.95%
30-34	0.983	19,666	145.2	508.0	932.6	98,332	0.95%
35-39	0.979	19,571	144.5	505.6	928.1	97,854	0.95%
40-44	0.972	19,442	143.5	502.3	922.0	97,211	0.95%
45-49	0.963	19,263	142.2	497.6	913.5	96,314	0.95%
50-54	0.950	19,003	140.3	490.9	901.2	95,017	0.95%
55-59	0.931	18,619	137.4	481.0	883.0	93,095	0.95%
60-64	0.902	18,041	133.2	466.1	855.5	90,204	0.95%
65-69	0.858	17,164	126.7	443.4	814.0	85,820	0.95%
70-74	0.792	15,837	116.9	409.1	751.0	79,183	0.95%
75-79	0.693	13,861	102.3	358.1	657.3	69,305	0.95%
80+	0.296	5,918	17.5	61.2	112.3	11,836	0.95%
Total Ages 18+			**1,700**	**5,950**	**10,923**	**1,151,710**	**0.95%**

Table 3: Years of Life Lived with Depression
in a British Columbia Female Birth Cohort of 20,000

Females

Age Group	Mean Survival Rate	Individuals in Birth Cohort	Estimated First MDE	Estimated Subsequent MDE	Years of Life with Depresion in Birth Cohort	Years of Life in Birth Cohort	% of Life Years with Depression
18-19	0.994	19,887	82.5	288.8	530.2	39,775	1.33%
20-24	0.993	19,868	206.1	721.3	1,324.1	99,339	1.33%
25-29	0.992	19,836	205.8	720.2	1,322.0	99,179	1.33%
30-34	0.990	19,799	205.4	718.8	1,319.6	98,997	1.33%
35-39	0.987	19,748	204.8	717.0	1,316.1	98,738	1.33%
40-44	0.984	19,672	204.1	714.2	1,311.1	98,358	1.33%
45-49	0.978	19,560	202.9	710.1	1,303.6	97,800	1.33%
50-54	0.970	19,395	201.2	704.2	1,292.7	96,977	1.33%
55-59	0.957	19,150	198.6	695.2	1,276.3	95,748	1.33%
60-64	0.939	18,774	194.7	681.6	1,251.3	93,872	1.33%
65-69	0.909	18,190	188.7	660.4	1,212.3	90,948	1.33%
70-74	0.863	17,265	179.1	626.8	1,150.7	86,325	1.33%
75-79	0.790	15,799	163.9	573.6	1,053.0	78,995	1.33%
80+	0.384	7,677	95.6	334.5	614.0	46,063	1.33%
Total Ages 18+			**2,533**	**8,867**	**16,277**	**1,221,114**	**1.33%**

- Depression increases an individual's mortality risk. Males living with depression are 21 times as likely to commit suicide as males without depression. For females, this ratio increases to 27 times.[369] Individuals living with depression also have higher rates of overall excess mortality with an early meta-analysis suggesting a RR of 1.81

[369] Lépine J-P and Briley M. The increasing burden of depression. *Neuropsychiatric Disease and Treatment*. 2011; 7(Suppl 1): 3-7.

(95% CI of 1.58 to 2.07).[370] This review, however, did not adjust for confounding variables such as chronic illness and lifestyle. After adjusting for tobacco smoking and heavy alcohol use, Murphy et al. found a non-significant increase in mortality associated with depression in men (RR 1.6, 95% CI of 0.8 to 3.1).[371] Other research has found that the effect of depression on mortality is independent of chronic illnesses such as diabetes[372] and congestive heart failure.[373] After adjusting for a number of potentially confounding covariates, including the presence of chronic disease, Schoevers, et al. found a 41% higher mortality rate associated with chronic depression.[374] A more recent meta-analysis of excess mortality associated with depression found a RR of 1.52 (95% CI of 1.45 to 1.59).[375] For modelling purposes we calculated the number of deaths occurring for males and females between the ages of 20 and 74 in our birth cohort and then estimated how many of these deaths would be in individuals living with depression. We assumed that depression would increase the premature mortality rate by 52% and varied this in the sensitivity analysis from 45% to 59%. In males, 20 deaths and 477 life years lost in the cohort are attributable to depression (see Table 4). In females, 18 deaths and 444 life years lost are attributable to depression (see Table 5).

Table 4: Deaths and Life Years Lost Attributable to Depression
in a British Columbia Male Birth Cohort of 20,000

Age Group	Individuals in Birth Cohort	Deaths	Proportion with Depression	Unadjusted Deaths in Pop. With Depression	Adjusted Deaths in Pop. With Depression	Deaths Attributable to Depression	Average Life Years Lived	Life Years Lost to Depression
18-19	19,862							
20-24	19,821	41	0.95%	0.4	0.6	0.2	58.9	12
25-29	19,742	79	0.95%	0.8	1.1	0.4	56.0	22
30-34	19,666	75	0.95%	0.7	1.1	0.4	51.1	19
35-39	19,571	96	0.95%	0.9	1.4	0.5	46.3	22
40-44	19,442	129	0.95%	1.2	1.9	0.6	41.5	26
45-49	19,263	179	0.95%	1.7	2.6	0.9	36.8	33
50-54	19,003	259	0.95%	2.5	3.7	1.3	32.2	41
55-59	18,619	384	0.95%	3.6	5.5	1.9	27.7	53
60-64	18,041	578	0.95%	5.5	8.3	2.9	23.4	67
65-69	17,164	877	0.95%	8.3	12.6	4.3	19.2	83
70-74	15,837	1,327	0.95%	12.6	19.1	6.5	15.3	100
Total		**4,025**		**38**	**58**	**20**		**477**

[370] Cuijpers P and Smit F. Excess mortality in depression: a meta-analysis of community studies. *Journal of Affective Disorders*. 2002; 72(3): 227-36.
[371] Murphy JM, Burke Jr JD, Monson RR et al. Mortality associated with depression: A forty-year perspective from the Stirling County Study. *Social Psychiatry and Psychiatric Epidemiology*. 2008; 43(8): 594-601.
[372] Lin EH, Heckbert SR, Rutter CM et al. Depression and increased mortality in diabetes: unexpected causes of death. *The Annals of Family Medicine*. 2009; 7(5): 414-21.
[373] Jiang W, Alexander J, Christopher E et al. Relationship of depression to increased risk of mortality and rehospitalization in patients with congestive heart failure. *Archives of Internal Medicine*. 2001; 161(15): 1849-56.
[374] Schoevers R, Geerlings M, Deeg D et al. Depression and excess mortality: evidence for a dose response relation in community living elderly. *International Journal of Geriatric Psychiatry*. 2009; 24(2): 169-76.
[375] Cuijpers P, Vogelzangs N, Twisk J et al. Comprehensive meta-analysis of excess mortality in depression in the general community versus patients with specific illnesses. *American Journal of Psychiatry*. 2014; 171(4): 453-62.

Table 5: Deaths and Life Years Lost Attributable to Depression
in a British Columbia Female Birth Cohort of 20,000

Age Group	Individuals in Birth Cohort	Female Deaths	Proportion with Depression	Unadjusted Deaths in Pop. With Depression	Adjusted Deaths in Pop. With Depression	Deaths Attributable to Depression	Average Life Years Lived	Life Years Lost to Depression
18-19	19,887							
20-24	19,868	20	1.33%	0.3	0.4	0.1	62.7	9
25-29	19,836	32	1.33%	0.4	0.6	0.2	57.8	13
30-34	19,799	36	1.33%	0.5	0.7	0.3	52.9	13
35-39	19,748	52	1.33%	0.7	1.0	0.4	48.1	17
40-44	19,672	76	1.33%	1.0	1.5	0.5	43.2	23
45-49	19,560	112	1.33%	1.5	2.3	0.8	38.5	30
50-54	19,395	165	1.33%	2.2	3.3	1.1	33.8	39
55-59	19,150	246	1.33%	3.3	5.0	1.7	29.2	50
60-64	18,774	375	1.33%	5.0	7.6	2.6	24.7	64
65-69	18,190	585	1.33%	7.8	11.8	4.1	20.4	83
70-74	17,265	925	1.33%	12.3	18.7	6.4	16.3	104
Total		**2,622**		**35**	**53**	**18**		**444**

- Diagnosing depression is challenging. "The diagnosis of a mental health disorder is a process that often takes time and develops in a context of trust. Both patient and doctor may need to be sure that the somatic symptoms of depression are exactly that, and not the symptoms of an underlying physical illness."[376]
- Based on a meta-analysis of 41 studies including 50,371 patients, for every 100 patients, GPs identify 10 true positive cases of depression, diagnose 15 patients with depression who do not have depression (false positives) and miss 10 cases of depression (false negatives). Accuracy is improved with prospective examination over an extended period of time (3-12 months) rather than relying on a one-time assessment or case-note records.[377]
- Those who meet screening criteria and were previously undiagnosed by their primary care physician tend to be less severely ill than those who were previously diagnosed.[378,379] Approximately half (52%) of primary care patients identified by screening have transient symptoms (possibly related to life events) lasting less than two weeks and do not require treatment.[380]
- Zimmerman et al. found that 71% of patients diagnosed with major depressive disorder in their outpatient practice had a Hamilton Depression Rating Scale (HDRS) score of less than 22.[381] Scores on the HDRS can be interpreted as follows: no

[376] Kessler D, Sharp D and Lewis G. Screening for depression in primary care. *British Journal of General Practice*. 2005; 55(518): 659-60.
[377] Mitchell AJ, Vaze A and Rao S. Clinical diagnosis of depression in primary care: a meta-analysis. *The Lancet*. 2009; 374(9690): 609-19.
[378] Ormel J, Koeter MW, Van den Brink W et al. Recognition, management, and course of anxiety and depression in general practice. *Archives of General Psychiatry*. 1991; 48(8): 700-6.
[379] Simon GE and VonKorff M. Recognition, management, and outcomes of depression in primary care. *Archives of Family Medicine*. 1995; 4(2): 99-105.
[380] Coyne JC, Klinkman MS, Gallo SM et al. Short-term outcomes of detected and undetected depressed primary care patients and depressed psychiatric patients. *General Hospital Psychiatry*. 1997; 19(5): 333-43.
[381] Zimmerman M, Posternak MA and Chelminski I. Symptom severity and exclusion from antidepressant efficacy trials. *Journal of Clinical Psychopharmacology*. 2002; 22(6): 610-4.

depression (0-7), mild depression (8-16), moderate depression (17-23) and severe depression (≥24).[382]

- When a longitudinal perspective is taken, 30% of patients with depression remain undetected at 1 year and only 14% at the end of 3 years, or approximately one out of seven patients with treatable depression.[383,384,385] For modelling purposes, we assumed that 14% of depression is undiagnosed treatable depression (see Table 6, row *i*) and increased this to 30% in the sensitivity analysis.
- 85% of patients diagnosed with depression were prescribed anti-depressant medication (ADM) in 2011/12 in Canada.[386]
- Approximately 60% of patients stay on ADM for at least 3 months and 45% for at least 6 months.[387,388]
- The use of ADM for major depression is associated with a 64% (OR = 0.36, 95% CI of 0.15 to 0.88) reduced risk of recurrent depression eight years later[389] and a 70% (OR = 0.30, 95% CI of 0.1 to 1.0) reduced risk after 10 years.[390]
- The theoretical cumulative effectiveness of achieving remission through four levels of treatment (primarily medication switching or augmentation) based on the Sequenced Treatment Alternatives to relieve Depression (STAR*D) trial is 36.8% at Level 1, 56.1% at Level 2, 62.1% at Level 3 and 67.1% at Level 4.[391,392] For modelling purposes we used Level 2 (56.1%) results as the base with sensitivity analysis using Level 1 and Level 4 results (see Table 6, row *n*).
- Depression has an important influence on a person's QoL. Studies have also shown that individuals with current or treated depression report lower preference scores for depression health states that the general population.[393,394] Pyne and colleagues suggest that "public stigma may result in the general population being less sympathetic to the suffering of individuals with depression and less willing to validate the impact of

[382] Zimmerman M, Martinez JH, Young D et al. Severity classification on the Hamilton depression rating scale. *Journal of Affective Disorders*. 2013; 150(2): 384-8.
[383] Kessler D, Heath I, Lloyd K et al. Cross sectional study of symptom attribution and recognition of depression and anxiety in primary care. *BMJ*. 1999; 318(7181): 436-40.
[384] Kessler D, Bennewith O, Lewis G et al. Detection of depression and anxiety in primary care: follow up study. *BMJ*. 2002; 325(7371): 1016-7.
[385] Tylee A and Walters P. Underrecognition of anxiety and mood disorders in primary care: why does the problem exist and what can be done? *The Journal of Clinical Psychiatry.* 2006; 68(2): 27-30.
[386] Wong ST, Manca D, Barber D et al. The diagnosis of depression and its treatment in Canadian primary care practices: an epidemiological study. *Canadian Medical Association Journal*. 2014; 2(4): e337-e42.
[387] Solberg LI, Trangle MA and Wineman AP. Follow-up and follow-through of depressed patients in primary care: the critical missing components of quality care. *The Journal of the American Board of Family Practice*. 2005; 18(6): 520-7.
[388] Cantrell CR, Eaddy MT, Shah MB et al. Methods for evaluating patient adherence to antidepressant therapy: a real-world comparison of adherence and economic outcomes. *Medical Care*. 2006; 44(4): 300-3.
[389] Colman I, Zeng Y, Ataullahjan A et al. The association between antidepressant use and depression eight years later: a national cohort study. *Journal of Psychiatric Research*. 2011; 45(8): 1012-8.
[390] Colman I, Croudace TJ, Wadsworth ME et al. Psychiatric outcomes 10 years after treatment with antidepressants or anxiolytics. *The British Journal of Psychiatry*. 2008; 193(4): 327-31.
[391] Howland RH. Sequenced Treatment Alternatives to Relieve Depression (STAR* D): Part 2: Study Outcomes. *Journal of Psychosocial Nursing & Mental Health Services*. 2008; 46(10): 21.
[392] Sinyor M, Schaffer A and Levitt A. The sequenced treatment alternatives to relieve depression (STAR* D) trial: a review. *Canadian Journal of Psychiatry*. 2010; 55(3): 126-35.
[393] Pyne JM, Fortney JC, Tripathi S et al. How bad is depression? Preference score estimates from depressed patients and the general population. *Health Services Research*. 2009; 44(4): 1406-23.
[394] Gerhards SA, Evers SM, Sabel PW et al. Discrepancy in rating health-related quality of life of depression between patient and general population. *Quality of Life Research*. 2011; 20(2): 273-9.

depression symptoms."[395] Revicki and Wood, based on input from patients with depression who had completed at least eight weeks of ADM, identified the following health state utilities: severe depression =0.30, moderate depression = 0.55 to 0.63, mild depression = 0.64 to 0.73 and antidepressant maintenance therapy = 0.72 to 0.83.[396] Whiteford and colleagues[397] suggest the following health utilities:

- Severe depression = 0.35 (95% CI of 0.18-0.53)
- Moderate depression = 0.59 (95% CI of 0.45-0.72)
- Mild depression = 0.84 (95% CI of 0.78-0.89)

For modelling purposes we assumed an equal proportion of individuals with mild, moderate and severe depression and used the average health utilities provided by Whiteford and colleagues (0.59, 95% CI of 0.47-0.72) adjusted for a general population QoL of 0.848 (see Reference Document) resulting in a QoL reduction of 0.30 (see Table 6, row *p*), ranging from 0.16 to 0.45.

- Other assumptions used in assessing the clinically preventable burden are detailed in the Reference Document.

Based on these assumptions, screening for depression results in a CPB of 92 quality-adjusted life years saved (see Table 6, row s). The CPB of 92 represents the gap between existing coverage (no coverage) and the 'best in the world' coverage estimated at 12%.

[395] Pyne JM, Fortney JC, Tripathi S et al. How bad is depression? Preference score estimates from depressed patients and the general population. *Health Services Research*. 2009; 44(4): 1406-23.
[396] Revicki DA and Wood M. Patient-assigned health state utilities for depression-related outcomes: differences by depression severity and antidepressant medications. *Journal of Affective Disorders*. 1998; 48(1): 25-36.
[397] Whiteford HA, Degenhardt L, Rehm J et al. Global burden of disease attributable to mental and substance use disorders: findings from the Global Burden of Disease Study 2010. *The Lancet*. 2013; 382(9904): 1575-86.

Table 6: CPB of Screening for Depression in a Birth Cohort of 40,000			
Row Label	**Variable**	**Base Case**	**Data Source**
a	Life years lived from age 18 to death in a birth cohort of 20,000 males	1,151,710	Table 2
b	Life years lived from age 18 to death in a birth cohort of 20,000 females	1,221,114	Table 3
c	Life years lived with depression in a birth cohort of 20,000 males	10,923	Table 2
d	Life years lived with depression in a birth cohort of 20,000 females	16,277	Table 3
e	Proportion of life years lived with depression in a birth cohort of 20,000 males	0.95%	= c / a
f	Proportion of life years lived with depression in a birth cohort of 20,000 females	1.33%	= d / b
g	Life years lost attributable to depression in a birth cohort of 20,000 males	477	Table 4
h	Life years lost attributable to depression in a birth cohort of 20,000 females	444	Table 5
i	Proportion of treatable depression undiagnosed	14%	√
j	Life years lived with undiagnosed treatable depression in a birth cohort of 20,000 males	1,529	= c * i
k	Life years lived with undiagnosed treatable depression in a birth cohort of 20,000 females	2,279	= d * i
l	Adherence with screening	12%	√
m	Life years lived with undiagnosed treatable depression identified by screening	457	= (j + k) * l
n	Effectiveness of ADM in achieving remission	56%	√
o	Life years lived in remission with treated depression identified by screening	256	= m * n
p	Quality of life reduction	30%	√
q	QALYs gained	77	= o * p
r	Life-years gained / death averted	15	= (g + h) * i * l
s	**Potential QALYs gained, Screening increasing from 0% to 12%**	**92**	= q + r

√ = Estimates from the literature

We also modified a number of major assumptions and recalculated the CPB as follows:

- Assume that the RR of excess mortality associated with depression is reduced from 1.52 to 1.45 (Table 4 and 5): CPB = 90.
- Assume that the RR of excess mortality associated with depression is increased from 1.52 to 1.59 (Table 4 and 5): CPB = 94.
- Assume the proportion of treatable depression that is undiagnosed is increased from 14% to 30% (Table 6, row *i*): CPB = 198.
- Assume the effectiveness of ADM in achieving remission is reduced from 56% to 37% (Table 6, row *l*): CPB = 66.
- Assume the effectiveness of ADM in achieving remission is increased from 56% to 67% (Table 6, row *n*): CPB = 107.
- Assume the QoL adjustment is reduced from 30% to 16% (Table 6, row *p*): CPB = 55.
- Assume the QoL adjustment is increased from 30% to 45% (Table 6, row *p*): CPB = 130.

To this point we have not considered some of the potential harms associated with screening for depression, including the negative side-effects of ADM or the possibility that individuals may be diagnosed with depression who do not have depression (false positives).

- There is a side effect burden associated with taking ADM: 48.7% of individuals taking ADM experienced side effects at least 50% of the time, with the maximum

side effect burden being at least moderate 34.2% of the time.[398] Based on input from patients with depression who had completed at least eight weeks of ADM, Revicki and Wood identified a health state utility of between 0.72 and 0.83 associated with antidepressant maintenance therapy.[399] With an average population health state utility of 0.848 (see Reference Document), this represents a disutility of between 0.02 (or 2.4%) and 0.13 (15.3%). For modelling purposes we assumed a disutility of 8.8% (the midpoint) and varied this assumption from 2.4% and 15.3% in the sensitivity analysis (Table 7, row *t*).

- Screening for depression may result in 15 patients being diagnosed with depression who do not have depression (false positives) for every 10 patients who are true positive cases of depression.[400] For modelling purposes, we have assumed a ratio of 1.5 to 1 false positives to true positives (Table 7, row *n*) and that false positive patients will be prescribed ADM the same as true positive patients.
- One of the harms associated with a diagnosis of depression is being rated (i.e. charged a higher life insurance premium) or being refused insurance coverage when the diagnosis of depression is included in the patient's medical chart. Bell suggests that this is one reason why underdiagnoses may be by design rather than accident.[401] We have not included this potential harm in the modelling.

Based on these additional assumptions, the calculation of CPB is reduced from 92 to -8 quality-adjusted life years saved (see Table 7, row *v*). ***That is, when these harms are taken into account, screening for depression does more harm than good.***

[398] Thase ME, Friedman ES, Biggs MM et al. Cognitive therapy versus medication in augmentation and switch strategies as second-step treatments: a STAR* D report. *The American Journal of Psychiatry*. 2007; 164(5): 739-52.
[399] Revicki DA and Wood M. Patient-assigned health state utilities for depression-related outcomes: differences by depression severity and antidepressant medications. *Journal of Affective Disorders*. 1998; 48(1): 25-36.
[400] Mitchell AJ, Vaze A and Rao S. Clinical diagnosis of depression in primary care: a meta-analysis. *The Lancet*. 2009; 374(9690): 609-19.
[401] Bell JR. Underdiagnosis of depression in primary care: by accident or design? *Journal of the American Medical Association*. 1997; 277(18): 1433-33.

Table 7: CPB of Screening for Depression in a Birth Cohort of 40,000			
Row Label	**Variable**	**Base Case**	**Data Source**
a	Life years lived from age 18 to death in a birth cohort of 20,000 males	1,151,710	Table 2
b	Life years lived from age 18 to death in a birth cohort of 20,000 females	1,221,114	Table 3
c	Life years lived with depression in a birth cohort of 20,000 males	10,923	Table 2
d	Life years lived with depression in a birth cohort of 20,000 females	16,277	Table 3
e	Proportion of life years lived with depression in a birth cohort of 20,000 males	0.95%	= c / a
f	Proportion of life years lived with depression in a birth cohort of 20,000 females	1.33%	= d / b
g	Life years lost attributable to depression in a birth cohort of 20,000 males	477	Table 4
h	Life years lost attributable to depression in a birth cohort of 20,000 females	444	Table 5
i	Proportion of treatable depression undiagnosed	14%	√
j	Life years lived with undiagnosed treatable depression in a birth cohort of 20,000 males	1,529	= c * i
k	Life years lived with undiagnosed treatable depression in a birth cohort of 20,000 females	2,279	= d * i
l	Adherence with screening	12%	√
m	Life years lived with undiagnosed treatable depression identified by screening	457	= (j + k) * l
n	Life years treated for depression - false positives	685	= m * 1.5
o	Effectiveness of ADM in achieving remission	56%	√
p	Life years lived in remission with treated depression identified by screening	256	= m * o
q	Quality of life adjustment	30%	√
r	QALYs gained	77	= p * q
s	Life-years gained / death averted	15	= (g + h) * i * l
t	Disutility associated with ADM	-8.8%	√
u	QALYs lost associated with ADM	-101	= (m + n) * t
v	**Potential QALYs gained, Screening increasing from 0% to 12%**	**-8**	= r + s + u

√ = Estimates from the literature

Modelling Cost-Effectiveness

In this section, we will calculate the CE associated with screening non-pregnant adults ages 18 and older for depression when staff-assisted depression care supports are in place to assure accurate diagnosis, effective treatment, and follow-up in a BC birth cohort of 40,000.

In modelling CE, we made the following assumptions:

- We did not include false positives or the potential disutility associated with taking ADM, as identified in Table 7.
- We assumed that screening would occur annually (Table 8, row *c*).
- For patient time and travel costs, we estimated two hours of patient time required per screening visit (Table 8, row *g*).
- We assumed that diagnosed depression results in an additional 6 physician visits per year and modified this assumption from 4 to 8 in the sensitivity analysis (see Table 8, row *m*).
- Other costs and assumptions used in assessing cost-effectiveness are detailed in the Reference Document.
- Discount rate of 1.5%, varied from 0% to 3% in the sensitivity analysis.

Based on these assumptions, the estimated cost per QALY would be $148,602 (see Table 8, row *s*).

Table 8: CE of Screening for Depression in a Birth Cohort of 40,000

Row Label	Variable	Base Case	Data Source
a	Life years lived from age 18 to death without diagnosed depression in a birth cohort of 20,000 males	1,140,786	Table 6, row a - row c
b	Life years lived from age 18 to death without diagnosed depression in a birth cohort of 20,000 females	1,204,837	Table 6, row b - row d
	Costs of intervention		
c	Frequency of screening (every x years)	1	Assumed
d	Total number of screens (100% adherence)	2,345,623	= (a + b) / c
e	Adherence with screening	12%	Table 6, row l
f	Cost of 10-minute office visit	$34.85	Ref Doc
g	Value of patient time and travel for office visit	$59.38	Ref Doc
h	Portion of 10-minute office visit for screen	50%	Assumed
i	Cost of screening	$13,261,683	= (d * e) * (f + g) * h
j	Life years treated for depression	457	Table 6, row m
k	Annual cost of ADM	$438	Ref Doc
l	Cost of ADM	$200,150	= j * k
m	Annual # of additional visits to a clinician associated with treatment for depression	6	Assumed
n	Cost of additional follow-up office visits to a clinician	$258,358	= (m * j) * (f + g)
	CE calculation		
o	Cost of intervention over lifetime of birth cohort	$13,720,192	= (i + l + n)
p	QALYs saved	92	Table 6, row s
q	Cost of intervention over lifetime of birth cohort (1.5% discount)	$8,692,068	Calculated
r	QALYs saved (1.5% discount)	58	Calculated
s	**CE ($/QALY saved)**	**$148,602**	= q / r

v = Estimates from the literature

We also modified a number of major assumptions and recalculated the CE as follows:

- Assume the proportion of treatable depression that is undiagnosed is increased from 14% to 30% (Table 6, row *i*): CE = $71,996.
- Assume the effectiveness of ADM in achieving remission is reduced from 56% to 37% (Table 6, row *n*): CE = $207,084.
- Assume the effectiveness of ADM in achieving remission is increased from 56% to 67% (Table 6, row *n*): CPB = CE = $127,720.
- Assume the QoL adjustment is reduced from 30% to 16% (Table 6, row *p*): CE = $248,053.
- Assume the QoL adjustment is increased from 30% to 45% (Table 6, row *p*): CE = $105,909.
- Assume that the proportion of an office visit required for screening is reduced from 50% to 33% (Table 8, row *h*): CE = $99,776.
- Assume that the proportion of an office visit required for screening is increased from 50% to 67% (Table 8, row *h*): CE = $197,438.
- Assume that diagnosed depression results in an additional 4 physician visits per year rather than 6 (see Table 8, row *m*): CE = $147,669.
- Assume that diagnosed depression results in an additional 8 physician visits per year rather than 6 (see Table 8, row *m*): CE = $149,535.

Summary – Excluding Harms

Applying a 1.5% discount rate, the clinically preventable burden (CPB) associated with screening non-pregnant adults ages 18 and older for depression (excluding harms) is estimated to be 58 quality-adjusted life years (QALYs) while the cost-effectiveness (CE) is estimated to be $148,602 per QALY (see Table 9).

Table 9: Screening for Depression in a Birth Cohort of 40,000

Summary Excluding Harms

	Base Case	Range	
CPB (Potential QALYs Gained)			
Gap between B.C. Current (0%) and 'Best in the World' (12%)			
1.5% Discount Rate	**58**	35	125
3% Discount Rate	39	23	84
0% Discount Rate	92	55	198
CE ($/QALY) **including** patient time costs			
1.5% Discount Rate	**$148,602**	$71,996	$207,084
3% Discount Rate	$148,602	$71,996	$207,084
0% Discount Rate	$148,602	$71,996	$207,084
CE ($/QALY) **excluding** patient time costs			
1.5% Discount Rate	$56,325	$27,993	$78,492
3% Discount Rate	$56,325	$27,993	$78,492
0% Discount Rate	$56,325	$27,993	$78,492

Summary – Including Harms

Applying a 1.5% discount rate, the clinically preventable burden (CPB) associated with screening non-pregnant adults ages 18 and older for depression (including harms) is estimated to be -5 (that is, harmful) quality-adjusted life years (QALYs). This results in the cost-effectiveness (CE) being dominated (see Table 10).

Table 10: Screening for Depression in a Birth Cohort of 40,000

Summary Including Harms

	Base Case	Range	
CPB (Potential QALYs Gained)			
Gap between B.C. Current (0%) and 'Best in the World' (12%)			
1.5% Discount Rate	**-5**	-29	18
3% Discount Rate	-3	-19	12
0% Discount Rate	-8	-45	29
CE ($/QALY) **including** patient time costs			
1.5% Discount Rate			**$472,872**
3% Discount Rate	Dominated	Dominated	$472,872
0% Discount Rate			$472,872
CE ($/QALY) **excluding** patient time costs			
1.5% Discount Rate			$179,234
3% Discount Rate	Dominated	Dominated	$179,234
0% Discount Rate			$179,234

Screening for Depression in Pregnant and Postpartum Women

Canadian Task Force on Preventive Health Care (2013)

> *For adults in subgroups of the population who may be at increased risk of depression,* [including pregnant and postpartum women, phrase added][402] *we recommend not routinely screening for depression.*[403] *(Weak recommendation; very-low-quality evidence)* [404]

United States Preventive Services Task Force Recommendations (2016)

> *The USPSTF recommends screening for depression in the general adult population,* ***including pregnant and postpartum women*** [emphasis added]. *Screening should be implemented with adequate systems in place to ensure accurate diagnosis, effective treatment, and appropriate follow-up. (B recommendation)* [405]

The Lifetime Prevention Schedule Expert Oversight Committee acknowledges the conflict between the two recommendations. Upon further examination, the USPSTF review included literature investigating screening and treatment of depression in perinatal and postpartum women. The CTFPHC included literature examining screening only, which was sparse; literature examining screening and treatment was excluded. In BC, the current standard for delivery of public health services is offering the Edinburgh Postnatal Depression Scale (EPDS) by eight weeks postpartum, with education/intervention/referral for treatment as needed. The USPSTF review includes a number of validation studies on perinatal and postpartum depression screening tools (including the Edinburgh Postnatal Depression Scale) in a variety of settings. These do not appear in the CTFPHC review. Finally, there are several studies on perinatal and postpartum depression screening and treatment that were published after the CTFPHC review in 2013, but were included in the more recent USPSTF review. Therefore, the LPS will use the USPSTF recommendation as the most current evidence of clinical effectiveness and proceed with the modelling of population health impact and cost-effectiveness of screening and treatment for depression in perinatal and postpartum women.

Modelling the Clinically Preventable Burden

In this section, we will calculate the CPB associated with screening pregnant and postpartum women for depression in a BC birth cohort of 40,000.

In modelling CPB, we made the following assumptions:

- On average, each female in a BC birth cohort would be expected to birth 1.42 children over their lifetime (Table 1, row *a*).[406]

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[402] Subgroups of the population who may be at increased risk of depression include people with a family history of depression, traumatic experiences as a child, recent traumatic life events, chronic health problems, substance misuse, perinatal and postpartum status, or Aboriginal origin.

[403] Clinicians should be alert to the possibility of depression, especially in patients with characteristics that may increase the risk of depression, and should look for it when there are clinical clues, such as insomnia, low mood, anhedonia and suicidal thoughts.

[404] Canadian Task Force on Preventive Health Care. Recommendations on screening for depression in adults. *Canadian Medical Association Journal*. 2013; 185(9): 775-82.

[405] Siu AL and the US Preventive Services Task Force (USPSTF). Screening for depression in adults: US Preventive Services Task Force recommendation statement. *JAMA*. 2016; 315(4): 380-7.

[406] British Columbia Vital Statistics Agency. *Selected Vital Statistics and Health Status Indicators, One Hundred and Fortieth Annual Report 2011*. Available at http://www2.gov.bc.ca/assets/gov/residents/vital-statistics/statistics-reports/annual-reports/2011/pdf/ann2011.pdf. Accessed March 2016.

- In 2003/04, 11.9% of pregnant women in BC visited a physician at least once for depression services during the 27 month time period surrounding their child's birth (9 months before conception to 9 months after giving birth).[407]
- A 2004 systematic review found prevalence rates of depression of 7.4%, 12.8% and 12.0% during the first, second and third trimesters.[408]
- A 2005 systematic review found that the point prevalence of minor and major depressions ranged from approximately 8-11% during pregnancy, peaked at approximately 13% three months after giving birth and then fell to about 6% eight months after giving birth. Less than half of the depressive episodes are MDE.[409] MDE is a distinct clinical syndrome for which treatment is clearly indicated.[410]
- The majority of depressive episodes resolve within three to six months postpartum. A subset of new mothers (approximately 30%), however, remain chronically depressed after this time period.[411]
- For modelling purposes we assumed that screening would occur at 7 weeks post birth (Table 1, row *d*) and modified this to screen at 30 weeks pregnancy in the sensitivity analysis (Table 1, row *e*).
- For modelling purposes we assumed a prevalence of depression of 7.4% during the first trimester, 12.8% during the second trimester, 12.0% during the third trimester and 13% during the eight months after giving birth. We also assumed an equal distribution between mild, moderate and severe depression, yielding a weighted average prevalence of 7.9% for moderate to severe depression (Table 1, row *v*). If we screen at 7 weeks post birth, a potential total of 1,274 years lived with moderate to severe depression between 7 weeks and eight months post birth would be identified in the cohort (Table 1, row *d*). If we screen at 30 weeks pregnant, a potential total of 1,996 years lived with moderate to severe depression between 30 weeks pregnant and eight months post birth would be identified in the cohort (Table 1, row *e*).
- Depression is associated with the following disutility:[412]
    - Severe depression = 0.65 (95% CI of 0.47-0.82)
    - Moderate depression = 0.41 (95% CI of 0.28-0.55)
    - Mild depression = 0.16 (95% CI of 0.11-0.22)

  We assumed an equal distribution between mild, moderate and severe depression, yielding an average disutility of 0.53 (95% CI of 0.38-0.69) for moderate to severe depression. The average QoL for a 18-39 year old is 0.90 (see Reference Document), resulting in a % reduction in QoL of 59% (0.53 / 0.90) (Table 1, row *f*).

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[407] BC Reproductive Mental Health Program. *Addressing Perinatal Depression - A Framework for BC's Health Authorities*. 2006. Available at http://www.health.gov.bc.ca/library/publications/year/2006/MHA_PerinatalDepression.pdf. Accessed March 2016.

[408] Bennett HA, Einarson A, Taddio A et al. Prevalence of depression during pregnancy: systematic review. *Obstetrics & Gynecology*. 2004; 103(4): 698-709.

[409] Gavin NI, Gaynes BN, Lohr KN et al. Perinatal depression: a systematic review of prevalence and incidence. *Obstetrics & Gynecology*. 2005; 106(5, Part 1): 1071-83.

[410] Gaynes BN, Gavin N, Meltzer-Brody S et al. Perinatal depression: Prevalence, screening accuracy, and screening outcomes: Summary. *Evidence Report/Technology Assessment (Summary)* 2005; (119): 1-8.

[411] Vliegen N, Casalin S and Luyten P. The course of postpartum depression: a review of longitudinal studies. *Harvard Review of Psychiatry*. 2014; 22(1): 1-22.

[412] Whiteford HA, Degenhardt L, Rehm J et al. Global burden of disease attributable to mental and substance use disorders: findings from the Global Burden of Disease Study 2010. *The Lancet*. 2013; 382(9904): 1575-86.

- Suicide during the perinatal period is rare, with estimates between one and five per 100,000 live births in high income settings. For modelling purposes we have used a rate of 3/100,000 as the base case and modified this from 1 to 5/100,000 in the sensitivity analysis (Table 1, row *h*). When suicides do occur during this period, the mean age of the mother is 30.5 years, resulting in a loss of 55 QALYs per suicide (Table 1, row *j*).[413] Women who commit suicide during the perinatal period are twice as likely (RR of 2.19, 95% CI of 1.43 to 3.34) to have a diagnosis of depression as women who commit suicide outside of the perinatal period (Table 1, row *k*).[414]
- Mothers with a high level of depressive symptoms report significantly poorer adherence with childhood safety prevention practices such as the consistent use of car seats, covering electrical plugs, and having syrup of ipecac in the home.[415]
- Postpartum depression does not appear to influence the number of well-baby visits or the likelihood of immunization but it may increase the likelihood of infant hospitalization and sick/emergency visits during the first year of life.[416,417]
- Postpartum depression is associated with a 59% (OR of 1.59, 95% CI of 1.24 to 2.04) increase in unintentional injury (Table 1, row *o*) and a 41% (OR of 1.41, 95% CI of 1.02 to 1.95) increase in falls in infants.[418]
- In BC, the rate of hospital separations due to unintentional injuries in children less than 5 years of age is 671 per 100,000 (Table 1, row *m*). The rate of deaths due to unintentional injuries is 10.7 per 100,000 (Table 1, row *n*).[419] If we assume that the average death occurs at age 2, then each death results in 80 years of life lost (Table 1, row *r*).[420]
- Pregnancy and postpartum depression are associated with a shorter duration of breastfeeding.[421] An Australian study found the median duration of breastfeeding to be 26-28 weeks in women with depression and 39 weeks in women without depression.[422] Maternal depressive symptoms at 2 to 4 months postpartum are associated with a 27% (95% CI of 12% to 39%) reduced odds of continuing breastfeeding.[423] For modelling purposes, we assumed a 27% reduction of exclusive

[413] See http://www.statcan.gc.ca/pub/84-537-x/2013005/tbl-eng.htm. Accessed December 2015.
[414] Khalifeh H, Hunt IM, Appleby L et al. Suicide in perinatal and non-perinatal women in contact with psychiatric services: 15 year findings from a UK national inquiry. *The Lancet Psychiatry*. 2016: 1-10.
[415] McLennan JD and Kotelchuck M. Parental prevention practices for young children in the context of maternal depression. *Pediatrics*. 2000; 105(5): 1090-5.
[416] Farr SL, Dietz PM, Rizzo JH et al. Health care utilisation in the first year of life among infants of mothers with perinatal depression or anxiety. *Paediatric and Perinatal Epidemiology*. 2013; 27(1): 81-8.
[417] Minkovitz CS, Strobino D, Scharfstein D et al. Maternal depressive symptoms and children's receipt of health care in the first 3 years of life. *Pediatrics*. 2005; 115(2): 306-14.
[418] Yamaoka Y, Fujiwara T and Tamiya N. Association between maternal postpartum depression and unintentional injury among 4-month-old infants in Japan. *Maternal and Child Health Journal*. 2015; 20: 326-36.
[419] Rajabali F, Han G, Artes S et al. *Unintentional Injuries in British Columbia: Trends and Patterns Among Children & Youth*. 2005. B.C. Injury Research and Prevention Unit. Available at https://northernhealth.ca/Portals/0/Your_Health/Programs/Injury%20Prevention/Unintentional%20Injuries%20in%20BC%20Trends%20Among%20Children%20and%20Youth%202005.pdf. Accessed March 2016.
[420] See http://www.statcan.gc.ca/pub/84-537-x/2013005/tbl-eng.htm. Accessed December 2015.
[421] Dias CC and Figueiredo B. Breastfeeding and depression: A systematic review of the literature. *Journal of Affective Disorders*. 2015; 171: 142-54.
[422] Henderson JJ, Evans SF, Straton JA et al. Impact of postnatal depression on breastfeeding duration. *Birth*. 2003; 30(3): 175-80.
[423] McLearn KT, Minkovitz CS, Strobino DM et al. Maternal depressive symptoms at 2 to 4 months post partum and early parenting practices. *Archives of Pediatrics & Adolescent Medicine*. 2006; 160(3): 279-84.

breastfeeding to six months associated with maternal depression (Table 1, row *u*) and varied this from 12% to 39% in the sensitivity analysis.

- Breastfeeding is associated with a reduced risk of excess weight, otitis media, atopic dermatitis, gastrointestinal infection, lower respiratory tract infection, asthma, type 1 diabetes, childhood leukemia and sudden infant death syndrome in infants and breast and ovarian cancers in the mother.[424,425] In a previous analysis of the promotion of breastfeeding, we calculated that exclusive breastfeeding to six months is associated with an increase of 0.40 QALYs per infant/mother pair (Table 1, row *t*).[426]
- Depression *in the year before birth* is independently associated with an increase in the risk of Sudden Infant Death Syndrome (SIDS) (OR of 4.9, 95% CI of 1.1 to 22.1). Depression *during pregnancy or after birth* is not significantly associated with SIDS.[427] Since the proposed screening for depression would take place during pregnancy or shortly after birth, we have not included SIDS in this analysis.
- An increased risk of preterm birth is associated with antenatal depression and has been estimated at 37% (OR of 1.37, 95% CI of 1.04 to 1.81) and 39% (OR of 1.39, 95% CI of 1.19 to 1.61) in two meta-analyses.[428,429]
- Preterm births, including late preterm births, are associated with a greater risk of developmental delay, mental retardation, cerebral palsy, and poor health related outcomes (and utilization) during their first year.[430,431,432]
- Children born preterm tend to have a lower overall QoL than their full term counterparts. The difference in QoL decreases with age (a disutility of 0.13 from birth to age 12 and a disutility of 0.06 from age 13 to 19) and tends to disappear when they become adults.[433]
- Screening and treatment for depression starting late in pregnancy or shortly after birth, however, is unlikely to have an impact on pre-term birth rates and has not been included in this analysis.
- Maternal depressive symptoms at 2 to 4 months postpartum are associated with a 19% reduced odds of showing books, 30% reduced odds of playing with the infant,

[424] Chung M, Raman G, Trikalinos T et al. Interventions in primary care to promote breastfeeding: an evidence review for the US Preventive Services Task Force. *Annals of Internal Medicine*. 2008; 149(8): 565-82.
[425] Bartick M and Reinhold A. The burden of suboptimal breastfeeding in the United States: a pediatric cost analysis. *Pediatrics*. 2010; 125(5): e1048-e56.
[426] H. Krueger & Associates Inc. *Establishing Priorities among Effective Clinical Prevention Services in British Columbia (Update): Technical Report for Breastfeeding, Screening for Type 2 Diabetes, STI Behavioural Counselling and Obesity in Adults.* March 30, 2015.
[427] Howard LM, Kirkwood G and Latinovic R. Sudden infant death syndrome and maternal depression. *The Journal of Clinical Psychiatry*. 2007; 68(8): 1279-83.
[428] Grigoriadis S, VonderPorten EH, Mamisashvili L et al. The impact of maternal depression during pregnancy on perinatal outcomes: a systematic review and meta-analysis. *The Journal of Clinical Psychiatry*. 2013; 74(4): e321-e41.
[429] Grote NK, Bridge JA, Gavin AR et al. A meta-analysis of depression during pregnancy and the risk of preterm birth, low birth weight, and intrauterine growth restriction. *Archives of General Psychiatry*. 2010; 67(10): 1012-24.
[430] Dong Y and Yu JL. An overview of morbidity, mortality and long-term outcome of late preterm birth. *World Journal of Pediatrics*. 2011; 7(3): 199-204.
[431] McGowan JE, Alderdice FA, Holmes VA et al. Early childhood development of late-preterm infants: a systematic review. *Pediatrics*. 2011; 127(6): 1111-24.
[432] Samra HA, McGrath JM and Wehbe M. An integrated review of developmental outcomes and late-preterm birth. *Journal of Obstetric, Gynecologic, and Neonatal Nursing*. 2011; 40(4): 399-411.
[433] Zwicker JG and Harris SR. Quality of life of formerly preterm and very low birth weight infants from preschool age to adulthood: a systematic review. *Pediatrics*. 2008; 121(2): e366-e76.

26% reduced odds of talking to the infant and 39% reduced odds of following routines, compared to mothers without depressive symptoms.[434]

- Few studies have assessed the benefits of treating depression during the perinatal period and the subsequent well-being of the child. The limited research available "has yielded a mixed pattern of results suggesting additional investigations are needed."[435]
- A commonly used depression screening instrument in postpartum and pregnant women is the Edinburgh Postnatal Depression Scale (EPDS). The sensitivity of the EPDS is 0.79 (95% CI of 0.72 to 0.85) and the specificity is always higher than 0.87.[436] This means that the test would identify 79% of true positive cases (women with perinatal depression) and would falsely identify 13% of cases as positive (the false positive rate) (Table 1, row *y*).
- Involvement in screening programs, with or without additional treatment components, is associated with an 18% to 59% (weighted mean of 32%) reduced risk of depression (Table 1, row *ab*).[437]
- The use of second generation antidepressants during pregnancy may be associated with increased risk of some serious side-effects,[438] although the research remains unclear.[439,440]
- Cognitive behavioural therapy (CBT) is associated with a 34% (RR of 1.34, 95% CI of 1.19 to 1.50) increase in the likelihood of remission.[441]
- Other assumptions used in assessing the clinically preventable burden are detailed in the Reference Document.

Based on these assumptions, the CPB is 109 quality-adjusted life years saved (see Table 1, row *ae*). The CPB of 109 represents the gap between no coverage and the 'best in the world' coverage estimated at 40%.

[434] McLearn KT, Minkovitz CS, Strobino DM et al. Maternal depressive symptoms at 2 to 4 months post partum and early parenting practices. *Archives of Pediatrics & Adolescent Medicine*. 2006; 160(3): 279-84.
[435] Stein A, Pearson RM, Goodman SH et al. Effects of perinatal mental disorders on the fetus and child. *The Lancet*. 2014; 384(9956): 1800-19.
[436] O'Connor E, Rossom RC, Henninger M et al. Primary care screening for and treatment of depression in pregnant and postpartum women: evidence report and systematic review for the US Preventive Services Task Force. *JAMA*. 2016; 315(4): 388-406.
[437] Ibid.
[438] Ibid.
[439] Molyneaux E, Trevillion K and Howard LM. Antidepressant treatment for postnatal depression. *JAMA*. 2015; 313(19): 1965-6.
[440] Furu K, Kieler H, Haglund B et al. Selective serotonin reuptake inhibitors and venlafaxine in early pregnancy and risk of birth defects: population based cohort study and sibling design. *BMJ*. 2015; 350: h1798-h806.
[441] O'Connor E, Rossom RC, Henninger M et al. Primary care screening for and treatment of depression in pregnant and postpartum women: evidence report and systematic review for the US Preventive Services Task Force. *JAMA*. 2016; 315(4): 388-406.

Table 1: Calculation of Clinically Preventable Burden (CPB) Estimate for Screening Pregnant and Postpartum Women for Depression in a Birth Cohort of 40,000 (B.C.)			
Row Label	**Variable**	**Base Case**	**Data Source**
a	Lifetime live births per female	1.42	√
b	Proportion of females surviving to age 20 in the cohort	99.39%	√
c	Number of pregnancies in the birth cohort	28,226	= (b * 20,000) * a
d	Estimated years lived with moderate to severe perinatal depression - 7 weeks post birth to 34 weeks post birth	1,274	√
e	Estimated years lived with moderate to severe perinatal depression - 30 weeks pregnant to 34 weeks post birth	1,996	√
f	Disutility associated with moderate to severe depression	0.59	√
g	QALYs lost due to moderate to severe perinatal depression	750	= d * f
h	Rate of suicide in perinatal women without depression	0.00003	√
i	Suicides in perinatal women without depression	0.85	= c * h
j	Years of life lost due to suicide	55	√
k	Increase in risk of suicide in perinatal women with depression	119%	√
l	QALYs lost due to suicide attributable to perinatal depression	55.4	= (i * k) * j
m	Rate of hospitalizations due to unintentional injuries in children age 0-4; mothers without depression	0.0067	√
n	Mortality rate due to unintentional injuries in children age 0-4; mothers without depression	0.00011	√
o	Increased risk of unintentional injuries; mothers with depression	59%	√
p	Hospitalizations due unintentional injuries in children age 0-4 attributable to mothers with depression	112	= (r * c) * t
q	Deaths due to unintentional injuries in children age 0-4 attributable to mothers with depression	1.8	= (s * c) * t
r	Years of life lost due to death of child from unintentional injury	80	√
s	QALYs lost due to unintentional injury attributable to perinatal depression	143	= q * r
t	QALYs lost per mother/infant pair due to not exclusively breastfeeding to six months	0.40	√
u	Reduced risk of exclusive breastfeeding to six months associated with maternal depression	27%	√
v	Estimated prevalence of moderate to severe perinatal depression	7.9%	√
w	QALYs lost due to shorter duration of breastfeeding	241	= v * c * t * u
x	**Total QALYs lost due to moderate to severe perinatal depression**	**1,189**	= g + j + s + w
y	Proportion of true positive cases identified by using the EPDS	79%	√
z	Adherence with screening	39%	Ref Doc
aa	Years lived with moderate to severe perinatal depression identified	366	= (w * z) * y
ab	Effectiveness of screening in reducing the risk of moderate to severe depression	32%	√
ac	Years lived with moderate to severe perinatal depression reduced by	117	= aa * ab
ad	% of years lived with moderate to severe perinatal depression reduced by screening	9.2%	= ac / d
ae	**Potential QALYs saved (CPB) - Screening increasing from 0% to 40%**	**109**	= x * ad

√ = Estimates from the literature

We also modified a number of major assumptions and recalculated the CPB as follows:

- Assume that screening would occur at 30 weeks pregnant and again at 7 weeks post birth instead of just at 7 weeks post birth (Table 1, row *e*): CPB = 202.
- Assume that the disutility associated with moderate to severe depression is reduced from 0.59 to 0.42 (Table 1, row *f*): CPB = 73.
- Assume that the disutility associated with moderate to severe depression is increased from 0.59 to 0.76 (Table 1, row *f*): CPB = 153.

- Assume that the increased risk of unintentional injuries in children (mothers with depression) is reduced from 59% to 24% (Table 1, row *o*): CPB = 94.
- Assume that the increased risk of unintentional injuries in children (mothers with depression) is increased from 59% to 104% (Table 1, row *o*): CPB = 130.
- Assume that the effectiveness of screening in reducing the risk of moderate to severe depression is reduced from 32% to 18% (Table 1, row *ab*): CPB = 62.
- Assume that the effectiveness of screening in reducing the risk of moderate to severe depression is increased from 32% to 59% (Table 1, row *ab*): CPB = 202.
- Assume that the reduced risk of exclusive breastfeeding to six months associated with maternal depression is reduced from 27% to 12% (Table 1, row *u*): CPB = 86.
- Assume that the reduced risk of exclusive breastfeeding to six months associated with maternal depression is increased from 27% to 39% (Table 1, row *u*): CPB = 130.

Modelling Cost-Effectiveness

In this section, we will calculate the CE associated with screening pregnant and postpartum women for depression in a BC birth cohort of 40,000.

In modelling CE, we made the following assumptions:

- **Expected screens** - We assumed that screening would occur once per pregnancy (Table 2, row *a*) and modified this to twice in the sensitivity analysis. [442,443]
- **Cost of office visit** - Screening with the EPDS takes approximately 5 minutes.[444] We therefore assumed that 50% of a 10-minute office visit would be required for the screening and varied this from 33% to 67% in the sensitivity analysis (Table 2, row *h*).
- **Evaluation of women with positive screens** – Women who test positive for depression on the EPDS should be offered a psychiatric diagnostic assessment.[445] We assumed a cost of $237.95 for this assessment, based on fee code 00610 – full diagnostic interview by a psychiatrist in the BC MSC Payment Schedule (Table 2, row *o*).[446] The assessment and fee applies to all true and false positive cases.
- **Treatment for depression** – For the base model, we assumed that women with severe depression would be treated with CBT rather than antidepressant medication, due to potential safety concerns. CBT can be provided in a group or to an individual. Individual therapy consists of 12 – 90 minute sessions with 1-2 follow-up sessions

[442] British Columbia. *Healthy Start Initiative: Provincial Perinatal, Child and Family Public Health Services.* April 2013
[443] BC Reproductive Mental Health Program and Perinatal Services BC. *Best Practice Guidelines for Mental Health Disorders in the Perinatal Period*. 2014. Available at http://www.perinatalservicesbc.ca/Documents/Guidelines-Standards/Maternal/MentalHealthDisordersGuideline.pdf. Accessed March 2016.
[444] Ibid.
[445] Wisner KL, Sit DK, McShea MC et al. Onset timing, thoughts of self-harm, and diagnoses in postpartum women with screen-positive depression findings. *JAMA Psychiatry*. 2013; 70(5): 490-8.
[446] Medical Services Commission. *MSC Payment Schedule*. 2017. Available online at https://www2.gov.bc.ca/assets/gov/health/practitioner-pro/medical-services-plan/msc-payment-schedule-july-2017.pdf. Accessed February 2018.

lasting from 10-30 minutes for a total therapy time of approximately 19 hours.[447] The cost of psychiatric treatment in BC is $169.75 per hour[448] for a total cost of $3,225 per individual. Group therapy general consists of 1 initial individual session lasting 90 minutes, eight individuals receiving 12 – 120 minute sessions with 1-2 follow-up sessions lasting from 10-30 minutes.[449] The cost of group therapy in BC with eight clients is $269 per hour.[450] The cost of group therapy would therefore be $1,231 per person (Table 2, row *q*). For modelling purposes, we assumed in the base model that CBT would be provided as group therapy and then included the costs for individual therapy in the sensitivity analysis. For patient time and travel costs associated with CBT we assumed 26.5 hours in therapy plus 1 hour travel for each session for a total of 41 hours. If antidepressant medication is used, the cost/day for antidepressant prescriptions in BC ranges from $1.00 for prescriptions paid by the provincial government to $1.19 for prescription paid for by uninsured patients and $1.27 paid for by private insurers.[451] The weighted average is $1.15/day or $420/year.

- **Hospitalizations avoided due to unintentional injury** – We assumed that the hospital costs per unintentional injury would be $20,524 (Table 2, row *u*).[452]
- **Costs avoided due to increased duration of breastfeeding** - In a previous analysis of the promotion of breastfeeding, we calculated that exclusive breastfeeding to six months is associated with costs avoided of $2,067 per infant/mother pair (Table 2, row *w*).[453]
- Other costs and assumptions used in assessing cost-effectiveness are detailed in the Reference Document.
- Discount rate of 1.5%, varied from 0% to 3% in the sensitivity analysis.

Based on these assumptions, the estimated cost per QALY would be $23,042 (Table 2, row *ad*).

[447] Stevenson M, Scope A, Sutcliffe P et al. Group cognitive behavioural therapy for postnatal depression: a systematic review of clinical effectiveness, cost-effectiveness and value of information analyses. *Health Technology Assessment*. 2010; 14(44): 1-135.
[448] Medical Services Commission. *MSC Payment Schedule*. 2017. Available online at https://www2.gov.bc.ca/assets/gov/health/practitioner-pro/medical-services-plan/msc-payment-schedule-july-2017.pdf. Accessed February 2018.
[449] Stevenson M, Scope A, Sutcliffe P et al. Group cognitive behavioural therapy for postnatal depression: a systematic review of clinical effectiveness, cost-effectiveness and value of information analyses. *Health Technology Assessment*. 2010; 14(44): 1-135.
[450] Medical Services Commission. *MSC Payment Schedule*. 2017. Available online at https://www2.gov.bc.ca/assets/gov/health/practitioner-pro/medical-services-plan/msc-payment-schedule-july-2017.pdf. Accessed February 2018.
[451] Morgan S, Smolina K, Mooney D et al. *The Canadian Rx Atlas, Third Edition*. 2013. UBC Centre for Health Services and Policy Research. Available at http://www.chspr.ubc.ca/sites/default/files/file_upload/publications/2013/RxAtlas/canadianrxatlas2013.pdf. Accessed December 2015.
[452] British Columbia Injury Research and Prevention Unit. *Economic Burden of Injury in British Columbia*. 2015. Available at http://www.injuryresearch.bc.ca/wp-content/uploads/2015/08/BCIRPU-EB-2015.pdf. Accessed March 2016.
[453] H. Krueger & Associates Inc. *Establishing Priorities among Effective Clinical Prevention Services in British Columbia (Update): Technical Report for Breastfeeding, Screening for Type 2 Diabetes, STI Behavioural Counselling and Obesity in Adults.* March 30, 2015.

Table 2. Calculation of Cost-effectiveness (CE) for Screening Pregnant and Postpartum Women for Depression in a Birth Cohort of 40,000			
Row Label	**Variable**	**Base Case**	**Data Source**
a	Number of screens per pregnancy	1	√
b	Number of pregnancies in the birth cohort	28,226	= Table 1, row c
c	Total # of screens in birth cohort - 100% adherence	28,226	= a * b
d	Adherence with screening	39%	= Table 1, row z
e	Total # of screens in birth cohort - 40% adherence	11,008	= c * d
f	Cost of 10-minute office visit	$34.85	Ref Doc
g	Value of patient time and travel for office visit	$59.38	Ref Doc
h	Portion of 10-minute office visit for screen	50%	√
i	Cost of screening	$518,652	= e* (f + g) * h
j	Estimated prevalence of perinatal depression	7.9%	= Table 1, row v
k	EPDS true positive %	79%	= Table 1, row y
l	EPDS false positive %	13%	√
m	# of true positive screens	688	= b * d * j * k
n	# of false positive screens	113	= b * d * j * l
o	Cost per psychiatric assessment	$237.95	√
p	Cost of psychiatric assessment	$238,068	= (m + n) * o + (m + n) * g
q	Cost of CBT / ADM per individual	$1,231	√
r	Costs of patient time for CBT per individual	$1,217	= 41 * (g / 2)
s	Cost of CBT	$1,683,308	= (q + r) *m
t	Hospitalizations due to unintentional injuries avoided with screening	10.3	= Table 1, row p * Table 1, row ad
u	Cost of hospital treatment	$20,524	√
v	Costs avoided due to unintentional injury hospitalizations avoided	-$211,015	= t * u
w	Costs avoided due to exclusive breastfeeding to six months per mother / infant pair	-$2,067	√
x	Reduced risk of exclusive breastfeeding associated with maternal depression	27%	= Table 1, row u
y	Costs avoided due to longer duration of breastfeeding	-$114,588	= Table 1, row v * Table 1, row c * Table 1, row ad * w * x
z	Net screening and patient costs (undiscounted)	$2,114,425	= i + p + s + v + y
aa	QALYs saved (undiscounted)	109	= Table 1, row ae
ab	Net screening and patient costs (1.5% discount)	$2,131,450	Calculated
ac	QALYs saved (1.5% discount)	93	Calculated
ad	**CE ($/QALY saved)**	**$23,042**	= ab / ac

√ = Estimates from the literature

We also modified a number of major assumptions and recalculated the CE as follows:

- Assume that screening would occur at 30 weeks pregnant and again at 7 weeks post birth instead of just at 7 weeks post birth (Table 1, row *e*): CE = $28,566.
- Assume that the disutility associated with moderate to severe depression is reduced from 0.59 to 0.42 (Table 1, row *f*): CE = $36,843.
- Assume that the disutility associated with moderate to severe depression is increased from 0.59 to 0.76 (Table 1, row *f*): CE = $15,632.
- Assume that the increased risk of unintentional injuries in children (mothers with depression) is reduced from 59% to 24% (Table 1, row *o*): CE = $27,714.
- Assume that the increased risk of unintentional injuries in children (mothers with depression) is increased from 59% to 104% (Table 1, row *o*): CE = $18,030.
- Assume that the effectiveness of screening in reducing the risk of depression is reduced from 32% to 18% (Table 1, row *ab*): CE = $43,255.

- Assume that the effectiveness of screening in reducing the risk of depression is increased from 32% to 59% (Table 1, row *ab*): CE = $11,149.
- Assume that the portion of a 10-minute office visit required for screening is reduced from 50% to 33% (Table 2, row *h*): CE = $21,163.
- Assume that the portion of a 10-minute office visit required for screening is increased from 50% to 67% (Table 2, row *h*): CE = $24,920.
- Assume that the cost of CBT per individual is increased from $1,231 to $3,225 (Table 2, row *q*): CE = $37,644.
- Assume that 50% of individuals use group CBT and 50% ADM (Table 2, row *q*): CE = $20,072.
- Assume that the reduced risk of exclusive breastfeeding to six months associated with maternal depression is reduced from 27% to 12% (Table 1, row *u*): CE = $29,016.
- Assume that the reduced risk of exclusive breastfeeding to six months associated with maternal depression is increased from 27% to 39% (Table 1, row *u*): CE = $19,357.

Summary

Applying a 1.5% discount rate, the clinically preventable burden (CPB) associated with screening pregnant and postpartum women for depression is estimated to be 93 quality-adjusted life years (QALYs) while the cost-effectiveness (CE) is estimated to be $23,042 per QALY (see Table 3).

Table 3: Offer of Screening Pregnant and Postpartum Women for Depression in a Birth Cohort of 40,000

Summary

	Base Case	Range	
CPB (Potential QALYs Gained)			
Gap between 0% and 'Best in the World' (39%)			
1.5% Discount Rate	**93**	52	171
3% Discount Rate	79	45	146
0% Discount Rate	109	62	202
CE ($/QALY) **including** patient time costs			
1.5% Discount Rate	**$23,042**	$11,149	$43,255
3% Discount Rate	$26,846	$13,163	$50,109
0% Discount Rate	$19,334	$9,124	$36,688
CE ($/QALY) **excluding** patient time costs			
1.5% Discount Rate	$10,140	$4,151	$20,319
3% Discount Rate	$12,002	$5,110	$23,715
0% Discount Rate	$8,258	$3,116	$16,997

Screening for Osteoporosis to Prevent Fractures

United States Preventive Services Task Force Recommendations[454]

The USPSTF recommends screening for osteoporosis with bone measurement testing to prevent osteoporotic fractures in women 65 years and older. (B recommendation)

The USPSTF recommends screening for osteoporosis with bone measurement testing to prevent osteoporotic fractures in postmenopausal women younger than 65 years at increased risk of osteoporosis, as determined by a formal clinical risk assessment tool. (B recommendation)

The USPSTF concludes that the current evidence is insufficient to assess the balance of benefits and harms of screening for osteoporosis to prevent osteoporotic fractures in men. (I statement)

In discussing the limitations of their recommendation, the USPSTF states that "…evidence is limited on the direct question of the benefits and harms of screening for elevated osteoporotic fracture risk. The indirect evidence pathway rests on studies evaluating (1) the accuracy of screening approaches in identifying osteoporosis and predicting fractures and (2) the benefits of treatment among those with osteoporosis or at high risk for fractures. Other limitations of the evidence base relate to underlying heterogeneity in baseline risk, prior fractures, prior treatment, and duration of follow-up."[455]

Canadian Task Force on Preventive Health Care Recommendations

The CTFPHC does not have a current published recommendation on screening for osteoporosis.[456]

We will follow the approach of the USPSTF and model the path of indirect evidence.

Modelling the Clinically Preventable Burden

In this section, we will calculate the CPB associated with screening for osteoporosis in females ages 65 and older.

In modelling CPB, we made the following assumptions:

- Using longitudinal peak bone mineral data from the Canadian multicentre osteoporosis study (CaMos), Berger et al estimate the prevalence of osteoporosis in Canadian women over 65 years old to be 37.1% (95% CI 33.6% – 42.7%).[457]

[454] Curry SJ, Krist AH, Owens DK et al. Screening for osteoporosis to prevent fractures: US Preventive Services Task Force recommendation statement. *Journal of the American Medical Association.* 2018; 319(24): 2521-31.
[455] Viswanathan M, Reddy S, Berkman N et al. Screening to Prevent Osteoporotic Fractures: An Evidence Review for the US Preventive Services Task Force. 2018: Available at https://www.ncbi.nlm.nih.gov/books/NBK532075/. Accessed December 2018.
[456] Canadian Task Force on Preventive Health Care. *Published Guidelines.* 2018. Available at https://canadiantaskforce.ca/guidelines/published-guidelines/ Accessed November 2018.
[457] Berger C, Goltzman D, Langsetmo L et al. Peak bone mass from longitudinal data: implications for the prevalence, pathophysiology, and diagnosis of osteoporosis. *Journal of Bone and Mineral Research*. 2010; 25(9): 1948-57.

- Cheng et al. evaluated Medicare claims in the US and estimated the following prevalence of osteoporosis in women by age:[458] 65 – 69 (29.8%), 70 – 74 (33.7%), and 75 – 79 (41.8%), 80 + (48.3%).
- The prevalence of osteoporosis in BC women by age, based on data from BBC's Chronic Disease Registry between 2001 and 2017, is as follows: 65 – 69 (19.2%), 70 – 74 (25.3%), and 75 – 79 (30.7%), 80 + (37.1%). [459]

Table 1: Screening for Osteoporosis in Women Ages 65 and Older
Prevalence of Osteoporosis
In a BC Birth Cohort of 40,000

Age	# in Cohort	Deaths in Cohort	Death Rate / 100,000	Years Lived	Prevalence of Osteoporosis	Years Lived with Osteoporosis
64	18,572					
65	18,456	116	629	18,392	19.2%	3,543
66	18,329	127	692	18,259	19.2%	3,519
67	18,190	139	765	18,113	19.2%	3,492
68	18,037	152	845	17,954	19.2%	3,463
69	17,870	167	936	17,778	19.2%	3,431
70	17,687	183	1,036	17,586	25.3%	4,475
71	17,486	201	1,151	17,375	25.3%	4,424
72	17,265	221	1,278	17,144	25.3%	4,368
73	17,023	242	1,422	16,890	25.3%	4,307
74	16,758	265	1,584	16,612	25.3%	4,240
75	16,467	291	1,766	16,307	30.7%	5,055
76	16,148	319	1,974	15,973	30.7%	4,957
77	15,799	349	2,209	15,608	30.7%	4,850
78	15,418	381	2,474	15,209	30.7%	4,733
79	15,001	417	2,777	14,774	30.7%	4,605
80	14,547	454	3,121	14,300	37.1%	5,397
81	14,053	494	3,514	13,785	37.1%	5,214
82	13,517	536	3,964	13,228	37.1%	5,015
83	12,938	579	4,477	12,626	37.1%	4,800
84	12,314	624	5,066	11,980	37.1%	4,569
85	11,645	669	5,747	11,288	37.1%	4,320
86	10,931	714	6,532	10,553	37.1%	4,055
Total		**7,640**		**341,738**	**28.3%**	**96,834**

- We used the age-specific estimates of prevalence from the BC Chronic Disease Registry applied to our BC cohort of women starting at age 65 and continuing to age 86 (based on the average life expectancy of 22 years for a 65 year old women) and estimated a prevalence in BC of 28.3% (see Table 1), lower than the 37.1% identified by Berger et al.[460]

[458] Cheng H, Gary L, Curtis J et al. Estimated prevalence and patterns of presumed osteoporosis among older Americans based on Medicare data. *Osteoporosis International*. 2009; 20(9): 1507-15.
[459] Aciemme (Sam) Ospan, Senior Manager, Lifetime Prevention Schedule, Healthy Living and Health Promotion Branch, BC Ministry of Health. September 13, 2019. Personal communication.
[460] Berger C, Goltzman D, Langsetmo L et al. Peak bone mass from longitudinal data: implications for the prevalence, pathophysiology, and diagnosis of osteoporosis. *Journal of Bone and Mineral Research*. 2010; 25(9): 1948-57.

- A study by Hopkins and colleagues calculated the total number of patients with fractures in Canada between April 1, 2010 and March 31, 2011, by sex, age and type of fracture using data from the Canadian Institute for Health Information (CIHI).[461] The various types of fractures were identified based on International Statistical Classification of Diseases and Related Health Problems, Tenth Revision, Canada (ICD-10-CA) codes. We compiled the relevant data for women ages 60-89 and calculated the incidence rate per 100,000 by age group (60-69, 70-79 and 80-89) by fracture type (see Table 2).

Table 2: Screening for Osteoporosis in Women Ages 65 and Older
Incidence of Fractures by Type of Fracture and Age

	Age Group			
	60 - 69	70 - 79	80 - 89	Total
Female Population in 2011	1,760,036	1,085,293	681,159	3,526,488
Number of Fractures in Canada in 2011				
Hip	1,826	4,238	9,612	15,676
Vertebral	904	1,673	2,540	5,117
All Other				
Wrist	7,584	5,131	4,486	17,201
Humerus	1,844	2,015	2,423	6,282
Other	8,867	8,055	11,779	28,701
Multiple	1,271	1,835	2,769	5,875
Subtotal All Other	19,566	17,036	21,457	58,059
Total	**22,296**	**22,947**	**33,609**	**78,852**
Fracture Rate per 100,000 person years				
Hip	104	390	1,411	445
Vertebral	51	154	373	145
All Other				
Wrist	431	473	659	488
Humerus	105	186	356	178
Other	504	742	1,729	814
Multiple	72	169	407	167
Subtotal All Other	1,112	1,570	3,150	1,646
Total	**1,267**	**2,114**	**4,934**	**2,236**

- For modelling purposes, we assumed a hip fracture rate of 104 / 100,000 person years in women ages 65-69, 390 / 100,000 person years in women ages 70-79 and 1,411 / 100,000 person years in women ages 80-86. Furthermore, we assumed a vertebral fracture rate of 51 / 100,000 person years in women ages 65-69, 154 / 100,000 person years in women ages 70-79 and 373 / 100,000 person years in women ages 80-86. Finally, we assumed a non-hip, non-vertebral fracture rate of 1,112 / 100,000 person years in women ages 65-69, 1,570 / 100,000 person years in women ages 70-79 and 3,150 / 100,000 person years in women ages 80-86.

[461] Hopkins R, Burke N, Von Keyserlingk C et al. The current economic burden of illness of osteoporosis in Canada. *Osteoporosis International*. 2016; 27(10): 3023-32.

- Lippuner and colleagues estimated that 71% of hip fractures in 65-74 year olds are attributable to osteoporosis.[462] This increases to 91% in 74-84 year olds. Similarly, approximately 81% of vertebral fractures in 65-84 year olds are attributable to osteoporosis. Finally, non-hip, non-vertebral, non-stress fractures attributable to osteoporosis ranged from 50-78% for ages 65-74 and between 60-91% for ages 75+.
- In their economic modelling, Hopkins et al assumed that 100% of hip and vertebral fractures are attributable to osteoporosis while 81.5% of all other fractures in women are attributable to osteoporosis.[463]

- For modelling purposes, we assumed that 71% of hip fractures in 65-74 year olds are attributable to osteoporosis, increasing to 91% at age 75, that 81% of vertebral fractures are attributable to osteoporosis and 81.5% of all other fractures are attributable to osteoporosis (see Table 3).

- In Table 3, we show that for the 22 years modelled for the cohort beginning at age 65, the total number of osteoporosis-attributable fractures is 7,379. Of these, 1,708 are hip fractures, 507 are vertebral fractures and 5,164 are other fractures.

Table 3: Screening for Osteoporosis in Women Ages 65 and Older
Number of Fractures Attributable to Osteoporosis
In a BC Birth Cohort of 40,000

				Rate per 100,000 Person Years			*Number of Fractures*			*Percent of Fractures Attributable to Osteoporosis*			*Fractures Attributable to Osteoporosis*		
Age	# in Cohort	Deaths in Cohort	Years Lived	Hip Fracture	Vertebral Fracture	All Other Fractures	Hip Fracture	Vertebral Fracture	All Other Fractures	Hip Fracture	Vertebral Fracture	All Other Fractures	Hip Fracture	Vertebral Fracture	All Other Fractures
64	18,572														
65	18,456	116	18,392	104	51	1,112	19	9	204	71.0%	81.0%	81.5%	14	8	167
66	18,329	127	18,259	104	51	1,112	19	9	203	71.0%	81.0%	81.5%	13	8	165
67	18,190	139	18,113	104	51	1,112	19	9	201	71.0%	81.0%	81.5%	13	8	164
68	18,037	152	17,954	104	51	1,112	19	9	200	71.0%	81.0%	81.5%	13	7	163
69	17,870	167	17,778	104	51	1,112	18	9	198	71.0%	81.0%	81.5%	13	7	161
70	17,687	183	17,586	390	154	1,570	69	27	276	71.0%	81.0%	81.5%	49	22	225
71	17,486	201	17,375	390	154	1,570	68	27	273	71.0%	81.0%	81.5%	48	22	222
72	17,265	221	17,144	390	154	1,570	67	26	269	71.0%	81.0%	81.5%	48	21	219
73	17,023	242	16,890	390	154	1,570	66	26	265	71.0%	81.0%	81.5%	47	21	216
74	16,758	265	16,612	390	154	1,570	65	26	261	71.0%	81.0%	81.5%	46	21	213
75	16,467	291	16,307	390	154	1,570	64	25	256	91.0%	81.0%	81.5%	58	20	209
76	16,148	319	15,973	390	154	1,570	62	25	251	91.0%	81.0%	81.5%	57	20	204
77	15,799	349	15,608	390	154	1,570	61	24	245	91.0%	81.0%	81.5%	55	19	200
78	15,418	381	15,209	390	154	1,570	59	23	239	91.0%	81.0%	81.5%	54	19	195
79	15,001	417	14,774	390	154	1,570	58	23	232	91.0%	81.0%	81.5%	52	18	189
80	14,547	454	14,300	1,411	373	3,150	202	53	450	91.0%	81.0%	81.5%	184	43	367
81	14,053	494	13,785	1,411	373	3,150	195	51	434	91.0%	81.0%	81.5%	177	42	354
82	13,517	536	13,228	1,411	373	3,150	187	49	417	91.0%	81.0%	81.5%	170	40	340
83	12,938	579	12,626	1,411	373	3,150	178	47	398	91.0%	81.0%	81.5%	162	38	324
84	12,314	624	11,980	1,411	373	3,150	169	45	377	91.0%	81.0%	81.5%	154	36	308
85	11,645	669	11,288	1,411	373	3,150	159	42	356	91.0%	81.0%	81.5%	145	34	290
86	10,931	714	10,553	1,411	373	3,150	149	39	332	91.0%	81.0%	81.5%	136	32	271
Total		**7,640**	**341,738**	**577**	**183**	**1,854**	**1,971**	**626**	**6,337**				**1,708**	**507**	**5,164**

- In their meta-analysis on morbidity associated with hip fractures, Haentjen and colleagues calculated a hazard ratio of 2.87 (95% CI 2.52 – 3.27) of death in the first year for women 50 and older with a hip fracture compared to those without.[464] A

[462] Lippuner K, Golder M and Greiner R. Epidemiology and direct medical costs of osteoporotic fractures in men and women in Switzerland. *Osteoporosis International*. 2005; 16(2): S8-S17.
[463] Hopkins R, Burke N, Von Keyserlingk C et al. The current economic burden of illness of osteoporosis in Canada. *Osteoporosis International*. 2016; 27(10): 3023-32.
[464] Haentjens P, Magaziner J, Colón-Emeric C et al. Meta-analysis: excess mortality after hip fracture among older women and men. *Annals of Internal Medicine.* 2010; 152(6): 380-90.

hazard ratio of 1.00 suggests that the death rate in the group of interest is the same as that in the general population.

- Tran and colleagues report that for women over 50 the hazard ratio (of excess mortality) of any fragility fracture is 1.51 (95% CI 1.31 – 1.75), 2.13 (1.58 – 2.87) for hip fractures, 1.82 (1.28 – 2.57) for vertebral fractures and 1.38 (1.18 – 1.62) for non-hip, non-vertebral fractures.[465]
- In his commentary on mortality after osteoporotic fractures, Schousboe discusses some of the links between fracture and mortality. He notes that "…after adjustment for comorbidity, and/or functional status, some studies report longer-term excess mortality after hip fracture and others do not."[466]

- We will model the risk of excess mortality for women with a hip fracture using a hazard ratio of 2.87 in the first year after hip fracture (and vary this from 2.52 to 3.27 in our sensitivity analysis). We will model the risk of excess mortality for women with vertebral fractures at 1.82 (varied between 1.28 and 2.57) and for all other fractures (i.e. non-hip, non-vertebral) we use a hazard ratio of 1.38 (varied between 1.18 and 1.62). We conservatively apply the excess mortality only in the year of the incident fracture.

- Based on the number of osteoporotic fractures calculated in Table 3, we calculate the number of deaths and life years lost attributable to osteoporotic fractures (see Table 4).
- In Table 4, we show that 181 excess deaths are attributable to osteoporosis-related fractures, 113 of which are due to hip fractures, 13 to vertebral fractures and 55 to other fractures. Combining the year when the deaths occur with life expectancy at the time of death, we further show that a total of 1,000 life years are lost due to osteoporosis-related fractures. Of these, 571 life years lost are due to hip fractures, 75 are due to vertebral fractures and 354 are due to other fractures.

[465] Tran T, Bliuc D, van Geel T et al. Population-wide impact of non-hip non-vertebral fractures on mortality. *Journal of Bone and Mineral Research*. 2017; 32(9): 1802-10.
[466] Schousboe JT. Mortality After Osteoporotic Fractures: What Proportion Is Caused by Fracture and Is Preventable? *Journal of Bone and Mineral Research*. 2017; 32(9): 1783-8.

Table 4: Screening for Osteoporosis in Women Ages 65 and Older
Number of Deaths Attributable to Osteoporotic Fracture
In a BC Birth Cohort of 40,000

					Fractures Attributable to Osteoporosis			*Hazard Ratio of Excess Death Due to Incident Fracture*			*Excess Deaths Due to Incident Fracture*				*Life Years Lost Due to Osteoporotic Fractures*		
Age	# in Cohort	Deaths in Cohort	Years Lived	Death Rate / 100,000	Hip Fracture	Vertebral Fracture	All Other Fractures	Hip Fracture	Vertebral Fracture	All Other Fractures	Hip Fracture	Vertebral Fracture	All Other Fractures	Life Expectancy	Hip Fracture	Vertebral Fracture	All Other Fractures
64	18,572																
65	18,456	116	18,392	629	14	8	167	2.87	1.82	1.38	0.16	0.04	0.40	22	4	1	9
66	18,329	127	18,259	692	13	8	165	2.87	1.82	1.38	0.17	0.04	0.43	21	4	1	9
67	18,190	139	18,113	765	13	8	164	2.87	1.82	1.38	0.19	0.05	0.48	20	4	1	10
68	18,037	152	17,954	845	13	7	163	2.87	1.82	1.38	0.21	0.05	0.52	19	4	1	10
69	17,870	167	17,778	936	13	7	161	2.87	1.82	1.38	0.23	0.06	0.57	18	4	1	10
70	17,687	183	17,586	1,036	49	22	225	2.87	1.82	1.38	0.94	0.19	0.89	17	16	3	15
71	17,486	201	17,375	1,151	48	22	222	2.87	1.82	1.38	1.04	0.20	0.97	16	17	3	16
72	17,265	221	17,144	1,278	48	21	219	2.87	1.82	1.38	1.14	0.22	1.06	15	17	3	16
73	17,023	242	16,890	1,422	47	21	216	2.87	1.82	1.38	1.24	0.25	1.17	14	17	3	16
74	16,758	265	16,612	1,584	46	21	213	2.87	1.82	1.38	1.36	0.27	1.28	13	18	4	17
75	16,467	291	16,307	1,766	58	20	209	2.87	1.82	1.38	1.91	0.29	1.40	12	23	4	17
76	16,148	319	15,973	1,974	57	20	204	2.87	1.82	1.38	2.10	0.32	1.53	11	23	4	17
77	15,799	349	15,608	2,209	55	19	200	2.87	1.82	1.38	2.29	0.35	1.68	10	23	4	17
78	15,418	381	15,209	2,474	54	19	195	2.87	1.82	1.38	2.50	0.39	1.83	9	23	3	16
79	15,001	417	14,774	2,777	52	18	189	2.87	1.82	1.38	2.73	0.42	1.99	8	22	3	16
80	14,547	454	14,300	3,121	184	43	367	2.87	1.82	1.38	10.72	1.11	4.35	7	75	8	30
81	14,053	494	13,785	3,514	177	42	354	2.87	1.82	1.38	11.63	1.20	4.73	6	70	7	28
82	13,517	536	13,228	3,964	170	40	340	2.87	1.82	1.38	12.59	1.30	5.12	5	63	6	26
83	12,938	579	12,626	4,477	162	38	324	2.87	1.82	1.38	13.57	1.40	5.51	4	54	6	22
84	12,314	624	11,980	5,066	154	36	308	2.87	1.82	1.38	14.57	1.50	5.92	3	44	5	18
85	11,645	669	11,288	5,747	145	34	290	2.87	1.82	1.38	15.58	1.61	6.33	2	31	3	13
86	10,931	714	10,553	6,532	136	32	271	2.87	1.82	1.38	16.55	1.71	6.72	1	17	2	7
Total		**7,640**	**341,738**		**1,708**	**507**	**5,164**				**113**	**13**	**55**		**571**	**75**	**354**

- In Table 5, we subtract the number of deaths from the number of osteoporosis fracture events to determine the number of people still living after osteoporosis-related fractures. This comes to 7,198 people in total, 1,594 of whom have had hip fractures, 494 of whom have had vertebral fractures and 5,110 of whom have had other fractures.

Table 5: Screening for Osteoporosis in Women Ages 65 and Older
Number Living with Fracture
In a BC Birth Cohort of 40,000

	Fractures Attributable to Osteoporosis			*Excess Deaths Due to Incident Fracture*			*Number Living with Fractures*		
Age	Hip Fracture	Vertebral Fracture	All Other Fractures	Hip Fracture	Vertebral Fracture	All Other Fractures	Hip Fracture	Vertebral Fracture	All Other Fractures
64									
65	14	8	167	0.2	0.0	0.4	13	8	166
66	13	8	165	0.2	0.0	0.4	13	8	165
67	13	8	164	0.2	0.0	0.5	13	7	164
68	13	7	163	0.2	0.1	0.5	13	7	162
69	13	7	161	0.2	0.1	0.6	13	7	161
70	49	22	225	0.9	0.2	0.9	48	22	224
71	48	22	222	1.0	0.2	1.0	47	21	221
72	48	21	219	1.1	0.2	1.1	46	21	218
73	47	21	216	1.2	0.2	1.2	46	21	215
74	46	21	213	1.4	0.3	1.3	45	20	211
75	58	20	209	1.9	0.3	1.4	56	20	207
76	57	20	204	2.1	0.3	1.5	55	20	203
77	55	19	200	2.3	0.4	1.7	53	19	198
78	54	19	195	2.5	0.4	1.8	52	19	193
79	52	18	189	2.7	0.4	2.0	50	18	187
80	184	43	367	10.7	1.1	4.4	173	42	363
81	177	42	354	11.6	1.2	4.7	165	40	349
82	170	40	340	12.6	1.3	5.1	157	39	334
83	162	38	324	13.6	1.4	5.5	149	37	319
84	154	36	308	14.6	1.5	5.9	139	35	302
85	145	34	290	15.6	1.6	6.3	129	32	283
86	136	32	271	16.6	1.7	6.7	119	30	264
Total	**1,708**	**507**	**5,164**	**113**	**13**	**55**	**1,594**	**494**	**5,110**

- Betram et al use a hip-fracture disability weight of 0.272 based on Global Burden of Disease data to model hip-fracture health burden. The authors state that "29% of hip fracture cases in the elderly do not reach their pre-fracture levels 1 year post-fracture. Those who do recover tend to reach their pre-fracture levels of functioning at around 6 months."[467]
- Vertebral fracture patients are often advised that it will be a full year before they reach their pre-fracture levels of functioning.[468]
- Kanis and colleagues[469] assign different disability weights based on expert opinion derived from a 1998 National Osteoporosis Foundation paper.[470] They suggest a first-year utility loss with vertebral, rib and pelvis fractures of 0.0502, with humerus, clavicle, scapula, sternum and distal forearm fractures of 0.0464 and hip, other femoral fractures and tibia and fibula fractures of 0.4681.[471]

[467] Bertram M, Norman R, Kemp L et al. Review of the long-term disability associated with hip fractures. *Injury Prevention*. 2011; 17: 365-70.
[468] Dr. Susan Purkiss, MD, FRCPC, Clinical Instructor, General Internal Medicine, Faculty of Medicine, UBC. January 16, 2019. Personal communication.
[469] Kanis J, Oden A, Johnell O et al. The burden of osteoporotic fractures: a method for setting intervention thresholds. *Osteoporosis International.* 2001; 12(5): 417-27.
[470] Eddy D, CC JJ, Cummings S et al. Osteoporosis: review of the evidence for prevention, diagnosis, and treatment and cost-effectiveness analysis. Status report. *Osteoporosis International.* 1998; 8(SUPPL. 4):
[471] Kanis J, Oden A, Johnell O et al. The burden of osteoporotic fractures: a method for setting intervention thresholds. *Osteoporosis International.* 2001; 12(5): 417-27.

- The USPSTF found no harms of screening in terms of anxiety or quality of life.[472]

- We model that 29% of hip fracture patients do not recover their pre-fracture functioning, and have a reduced quality of life for their remaining years of life. We model that the remaining hip fracture patients recover within an average of 6 months. We model vertebral fracture patients recover to pre-fracture levels of functioning in one year and assume that all other fracture types recover in an average of 6 months. We model a 0.27 reduction in QoL following a hip fracture, a 0.050 reduction in QoL for vertebral fractures and a 0.046 QoL reduction for other fractures. Compared to an average quality of life of 0.76 of a 70-79 year old (see Reference Document), this results in a 35.5% (0.27 / 0.76) reduction in QoL due to hip fracture, a 6.6% reduction due to vertebral fracture and a 6.0% reduction due to other fractures.

- We apply our assumptions to the individuals living with fractures and calculate QALYs lost attributable to osteoporotic fractures in Table 6. For example, at age 65, 29% of the 13.4 hip fractures (3.9) will have a lifelong quality decrement. The QALYs lost in this group is the number multiplied by the decrement multiplied by the number of life years remaining, and comes to 30.5 (= 3.9 * 0.355 * 22). The remaining 9.5 hip fractures have the decrement applied for half a year, resulting in 1.7 QALY lost (9.5 * 0.355 * 0.5). The total QALYs lost due to hip fracture is the sum of these two, or 32 QALYs.

- Table 6 shows that the total QALYs lost due to osteoporosis-related fractures is 1,606. Hip fractures account for 1,420 of the QALYs lost, with vertebral fractures and other fractures accounting for 33 and 153 QALYs lost respectively.

[472] Viswanathan M, Reddy S, Berkman N et al. Screening to Prevent Osteoporotic Fractures: An Evidence Review for the US Preventive Services Task Force. 2018: Available at https://www.ncbi.nlm.nih.gov/books/NBK532075/. Accessed December 2018.

Table 6: Screening for Osteoporosis in Women Ages 65 and Older
Quality Adjusted Life Years for those Living with Fracture
In a BC Birth Cohort of 40,000

	Number Living with Fractures			*Lifetime Disability in Hip Fracture Cases*		*QoL Decrement*			*Length of Time for QoL Decrement*			*Quality Adjusted Life Years Lost Due to Osteoporotic Fractures*		
Age	Hip Fracture	Vertebral Fracture	All Other Fractures	Percentage	Number	Hip Fracture	Vertebral Fracture	All Other Fractures	Lifetime Hip Cases	Vertebral Fracture Cases	All other cases	Hip Fracture	Vertebral Fracture	All Other Fractures
64														
65	13	8	166	29%	3.9	0.36	0.07	0.06	22	1.0	0.5	32	0.5	5.0
66	13	8	165	29%	3.9	0.36	0.07	0.06	21	1.0	0.5	30	0.5	4.9
67	13	7	164	29%	3.8	0.36	0.07	0.06	20	1.0	0.5	29	0.5	4.9
68	13	7	162	29%	3.8	0.36	0.07	0.06	19	1.0	0.5	27	0.5	4.9
69	13	7	161	29%	3.7	0.36	0.07	0.06	18	1.0	0.5	25	0.5	4.8
70	48	22	224	29%	13.9	0.36	0.07	0.06	17	1.0	0.5	90	1.4	6.7
71	47	21	221	29%	13.7	0.36	0.07	0.06	16	1.0	0.5	84	1.4	6.6
72	46	21	218	29%	13.5	0.36	0.07	0.06	15	1.0	0.5	77	1.4	6.5
73	46	21	215	29%	13.2	0.36	0.07	0.06	14	1.0	0.5	71	1.4	6.4
74	45	20	211	29%	13.0	0.36	0.07	0.06	13	1.0	0.5	65	1.4	6.3
75	56	20	207	29%	16.3	0.36	0.07	0.06	12	1.0	0.5	76	1.3	6.2
76	55	20	203	29%	15.9	0.36	0.07	0.06	11	1.0	0.5	69	1.3	6.1
77	53	19	198	29%	15.4	0.36	0.07	0.06	10	1.0	0.5	61	1.3	5.9
78	52	19	193	29%	14.9	0.36	0.07	0.06	9	1.0	0.5	54	1.2	5.8
79	50	18	187	29%	14.4	0.36	0.07	0.06	8	1.0	0.5	47	1.2	5.6
80	173	42	363	29%	50.1	0.36	0.07	0.06	7	1.0	0.5	146	2.8	10.9
81	165	40	349	29%	48.0	0.36	0.07	0.06	6	1.0	0.5	123	2.7	10.5
82	157	39	334	29%	45.6	0.36	0.07	0.06	5	1.0	0.5	101	2.6	10.0
83	149	37	319	29%	43.1	0.36	0.07	0.06	4	1.0	0.5	80	2.4	9.6
84	139	35	302	29%	40.4	0.36	0.07	0.06	3	1.0	0.5	61	2.3	9.0
85	129	32	283	29%	37.5	0.36	0.07	0.06	2	1.0	0.5	43	2.1	8.5
86	119	30	264	29%	34.5	0.36	0.07	0.06	1	1.0	0.5	27	2.0	7.9
Total	**1,594**	**494**	**5,110**		**462**							**1,420**	**33**	**153**

- The USPSTF found convincing evidence that "…screening can detect osteoporosis and that treatment of women with osteoporosis can provide at least a moderate benefit in preventing fractures."[473]

- We have assumed a potential screening rate of 57.8% (Table 7, row *p*).[474] We assume that all persons with a positive screen for osteoporosis are prescribed medication.

- Fraser and colleagues report on the accuracy of a Canadian modification of the FRAX® fracture prediction screening tool. Combining FRAX® with BMD (bone mineral density) testing resulted in an area under the receiver operator curve of 0.69 (a poor to fair score) for predicting major osteoporotic fractures and 0.80 (a good score) for predicting hip fractures. When just the BMD testing results are used, the equivalent results are 0.66 for major osteoporotic fractures and 0.76 for hip fractures.[475]

- For women over 65, the USPSTF[476] does not explicitly recommend a risk assessment, only DXA screening.[477] We model accordingly.

[473] Curry SJ, Krist AH, Owens DK et al. Screening for osteoporosis to prevent fractures: US Preventive Services Task Force recommendation statement. *Journal of the American Medical Association.* 2018; 319(24): 2521-31.
[474] Amarnath ALD, Franks P, Robbins JA et al. Underuse and Overuse of Osteoporosis Screening in a Regional Health System: a Retrospective Cohort Study. *Journal of General Internal Medicine*. 2015; 12(30): 1733-40.
[475] Fraser L-A, Langsetmo L, Berger C et al. Fracture prediction and calibration of a Canadian FRAX® tool: a population-based report from CaMos. *Osteoporosis International*. 2011; 22(3): 829-37.
[476] Viswanathan M, Reddy S, Berkman N et al. Screening to Prevent Osteoporotic Fractures: An Evidence Review for the US Preventive Services Task Force. 2018: Available at https://www.ncbi.nlm.nih.gov/books/NBK532075/. Accessed December 2018.
[477] The USPSTF suggests that a risk assessment, such as FRAX®, is "a reasonable approach" to use on women less than 65 who present with at least one risk factor.

- We model a single screening at age 65 to detect osteoporosis and assume that 76% of hip fractures and 66% of all other fractures could be predicted by screening with DXA alone (Table 7, rows *q* & *r*).

- Bisphosphonates have been shown effective in building back bone mineral density and were the most frequently studied medication referenced by the USPSTF.[478] We therefore model treatment as being carried out with bisphosphonates.

- The review by the USPSTF found that bisphosphonates were found to significantly reduce vertebral fractures (RR of 0.57, 95% CI, 0.41-0.78) and nonvertebral fractures (RR of 0.84, 95% CI, 0.76-0.92) but not hip fractures (RR of 0.70, 95% CI, 0.44-1.11).[479]

- Long-term treatment compliance is critical in achieving a reduced risk of fracture. In a study of 19,987 (mostly [97%]) females ages 65 and older, Patrick et al. calculated that 36.5% of the study cohort took their medication between 80% and 100% of the time during the 300-day medication study compliance period.[480] A further 31.8% of the cohort were in the 0-19% compliance group, 11.3% were in the 20-39% compliance group, 8.8% were in the 40-59% compliance group and 11.5% in the 60-79% compliance group.

- It was in the high compliance group (80-100%) that Patrick et al. found a statistically significant 5-year reduction of 23% (95% CI of 8% to 36%) in hip fractures, 26% (95% CI of 12% to 38%) reduction in vertebral fractures and a 20% (95% CI of 9% to 29%) reduction in other non-hip fractures when compared to the group with poor or no compliance.[481] The only other compliance group that saw a significant reduction in hip fractures was the 60-79% group (24%, 95% CI of 1% to 42%).

- For the 36.5% of patients in the high compliance group (the 80-100% group) (Table 7, row *s*), we model a 23% reduction in hip fractures, a 26% reduction in vertebral fractures and a 20% reduction in all other fractures (Table 7, rows *t* to *v*).

- Shepstone and colleagues[482] recently published an RCT investigating the potential benefits of a fracture-risk based, community screening program in older women (ages 70-85) in the UK. BMD measurement was only applied to a selected subgroup of these women based on their risk assessment using the Fracture Risk Assessment Tool (FRAX). They found that this screening approach, followed by appropriate osteoporosis medication, did not reduce the overall incidence of osteoporosis-related fractures (hazard ratio [HR] 0.94, 95% CI 0.85 – 1.03), nor the overall incidence of all clinical fractures (0.94, 0.86 – 1.03). It did, however, reduce the incidence of hip fractures (0.72, 0.59 – 0.89). As noted previously, we do not assume any risk stratification in our modelling.

[478] Curry SJ, Krist AH, Owens DK et al. Screening for osteoporosis to prevent fractures: US Preventive Services Task Force recommendation statement. *Journal of the American Medical Association.* 2018; 319(24): 2521-31.
[479] Curry SJ, Krist AH, Owens DK et al. Screening for osteoporosis to prevent fractures: US Preventive Services Task Force recommendation statement. *Journal of the American Medical Association.* 2018; 319(24): 2521-31.
[480] Patrick AR, Brookhart MA, Losina E et al. The complex relation between bisphosphonate adherence and fracture reduction. *The Journal of Clinical Endocrinology & Metabolism*. 2010; 95(7): 3251-9.
[481] Patrick AR, Brookhart MA, Losina E et al. The complex relation between bisphosphonate adherence and fracture reduction. *The Journal of Clinical Endocrinology & Metabolism*. 2010; 95(7): 3251-9.
[482] Shepstone L, Lenaghan E, Cooper C et al. Screening in the community to reduce fractures in older women (SCOOP): a randomised controlled trial. *The Lancet*. 2018; 391(10122): 741-7.

Based on these assumptions, the CPB associated with screening for osteoporosis in females ages 65 and older is 91 QALYs (see Table 7, row *af*).

Table 7: CPB of Screening for Osteoporosis in Women 65+
In a BC Birth Cohort of 40,000

Row Label	Variable	Base case	Data Source
a	Expected life-years between age 65 and 86	341,738	Table 1
b	Prevalence of osteoporosis	38.5%	Table 1
c	Years lived with osteoporosis	131,418	= a * b
d	Expected number of hip fractures	1,971	Table 3
e	Expected number of vertebral fractures	626	Table 3
f	Expected number of all other fractures	6,337	Table 3
g	Expected number of hip fractures attributable to osteoporosis	1,708	Table 3
h	Expected number of vertebral fractures attributable to osteoporosis	507	Table 3
i	Expected number of all other fractures attributable to osteoporosis	5,164	Table 3
j	Life years lost due **death from** to osteoporotic hip fractures	571	Table 4
k	Life years lost due to **death from** osteoporotic vertebral fractures	75	Table 4
l	Life years lost due to **death from** all other osteoporotic fractures	354	Table 4
m	QALYs lost due to **living with** osteoporotic hip fractures	1,420	Table 6
n	QALYs lost due to **living with** osteoporotic vertebral fractures	33	Table 6
o	QALYs lost due to **living with** osteoporotic other fractures	153	Table 6
p	Screening Rate	57.8%	√
q	Accuracy of bone density screening to predict hip fractures	76%	√
r	Accuracy of bone density screening to predict non-hip fractures	66%	√
s	Long term compliance rate with medical treatment	36.5%	√
t	Hip fracture reduction rate due to treatment	23.0%	√
u	Vertebral fracture reduction rate due to treatment	26.0%	√
v	Other fracture reduction rate due to treatment	20.0%	√
w	Hip fractures avoided due to treatment	63	= g * p * q * s * t
x	Vertebral fractures avoided due to treatment	18	= h * p * r * s * u
y	Other fractures avoided due to treatment	144	= i * p * r * s * v
z	Life years gained **(deaths avoided)** due to screening, osteoporotic hip fractures	21	= j * p * q * s * t
aa	Life years gained **(deaths avoided)** due to screening, osteoporotic vertebral fractures	2.7	= k * p * r * s * u
ab	Life years gained **(deaths avoided)** due to screening, osteoporotic other fractures	10	= l * p * r * s * v
ac	QALYs gained due to screening in those **living with** osteoporotic hip fractures	52.4	= m * p * q * s * t
ad	QALYs gained due to screening in those **living with** osteoporotic vertebral fractures	1.2	= n * p * r * s * u
ae	QALYs gained due to screening in those **living with** osteoporotic other fractures	4.3	= o * p * r * s * v
af	Total QALYs gained due to screening (going from 0% to 57.8%)	**91**	= z + aa + ab + ac + ad + ae

√ = Estimates from the literature

For the sensitivity analysis, we modified a number of major assumptions and recalculated the CPB as follows:

- Assume that the hazard ratio (HR) for death after hip fracture is reduced from 2.87 to 2.52, the HR for death after vertebral fractures is reduced from 1.82 to 1.28 and the HR for death after other fractures is reduced from 1.38 to 1.18 (Table 4): CPB = 88
- Assume that the hazard ratio (HR) for death after hip fracture is increased from 2.87 to 3.27, the HR for death after vertebral fractures is increased from 1.82 to 2.57 and the HR for death after other fractures is increased from 1.38 to 1.62 (Table 4): CPB = 96
- Assume that the hip fracture reduction rate is reduced from 23% to 8% (Table 7, row *t*), the vertebral fracture reduction rate is reduced from 26% to 12% (Table 7, row *u*) and the other fracture reduction rate is reduced from 20% to 9% (Table 7, row *v*): CPB = 34
- Assume that the hip fracture reduction rate is increased from 23% to 36% (Table 7, row *t*), the vertebral fracture reduction rate is increased from 26% to 38% (Table 7,

row *u*) and the other fracture reduction rate is increased from 20% to 29% (Table 7, row *v*): CPB = 141

Modelling Cost-Effectiveness

In this section, we will calculate the CE associated with screening for osteoporosis in women ages 65 and older.

In modelling CE, we made the following assumptions:

- We model that 57.8%[483] of 65 year old women are referred to and receive a bone density (DXA) scan (Table 8, row *b*). This rate takes into account both physician adherence (willingness to make the referral) and patient adherence (willingness to get the scan done).
- The cost of each 10 minute primary care provider office visit is $34.85 (Reference Document) (Table 8, row *d)*
- The value of patient time for each visit to a primary care office and for bone density scanning is $59.38 (Reference Document) (Table 8, row *e*).
- The proportion of each office visit attributable to screening is 50% (Reference Document) (Table 8, row *f*).
- We model that all those who receive a DXA scan have also visited their primary care provider to receive the referral for the scan. During this appointment, a risk assessment (e.g. FRAX®) could be conducted within the portion of the office visit attributable to screening. The FRAX® tool adapted for the Canadian population can be found online at no cost.[484]
- According to the BC Medical Services Plan Fee-For-Service Payment Analysis for 2012/13 – 2016/17, a single area bone density scan (fee item 8688) averages $66.94 per scan. Adding a second area (fee item 8689) costs an additional $45.88 per scan. A second area scan occurred at a rate of approximately 95.2% of single area scans.[485]
- We assume that bone scans to determine bone mineral density are conducted by means of DXA and model the cost of the average bone scan as $66.94 + (0.952 * 45.88) = $110.62 (Table 8, row *h*).
- In the study by Patrick et al[486] of 19,987 individuals initiating treatment with bisphosphonates, they found that 31.8% had a cumulative proportion of days covered (i.e. the proportion of days taking medication) between 0 – 19%, 11.3% had a proportion of days covered (PDC) between 20 – 39%, 8.8% had a PDC between 40 – 59%, 11.5% had a PDC between 60 – 79% and 36.5% had a PDC between 80 -100%. (Table 8, rows *l* to *p*). Their study assessed medication compliance rates over a 300 day period.

[483] Amarnath ALD, Franks P, Robbins JA et al. Underuse and Overuse of Osteoporosis Screening in a Regional Health System: a Retrospective Cohort Study. *Journal of General Internal Medicine*. 2015; 12(30): 1733-40.
[484] University of Sheffield. *FRAX® Fracture Risk Assessment Tool*. 2018. Available at https://www.sheffield.ac.uk/FRAX/tool.aspx?country=19. Accessed January 2019.
[485] B.C. Ministry of Health, Health Sector Information, Analysis & Reporting Division. *MSP Fee-For-Service Payment Analysis 2012/2013 - 2016/2017*. 2017. Available at https://www2.gov.bc.ca/assets/gov/health/practitioner-pro/medical-services-plan/ffs_complete.pdf. Accessed November 2018.
[486] Patrick AR, Brookhart MA, Losina E et al. The complex relation between bisphosphonate adherence and fracture reduction. *The Journal of Clinical Endocrinology & Metabolism*. 2010; 95(7): 3251-9.

- For modelling purposes, we assume that each PDC group has a compliance rate at the midpoint of their range. Groups with a PDC of between 0 - 79% stop taking medication after 300 days. For the high compliance group, we assume that the medication is taken for 5 years in the base model (Table 8, row *y*). In the sensitivity analysis, we model 5 years of taking medication, followed by a 5 year medication 'holiday' followed by a further 5 years of taking medication.

- Alendronate is the most commonly prescribed bisphosphonate in BC and is typically prescribed to be taken orally once per week at a dose of 70mg.[487]

- We model weekly treatment with 70mg alendronate. The cost per 70mg pill ranges from $2.17 - $13.88 in BC.[488] Only two records for BC, however, showed a price above $3.21. We assume pricing above $3.21 per 70mg are outliers and model using the mid-point of the $2.17 - $3.21 range for the pills, or $2.69. The dispensing fee ranges from $4.49 - $13.99, with only a single dispensing fee below $9.95. We assume a dispensing fee at the midpoint of $9.95 - $13.99 (or $11.97) and assume a 3-month dose is dispensed each time.

- We model the annual cost of treatment as $187.76 (($2.69 * 52) + (4 * $11.97)). Translating this into a daily cost results in $0.51 / day ($187.76 / 365). Using the low and high numbers of the ranges above (excluding outliers), we use a range of between $0.42 and $0.62 / day in the sensitivity analysis (Table 8, row *v*).

- A December 20, 2018 publication by Reid and colleagues assessed the efficacy of 4 infusions of 5mg zoledronate (or zoledronic acid) at 18-month intervals vs. placebo in older women (mean age of 71) with osteopenia.[489] They noted a 37% (HR of 0.63, 94% CI 0.50 – 0.79) reduction in fragility fractures in women receiving zoledronate. The efficacy of such a reduction in medication dose and frequency is encouraging for the potential compliance with and cost of treatment.

- In comparing less-frequent zoledronic acid infusions with more frequent bisphosphonate treatment regimes, Lozano and Sanchez-Fidalgo report that "patients appear to have (a) preference for less frequent dosing. Switching from oral to intravenous therapy…may allow obtaining better outcomes in adherence to osteoporosis treatment."[490]

- Potential changes in adherence and the costs associated with zoledronic acid infusions are two important variables that should be considered in future updates of this model, should the results observed by Reid and colleagues[491] be confirmed for patients with osteoporosis.

- We model one additional visit to a primary care provider for monitoring medication for those with low compliance (PDC of 0 – 79%) (Table 8, row ab) and one **annual** visit to a primary care provider for monitoring medication for those with high compliance (PDC of 80 – 100%) (Table 8, row *i*).

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[487] Dr. Susan Purkiss, MD, FRCPC, Clinical Instructor, General Internal Medicine, Faculty of Medicine, UBC. January 16, 2019. Personal communication.

[488] Pacific Blue Cross. *Pharmacy Compass*. 2018. Available online at https://www.pac.bluecross.ca/pharmacycompass. Accessed January 2019.

[489] Reid IR, Horne AM, Mihov B et al. Fracture prevention with zoledronate in older women with osteopenia. *New England Journal of Medicine*. 2018; 379(25): 2407-16.

[490] Lozano MJF and Sánchez-Fidalgo S. Adherence and preference of intravenous zoledronic acid for osteoporosis versus other bisphosphonates. *European Journal of Hospital Pharmacy*. 2019; 26(1): 4-9.

[491] Reid IR, Horne AM, Mihov B et al. Fracture prevention with zoledronate in older women with osteopenia. *New England Journal of Medicine*. 2018; 379(25): 2407-16.

- A recent Canadian study by Hopkins et al. estimated the annual direct medical costs of a hip fracture to be $61,540, the cost of a vertebral fracture to be $25,965 and the cost of "other" fractures to be $13,579 (all in 2014 CAD).[492] Costs included acute care, rehabilitation care, long term care, home care, outpatient physician services and mobility devices.

- We adjusted the costs calculated by Hopkins et al. to 2017 CAD and use $62,152 for the total cost per hip fracture (Table 8, row *ai*), $26,223 (Table 8, row *aj*) per vertebral fracture and $13,714 for all other fractures (Table 8, row *ak*).

Based on these assumptions, the CE associated with screening for osteoporosis in women ages 65 and older is cost saving (-$29,412/QALY) (see Table 8, row *ar*).

Table 8: Cost Effectiveness of Osteoporosis Screening in Women 65+
In a BC Birth Cohort of 40,000

Row Label	Variable	Base case	Data Source
a	Population in cohort, age 65	18,456	BC Life Table
b	Proportion screened for osteoporosis	0.578	Table 7, row p
c	Number in cohort receiving bone density screen (DXA)	10,667	= a * b
d	Cost of 10 minute office visit	$34.85	Ref Doc
e	Value of patient time and travel for office visit	$59.38	Ref Doc
f	Portion of 10-minute visit for screening	50%	Ref Doc
g	Cost of initial screening visit	**$502,592**	= c * f * (d + e)
h	Bone density screening cost, per screen	$110.62	√
i	Cost of bone density screening	**$1,813,447**	c * (e + h)
j	Number of osteoporotic patients at age 65	3,543	Table 1
k	Number of osteoporotic patients identified via screening	2,048	= j * b
l	Percent of patients with proportion of days covered (PDC) 0 -19%	31.8%	√
m	Percent of patients with PDC of 20 - 39%	11.3%	√
n	Percent of patients with PDC of 40 - 59%	8.8%	√
o	Percent of patients with PDC of 60 - 79%	11.5%	√
p	Percent of patients with PDC of 80 - 100%	36.5%	Table 7, row s
q	Average days taking medication - PDC 0 -19% group	30	= 300 * 0.10
r	Average days taking medication - PDC 20 - 39% group	90	= 300 * 0.30
s	Average days taking medication - PDC 40 - 59% group	150	= 300 * 0.50
t	Average days taking medication - PDC 60 - 79% group	210	= 300 * 0.70
u	Total days taking medication - PDC 0 - 79% group	116,866	= (k * l * q) + (k * m * r) + (k * n * s) + (k * o * t)
v	Daily cost of medication	$0.51	√
w	Total cost of medication - PDC 0-79%	**$60,117**	= u * v
x	Average days taking medication - PDC 80-100% group	329	= 365 * 0.90
y	Years of treatment - PDC 80-100% group	5	√
z	Total days taking medication - PDC 80-100% group	1,227,879	= k * p * x * y
aa	Total cost of medication - PDC 80-100% group	**$631,634**	= z * v
ab	Annual office visits required to monitor medication	1	Assumption
ac	Cost of annual visits to monitor medication - PDC 0 - 79% group	**$61,276**	= (1 - p) * k * ab * (d + e) * f
ad	Cost of annual visits to monitor medication - PDC 80 - 100% group	**$176,108**	= p * k * y * ab * (d + e) * f
ae	Total cost of screening and treatment	**$3,245,174**	= g + i + w + aa + ac + ad
	Potential Costs Avoided		
af	Total hip fractures avoided	63	Table 7, row w
ag	Total vertebral fractures avoided	18	Table 7, row x
ah	Other fractures avoided	144	Table 7, row y
ai	Average cost per hip fracture in the year following the fracture	$62,152	√
aj	Average cost per vertebral fracture in the year following the fracture	$26,223	√
ak	Average cost per other fracture in the year following the fracture	$13,714	√
al	Total costs avoided	**$6,367,537**	= (af * ai) + (ag * aj) + (ah * ak)
am	**Net cost of intervention**	**-$3,122,363**	= ae - al
an	QALYs gained	91	Table 7, row af
ao	Cost effectiveness (CE) of intervention, $/QALY	-$34,145	= am / an
ap	Net Cost of Intervention (1.5% Discount)	-$2,248,682	Calculated
aq	Net QALYs Gained (1.5% Discount)	76	Calculated
ar	Cost Effectiveness (CE) of Intervention, $/QALY (1.5% Discount)	-$29,412	= ap / aq

√ = Estimates from the literature

[492] Hopkins R, Burke N, Von Keyserlingk C et al. The current economic burden of illness of osteoporosis in Canada. *Osteoporosis International*. 2016; 27(10): 3023-32.

For the sensitivity analysis, we modified a number of major assumptions and recalculated the CE as follows:

- Assume that the hazard ratio (HR) for death after hip fracture is reduced from 2.87 to 2.52, the HR for death after vertebral fractures is reduced from 1.82 to 1.28 and the HR for death after other fractures is reduced from 1.38 to 1.18 (Table 4): CE = - $30,527
- Assume that the hazard ratio (HR) for death after hip fracture is increased from 2.87 to 3.27, the HR for death after vertebral fractures is increased from 1.82 to 2.57 and the HR for death after other fractures is increased from 1.38 to 1.62 (Table 4): CE = - $28,234
- Assume that the hip fracture reduction rate is reduced from 23% to 8% (Table 7, row *t*), the vertebral fracture reduction rate is reduced from 26% to 12% (Table 7, row *u*) and the other fracture reduction rate is reduced from 20% to 9% (Table 7, row *v*): CE = $38,997
- Assume that the hip fracture reduction rate is increased from 23% to 36% (Table 7, row *t*), the vertebral fracture reduction rate is increased from 26% to 38% (Table 7, row *u*) and the other fracture reduction rate is increased from 20% to 29% (Table 7, row *v*): CE = - $43,257
- Assume that the cost of treatment is increased from $0.51 / day to $0.61 / day (Table 8, row *v*): CE = - $27,765
- Assume that the cost of treatment is reduced from $0.51 / day to $0.42 / day (Table 8, row *v*): CE = - $31,060
- Assume that treatment pattern for the PDC 80 – 100% group changes from five years of treatment to five years of treatment followed by five years untreated followed by another five years of treatment, for a total treatment time of 10 years (Table 8, row *y*): CE = - $20,574

A number of others have calculated the cost-effectiveness of screening and treatment options for osteoporosis in women ages 65 and older.[493,494,495,496] In a Canadian cost-effectiveness analysis published in 2006, Goeree and colleagues estimated a CE of $32,571 / QALY for etidronate when compared with no intervention.[497] The CE / QALY was $38,623 for alendronate and $114,070 for raloxifine. Their study made a number of different key assumptions than we have. First, they assumed that 100% of patients with osteoporosis would adhere to medication regimens for a five year period. Based on a large real-world adherence study published in 2010,[498] we assume that just 36.5% of patients with osteoporosis would adhere to a medication regimens for a five year period. In addition, their estimated annual cost of drugs was between $546 and $969 compared to our base case scenario of $188.

[493] Mobley LR, Hoerger TJ, Wittenborn JS et al. Cost-effectiveness of osteoporosis screening and treatment with hormone replacement therapy, raloxifene, or alendronate. *Medical Decision Making*. 2006; 26(2): 194-206.
[494] Hiligsmann M, Gathon HJ, Bruyère O et al. Cost–effectiveness of osteoporosis screening followed by treatment: the impact of medication adherence. *Value in Health*. 2010; 13(4): 394-401.
[495] Nayak S, Roberts MS and Greenspan SL. Cost-effectiveness of different screening strategies for osteoporosis in postmenopausal women. *Annals of Internal Medicine.* 2011; 155(11): 751-61.
[496] Nayak S, Roberts MS and Greenspan SL. Impact of generic alendronate cost on the cost-effectiveness of osteoporosis screening and treatment. *PloS one*. 2012; 7(3): e32879.
[497] Goeree R, Blackhouse G and Adachi J. Cost-effectiveness of alternative treatments for women with osteoporosis in Canada. *Current Medical Research and Opinion.* 2006; 22(7): 1425-36.
[498] Patrick AR, Brookhart MA, Losina E et al. The complex relation between bisphosphonate adherence and fracture reduction. *The Journal of Clinical Endocrinology & Metabolism*. 2010; 95(7): 3251-9.

Applying an annual drug cost of $546 to our model results in a cost / QALY of -$12,608. An annual drug cost of $969 would increase the cost / QALY to $7,234.

Summary

Applying a 1.5% discount rate, the clinically preventable burden (CPB) associated with screening for, and treatment of, osteoporosis in females ages 65 and older in order to prevent fractures is estimated to be 76 quality-adjusted life years (QALYs) while the cost-effectiveness (CE) is estimated to result in cost savings of $29,412 per QALY (see Table 9).

Table 9: Osteoporosis Screening in Women 65+ in a BC Birth Cohort of 40,000

Summary

	Base Case	Range	
CPB (Potential QALYs Gained)			
Assume No Current Service			
1.5% Discount Rate	**76**	28	118
3% Discount Rate	65	24	100
0% Discount Rate	91	34	141
CE ($/QALY) ***including*** patient time costs			
1.5% Discount Rate	**-$29,412**	-$43,257	$38,997
3% Discount Rate	-$24,048	-$40,489	$57,000
0% Discount Rate	-$34,145	-$45,672	$22,976
CE ($/QALY) ***excluding*** patient time costs			
1.5% Discount Rate	-$43,755	-$52,552	$81
3% Discount Rate	-$40,996	-$51,474	$11,028
0% Discount Rate	-$46,171	-$53,466	-$9,663

Screening for Abdominal Aortic Aneurysms

United States Preventive Services Task Force Recommendations[499]

> *The USPSTF recommends 1-time screening for AAA with ultrasonography in men aged 65 to 75 years who have ever smoked. (B recommendation).*

Canadian Task Force on Preventive Health Care Recommendations[500]

> *We recommend one-time screening with ultrasonography for AAA of men aged 65 to 80 years (weak recommendation; moderate quality of evidence).*
>
> *We recommend not screening men older than 80 years of age for AAA (weak recommendation; low quality of evidence).*

The Canadian Task force acknowledged "evidence showing increased risk of AAA among smokers" but did not make a separate recommendation on screening this population "because there is no evidence on outcomes of screening smokers for AAA."[501]

Modelling the Clinically Preventable Burden

In this section, we will calculate the CPB associated with screening for abdominal aortic aneurysms in males ages 65 to 75 who have ever smoked.

An abdominal aortic aneurysm is conventionally diagnosed when the diameter of the aorta below the kidneys is 30 mm (3.0 cm) or greater.[502]

The USPSTF considers an "ever-smoker" someone who has smoked at least 100 cigarettes in their lifetime.[503]

Unless otherwise noted, we apply these conventions and definitions in our modelling.

In modelling CPB, we made the following assumptions:

- The single screen recommended by the USPSTF is conducted at age 65.
- Jacomelli and colleagues report that the National Health Service in England's AAA screening programme had mean uptake across the country of 78.1%, but varied regionally between 61.7 – 85.8%.[504] We use 85.8% as the best in the world screening rate for AAA.

[499] LeFevre ML. Screening for abdominal aortic aneurysm: US Preventive Services Task Force recommendation statement. *Annals of Internal Medicine.* 2014; 161(4): 281-90.
[500] Singh H, Dickinson JA, Lewin G et al. Recommendations on screening for abdominal aortic aneurysm in primary care. *Canadian Medical Association Journal*. 2017; 189(36): E1137-E45.
[501] Singh H, Dickinson JA, Lewin G et al. Recommendations on screening for abdominal aortic aneurysm in primary care. *Canadian Medical Association Journal*. 2017; 189(36): E1137-E45.
[502] Sakalihasan N, Limet R and Defawe OD. Abdominal aortic aneurysm. *The Lancet*. 2005; 365(9470): 1577-89.
[503] LeFevre ML. Screening for abdominal aortic aneurysm: US Preventive Services Task Force recommendation statement. *Annals of Internal Medicine.* 2014; 161(4): 281-90.
[504] Jacomelli J, Summers L, Stevenson A et al. Impact of the first 5 years of a national abdominal aortic aneurysm screening programme. *British Journal of Surgery*. 2016; 103(9): 1125-31.

- The large, population-based randomized controlled trials (RCTs) used by the USPSTF in making their recommendation found an abdominal aortic aneurysm (AAA) in 4.0 – 7.7% of male screening participants.[505]
- Citing more recent epidemiologic evidence from Europe and New Zealand, the USPSTF acknowledged a "substantial decrease in AAA prevalence in men aged 65 years or older in the past 2 decades"[506] and referenced a study by Svensjö et al. citing an AAA prevalence rate of 1.7% in Sweden.[507]
- In the UK, the AAA prevalence rate in 65-year old men has decreased from 5.0% in 1991 to 1.3% in 2015.[508] In Denmark, the prevalence rate in 65-year old men was 2.6% during 2008-2011.[509]

- For modelling purposes we use an AAA prevalence rate in 65-year old men of 2.35% (Table 5, row *e*). Using 2.35% prevalence in our model brings the model results with screening reasonably close to actual BC results. The 2.35% prevalence rate used is between the values reported for the UK and Denmark.

- The USPSTF rated the quality of the population-based randomized controlled trials (RCTs) used by the USPSTF in making their recommendation. The USPSTF considered the Multicentre Aneurysm Screening Study (MASS) and the Viborg AAA studies as "good-quality", and the Chichester and Western Australia AAA studies as "fair-quality".[510] Neither good-quality study included men over the age of 74. On the other hand, both fair-quality studies included older men up to ages 80 (Chichester) and 83 (Western Australia).
- The prevalence of AAA increases with increasing age.[511]
- In the MASS study, 4.9% of screened men were diagnosed with AAA and the total AAA-related death rate was 109 per 100,000 person years in the control group.[512] In the Viborg study, 4.0% of screened men were diagnosed with AAA and the total AAA-related death rate was 87 per 100,000 person years in the control group.[513]
- Based on 25 years of experience with an ultrasound screening program for AAA in the UK, Oliver-Williams and colleagues report that while the "prevalence of screen-

[505] LeFevre ML. Screening for abdominal aortic aneurysm: US Preventive Services Task Force recommendation statement. *Annals of Internal Medicine.* 2014; 161(4): 281-90.
[506] Guirguis-Blake JM, Beil TL, Senger CA et al. Ultrasonography screening for abdominal aortic aneurysms: a systematic evidence review for the US Preventive Services Task Force. *Annals of Internal Medicine.* 2014; 160(5): 321-9.
[507] Svensjö S, Björck M, Gürtelschmid M et al. Low prevalence of abdominal aortic aneurysm among 65-year-old Swedish men indicates a change in the epidemiology of the disease. *Circulation*. 2011; 124(10): 1118-23.
[508] Oliver-Williams C, Sweeting MJ, Turton G et al. Lessons learned about prevalence and growth rates of abdominal aortic aneurysms from a 25-year ultrasound population screening programme. *British Journal of Surgery*. 2018; 105(1): 68-74.
[509] Grøndal N, Søgaard R and Lindholt JS. Baseline prevalence of abdominal aortic aneurysm, peripheral arterial disease and hypertension in men aged 65–74 years from a population screening study (VIVA trial). *British Journal of Surgery*. 2015; 102(8): 902-6.
[510] Guirguis-Blake JM, Beil TL, Senger CA et al. Ultrasonography screening for abdominal aortic aneurysms: a systematic evidence review for the US Preventive Services Task Force. *Annals of Internal Medicine.* 2014; 160(5): 321-9.
[511] Grøndal N, Søgaard R and Lindholt JS. Baseline prevalence of abdominal aortic aneurysm, peripheral arterial disease and hypertension in men aged 65–74 years from a population screening study (VIVA trial). *British Journal of Surgery*. 2015; 102(8): 902-6.
[512] Thompson S, Ashton H, Gao L et al. Final follow-up of the Multicentre Aneurysm Screening Study (MASS) randomized trial of abdominal aortic aneurysm screening. *British Journal of Surgery*. 2012; 99(12): 1649-56.
[513] Lindholt JS, Sørensen J, Søgaard R et al. Long-term benefit and cost-effectiveness analysis of screening for abdominal aortic aneurysms from a randomized controlled trial. *British Journal of Surgery*. 2010; 97(6): 826-34.

detected small and medium AAAs has decreased over the past 25 years, …growth rates have remained similar. Men with a subaneurysmal aorta at age 65 years have a substantial risk of developing a large AAA by the age of 80 years."[514]

- For modelling purposes, we assume that the death rate / 100,000 person years of 98.0 observed in the control groups of the MASS and Viborg studies would be reduced linearly to 51.7 / 100,000 person years due to the lower estimated prevalence of AAA (2.35%) used in our model (see Table 1).

Table 1: Screening for Abdominal Aortic Aneurysm Men Ages 65+
Adjusted Study Results Based on Lower AAA Prevalence

Study	USPSTF Study Rating	Study Prevalence of AAA	Study Death Rate in Control Group per 100,000 person years	Model Prevalence of AAA	Adjusted Death Rate per 100,000 person years
MASS (Thompson et al., 2012)	Good	4.9%	109	2.35%	52.3
Viborg (Lindholt et al.)	Good	4.0%	87	2.35%	51.1
Average of Good Quality Studies			**98.0**		**51.7**

- As early as 1998, Semmens et al. reported a decline in AAA-related emergency and elective procedures in Western Australia, ahead of similar results being reported in Europe and theorized that this may be due to "significant changes in the health of the Australian community" including "the success of the anti-smoking movement".[515]
- In Sweden, Johansson and colleagues observed that AAA mortality declined from 36 to 10 deaths per 100,000 for men aged 65-74 between the early 2000s and 2015.[516] They note, however, that only an estimated 30% of this reduction was associated with the introduction of screening for AAA and that 70% is due to other factors, most notably a reduction in smoking. Between 1970 and 2010, the prevalence of smoking in Sweden decreased from 44% to 15%.[517]
- In a 2018 systematic review and meta-analysis of tobacco smoking and AAA, Aune and colleagues report that the relative risk of AAA in current smokers is 4.87 (95% CI 3.93 – 6.02) and in former smokers is 2.10 (95% CI 1.76 – 2.50) compared to never smokers.[518]
- The Canadian Tobacco, Alcohol and Drugs Survey, 2017 indicated that 16.8% (95% CI 11.6 – 22.0%) of **men 45+ in BC** are current smokers, 36.3% (95% CI 29.6 – 43.0%) are former smokers and 47% (95% CI 39.6 – 54.3) have never smoked.[519]

[514] Oliver-Williams C, Sweeting MJ, Turton G et al. Lessons learned about prevalence and growth rates of abdominal aortic aneurysms from a 25-year ultrasound population screening programme. *British Journal of Surgery*. 2018; 105(1): 68-74.
[515] Semmens J, Norman P, Lawrence-Brown M et al. Population-based record linkage study of the incidence of abdominal aortic aneurysm in Western Australia in 1985–1994. *British Journal of Surgery.* 1998; 85(5): 648-52.
[516] Johansson M, Zahl PH, Siersma V et al. Benefits and harms of screening men for abdominal aortic aneurysm in Sweden: a registry-based cohort study. *The Lancet.* 2018; 391(10138): 2441-7.
[517] Johansson M, Zahl PH, Siersma V et al. Benefits and harms of screening men for abdominal aortic aneurysm in Sweden: a registry-based cohort study. *The Lancet.* 2018; 391(10138): 2441-7.
[518] Aune D, Schlesinger S, Norat T et al. Tobacco smoking and the risk of abdominal aortic aneurysm: a systematic review and meta-analysis of prospective studies. *Scientific Reports.* 2018; 8(1): 14786.
[519] Government of Canada. *Canadian Tobacco, Alcohol and Drugs (CTADS) Survey: 2017 Detailed Tables.* 2017. Available at https://www.canada.ca/en/health-canada/services/canadian-tobacco-alcohol-drugs-survey/2017-summary/2017-detailed-tables.html#t2. Accessed January 2019.

- Based on Canadian Community Health Survey data from 2014, 12.9% of BC men ages **65-69** are daily or occasional smokers.[520]

- For modelling purposes, we assume that 12.9% of men 65 years of age are current smokers (Table 5, row *d*), 47% are never smokers (Table 5, row *b*) and the balance (40.1%) are former smokers (Table 5, row *c*).

- In Table 2 we combine the estimated AAA-related death rate for the population as a whole (51.7 / 100,000 person years, see Table 1), the proportion of 65 year old BC men by smoking category and the relative risk of AAA for current-smokers, former-smokers and never-smokers. At the same time, we calculated the prevalence of AAA in each group, using our model prevalence of 2.35% for the whole population (Table 5, row *e*).

- The results suggest a prevalence of 1.21% (Table 5, row *f*) and an AAA-related death rate of 26.6 / 100,000 in never-smokers, a prevalence of 2.54% (Table 5, row *g*) and an AAA-related death rate of 55.9 / 100,000 in former-smokers and a prevalence of 5.90% (Table 5, row *h*) and an AAA-related death rate of 129.7 / 100,000 in current-smokers.

Table 2: Screening for Abdominal Aortic Aneurysm Men 65+
AAA Prevalence and Death Rates by Smoking Category

	Total	Never-Smoker	Former-Smoker	Current-Smoker
Proportion of Population	1.00	0.470	0.401	0.129
Relative Risk of AAA		1.00	2.10	4.87
Prevalence of AAA	2.35%	1.21%	2.54%	5.90%
Death Rate per 100,000	51.7	26.6	55.9	129.7

- Howard et al. report the incidence of acute AAA events to be 55 / 100,000 per year in 65-74 year olds and 112 / 100,000 per year in 75-84 year olds. Of these acute AAA events, 59.2% were fatal within 30 days.[521] This works out to AAA-related death rates of 32.6 (55 * 0.592) and 66.3 (112 * 0.592) / 100,000 for 65-74 and 75-84 year olds respectively.

- Howard and colleagues also report that 22.3% of incident AAA-events took place in 65 – 74 year olds, with only 13.1% of AAA-related deaths occurring in this age group.[522]

- We adjust the rates for age groups from 65 – 74 and 75 – 84 to reflect that 86.9% of AAA-related deaths are in the 75+ age group, while ensuring the total population rates still reflect what was calculated in Table 2. The deaths and life-years lost in a cohort of BC men 65+ due to AAA is shown in Table 3. We model from AAA screening at age 65 through to age 84, in keeping with the average life expectancy of 19.5 years for a 65 year old male from the BC Life Table.

[520] Based on the Statistics Canada's Canadian Community Health Survey 2014 Public Use Microdata File. All computations, use and interpretation of these data are entirely that of H. Krueger & Associates Inc.
[521] Howard D, Banerjee A, Fairhead J et al. Age-specific incidence, risk factors and outcome of acute abdominal aortic aneurysms in a defined population. *British Journal of Surgery*. 2015; 102(8): 907-15.
[522] Howard D, Banerjee A, Fairhead J et al. Age-specific incidence, risk factors and outcome of acute abdominal aortic aneurysms in a defined population. *British Journal of Surgery*. 2015; 102(8): 907-15.

- AAA is usually asymptomatic prior to rupture,[523] therefore reduced quality of life in those living with AAA is not presented in Table 3 or considered in our model.
- Table 3 indicates that, in our birth cohort, we would expect 36 AAA-related deaths in male never-smokers (Table 5, row *p*), 65 AAA-related deaths in former-smokers (Table 5, row *q*) and 48 AAA-related deaths in current-smokers (Table 5, row *r*). These 149 AAA-related deaths represent 1.90% of the total 7,872 deaths in the cohort between the ages of 65 and 84. Research from other jurisdictions suggests an AAA-related death rate of between 1-2% of total deaths.[524,525] These 149 deaths would result in the loss of 1,068 (259 + 464 + 346) QALYs in our cohort.
- BC Vital Statistics annual reports provide a detailed listing (by ICD-10 code) of annual deaths by age and sex. ICD-10 code I71 is for deaths due to "aortic aneurysm & dissection." If we combine deaths due to ICD-10 code I71 from the 2013[526], 2014[527] and 2015[528] BC Vital Statistics annual reports, 0.78% of deaths in males 65 – 79 and 0.72% of deaths in males 80 and over were attributed to ICD-10 code I71. In males over 65, 0.74% of deaths were attributed to ICD-10 code I71. This proportion of deaths attributable to ICD-10 code I71 is considerably lower than our modelled estimate of 1.90%. Using cause of death data from vital statistics can be somewhat challenging as research has indicted that at least 15% of all deaths are miscoded in vital statistics data in the US and Canada.[529] It is possible, therefore, that the 0.74% is an underrepresentation of the actual proportion of deaths due to AAA in BC males 65 years of age and older due to AAA. We include the 0.74% in our sensitivity analysis.

[523] Kapila V, Jetty P, Doug Wooster M et al. 2018 Screening for abdominal aortic aneurysms in Canada: review and position statement from the Canadian Society of Vascular Surgery. Available at https://canadianvascular.ca/resources/Documents/Clinical-Guidelines/FINAL-2018-CSVS-Screening-Recommendations.pdf. Accessed January 2019.

[524] Howard D, Banerjee A, Fairhead J et al. Age-specific incidence, risk factors and outcome of acute abdominal aortic aneurysms in a defined population. *British Journal of Surgery*. 2015; 102(8): 907-15.

[525] Sandiford P, Mosquera D and Bramley D. Trends in incidence and mortality from abdominal aortic aneurysm in New Zealand. *British Journal of Surgery*. 2011; 98(5): 645-51.

[526] BC Vital Statistics Agency. *Annual Report 2013. Selected Vital Statistics and Health Status Indicators.* 2015. Available at https://www2.gov.bc.ca/assets/gov/birth-adoption-death-marriage-and-divorce/statistics-reports/annual-reports/2013/pdf/annual-report-2013.pdf. Accessed February 2019.

[527] BC Vital Statistics Agency. *Annual Report 2014. Selected Vital Statistics and Health Status Indicators.* 2015. Available at https://www2.gov.bc.ca/assets/gov/birth-adoption-death-marriage-and-divorce/statistics-reports/annual-reports/2014/pdf/annual-report-2014.pdf. Accessed February 2019.

[528] BC Vital Statistics Agency. *Annual Report 2015. Selected Vital Statistics and Health Status Indicators.* 2015. Available at https://www2.gov.bc.ca/assets/gov/birth-adoption-death-marriage-and-divorce/statistics-reports/annual-reports/2015/pdf/annual-report-2015.pdf. Accessed February 2019.

[529] Naghavi M, Makela S, Foreman K. Research Algorithms for enhancing public health utility of national causes-of-death data. *Population Health Metrics*. 2010; 8: 9.

Table 3: Screening for Abdominal Aortic Aneurysm in Men 65+
Deaths and Life Years Lost Due to Abdominal Aortic Aneurysm
In a BC Birth Cohort of 40,000

		Never Smokers			*Former Smokers*			*Current Smokers*					*Life Years Lost Due to Death*		
Age	# in Cohort	Proportion of Population	AAA-Related Deaths per 100,000 person years	AAA-Related Deaths	Proportion of Population	AAA-Related Deaths per 100,000 person years	AAA-Related Deaths	Proportion of Population	AAA-Related Deaths per 100,000 person years	AAA-Related Deaths	AAA-Deaths in **Ever Smokers**	Life Expectancy	*Never Smokers*	*Former Smokers*	*Current Smokers*
65	17,559	47.0%	6.1	0.5	40.1%	12.9	0.9	12.9%	29.8	0.7	1.6	20	10.1	18.1	13.5
66	17,370	47.0%	6.1	0.5	40.1%	12.9	0.9	12.9%	29.8	0.7	1.6	19	9.5	17.0	12.7
67	17,164	47.0%	6.1	0.5	40.1%	12.9	0.9	12.9%	29.8	0.7	1.5	18	8.9	15.9	11.9
68	16,940	47.0%	6.1	0.5	40.1%	12.9	0.9	12.9%	29.8	0.7	1.5	17	8.3	14.8	11.1
69	16,697	47.0%	6.1	0.5	40.1%	12.9	0.9	12.9%	29.8	0.6	1.5	16	7.7	13.8	10.3
70	16,434	47.0%	6.1	0.5	40.1%	12.9	0.8	12.9%	29.8	0.6	1.5	15	7.1	12.7	9.5
71	16,147	47.0%	6.1	0.5	40.1%	12.9	0.8	12.9%	29.8	0.6	1.5	14	6.5	11.7	8.7
72	15,837	47.0%	6.1	0.5	40.1%	12.9	0.8	12.9%	29.8	0.6	1.4	13	5.9	10.6	7.9
73	15,500	47.0%	6.1	0.4	40.1%	12.9	0.8	12.9%	29.8	0.6	1.4	12	5.4	9.6	7.2
74	15,136	47.0%	6.1	0.4	40.1%	12.9	0.8	12.9%	29.8	0.6	1.4	11	4.8	8.6	6.4
75	14,743	47.0%	53.9	3.7	40.1%	113.1	6.7	12.9%	262.3	5.0	11.7	10	37.3	66.9	49.9
76	14,318	47.0%	53.9	3.6	40.1%	113.1	6.5	12.9%	262.3	4.8	11.3	9	32.6	58.4	43.6
77	13,861	47.0%	53.9	3.5	40.1%	113.1	6.3	12.9%	262.3	4.7	11.0	8	28.1	50.3	37.5
78	13,370	47.0%	53.9	3.4	40.1%	113.1	6.1	12.9%	262.3	4.5	10.6	7	23.7	42.4	31.7
79	12,844	47.0%	53.9	3.3	40.1%	113.1	5.8	12.9%	262.3	4.3	10.2	6	19.5	35.0	26.1
80	12,283	47.0%	53.9	3.1	40.1%	113.1	5.6	12.9%	262.3	4.2	9.7	5	15.5	27.9	20.8
81	11,686	47.0%	53.9	3.0	40.1%	113.1	5.3	12.9%	262.3	4.0	9.3	4	11.8	21.2	15.8
82	11,053	47.0%	53.9	2.8	40.1%	113.1	5.0	12.9%	262.3	3.7	8.8	3	8.4	15.0	11.2
83	10,386	47.0%	53.9	2.6	40.1%	113.1	4.7	12.9%	262.3	3.5	8.2	2	5.3	9.4	7.0
84	9,688	47.0%	53.9	2.5	40.1%	113.1	4.4	12.9%	262.3	3.3	7.7	1	2.5	4.4	3.3
Total			**26.6**	**36**		**55.9**	**65**		**129.7**	**48**	**113**		**259**	**464**	**346**

- There are three primary AAA-related modes of death considered by the randomized controlled trials: death as a result of AAA rupture before receiving emergency surgery at a hospital, death as a result of AAA rupture after receiving emergency surgery, and death due to complications following elective surgery.
- Only one good quality USPSTF referenced study reported on rates of elective and emergency surgery in the control and screening intervention groups; the Viborg study reported by Lindholt and colleagues.[530] They report an elective surgery rate of 70 / 100,000 and an emergency surgery rate of 70 / 100,000 in the control population at a reported AAA prevalence of 4.0%.
- We model that these rates would be reduced linearly to 41 / 100,000 person years (Table 5, row *v*) and 41 / 100,000 person years (Table 5, row *ac*) for elective and emergency procedures respectively due to the lower estimated prevalence of AAA (2.35%) used in our model (see Table 4).

Table 4: Screening for Abdominal Aortic Aneurysm Men Ages 65+
Adjusted Surgery Rates Based on Lower AAA Prevalence [1]

Variable	Study Prevalence of AAA	Incidence per 100,000 person years	Model Prevalence of AAA	Adjusted Incidence per 100,000 person years
Elective Operations, Control	4.0%	70	2.35%	41
Acute Operation, with Rupture, Control	4.0%	57	2.35%	33
Acute Operation, **without** rupture, Control	4.0%	13	2.35%	8
Total for Acute Operations, Control	4.0%	70	2.35%	41

[1] Source: Lindholt et al. (2010)

[530] Lindholt J, Juul S, Fasting H et al. Screening for abdominal aortic aneurysms: single centre randomised controlled trial. *BMJ*. 2005; 330: 750.

- Guirguis-Blake and colleagues conducted a pooled analysis of RCTs reporting 13-15 year follow up results and calculated the following relative risks in the screening group: [531]
    - RR of elective operations for AAA: 2.15 (95% CI, 1.89 – 2.44)
    - RR of emergency operations for AAA: 0.52 (95% CI, 0.40 – 0.66)
    - RR of AAA-related mortality: 0.58 (95% CI, 0.39 – 0.88)

- We model the RR after the pooled analysis by Guirguis-Blake et al. with a relative risk of elective operations of 2.15 (Table 5, row *al*), a relative risk of emergency operations of 0.52 (Table 5, row *au*), and an overall relative risk of AAA-related death of 0.58 in the screening group (Table 5, row *az*).

- There are a number of cases of asymptomatic AAA that could be found without screening. This number ranges from 7 - 25% in economic analyses and studies reporting this variable.[532,533,534,535,536]

- For modelling purposes we use the mid-point between 7% and 25% (13%) and vary this from 7 – 25% in our sensitivity analysis (Table 5, row *ak*).

- Reporting on the years 2003 – 2004 for Canada, Forbes et al. reported that 8.9% of elective AAA-repair was carried out by endovascular surgery, with the balance being open surgery.[537]
- Jetty and Husereau reported on Canadian trends from 2004 – 2009 and reported that endovascular aneurysm repair (EVAR) rates rose from 11.5% to 35.5% in Canada during that time. They also report substantial regional differences in elective endovascular repair rates, from a low of 15.8% in Manitoba to a high of 45.0% in BC in 2009. BC's rate increased each year from 7.5% in 2005 to 45.0% in 2009.[538]
- Of the 1,958 surgeries for AAA in BC between 2013/14 and 2017/18, 1,142 were EVAR (58%) and 816 were open (42%).[539]

[531] Guirguis-Blake J, Beil T, Sun X et al. Primary Care Screening for Abdominal Aortic Aneurysm: A Systematic Evidence Review for the US Preventive Services Task Force. Evidence Synthesis No. 109. 2014: Available at https://www.ncbi.nlm.nih.gov/books/NBK184793/. Accessed January 2019.
[532] Montreuil B and Brophy J. Screening for abdominal aortic aneurysms in men: a Canadian perspective using Monte Carlo–based estimates. *Canadian Journal of Surgery*. 2008; 51(1): 23.
[533] Silverstein MD, Pitts SR, Chaikof EL et al. Abdominal aortic aneurysm (AAA): cost-effectiveness of screening, surveillance of intermediate-sized AAA, and management of symptomatic AAA. *Baylor University Medical Center Proceedings*. 2005; 18(4): 345-67.
[534] Wanhainen A, Lundkvist J, Bergqvist D et al. Cost-effectiveness of different screening strategies for abdominal aortic aneurysm. *Journal of Vascular Surgery.* 2005; 41(5): 741-51.
[535] Wanhainen A, Hultgren R, Linné A et al. Outcome of the Swedish nationwide abdominal aortic aneurysm screening program. *Circulation*. 2016; 134(16): 1141-8.
[536] Howard D, Banerjee A, Fairhead J et al. Age-specific incidence, risk factors and outcome of acute abdominal aortic aneurysms in a defined population. *British Journal of Surgery*. 2015; 102(8): 907-15.
[537] Forbes TL, Lawlor DK, DeRose G et al. National audit of the recent utilization of endovascular abdominal aortic aneurysm repair in Canada: 2003 to 2004. *Journal of Vascular Surgery.* 2005; 42(3): 410-4.
[538] Jetty P and Husereau D. Trends in the utilization of endovascular therapy for elective and ruptured abdominal aortic aneurysm procedures in Canada. *Journal of Vascular Surgery.* 2012; 56(6): 1518-26.
[539] Aciemme (Sam) Ospan, Senior Manager, Lifetime Prevention Schedule, Healthy Living and Health Promotion Branch, BC Ministry of Health. June 3, 2019. Personal communication.

- Recent evidence from the UK and Sweden also indicate a rate for elective EVAR of 59%. [540,541]

- We model an EVAR rate of 58% in BC (Table 5, rows *x* & *ap*).

- The USPSTF referenced two key studies comparing early open surgery with surveillance in their analysis of the harms of screening.[542] One study was conducted in the UK (UKSAT)[543] and the other in the US (ADAM).[544]

- Greenhalgh and colleagues reported a 30-day mortality rate of 5.8% in patients receiving open surgery in the UK Small Aneurysm Trial (UKSAT). The authors acknowledge that this rate was "about half the national in-hospital mortality rate for elective repair" of AAA. [545] This study was conducted at a time when endovascular surgery was "still under development".

- Lederle and colleagues reported a 30-day mortality rate of 2.0% in patients receiving open surgery in the Aneurysm Detection and Management (ADAM) study.[546]

- Thompson and colleagues reported a 30-day mortality of 1.8% and 4.6% for elective endovascular and elective open AAA surgeries respectively (MASS study in UK).[547]

- Several studies published since the USPSTF recommendation in 2014 have reported on elective surgery mortalities. A study of Medicare beneficiaries in the US reported a perioperative (within 30-days of surgery) mortality rate of 1.6% for endovascular repair of AAA and 5.2% for open repair. The mean age was 75.6 for those receiving surgery and the data used was from 2001 - 2008.[548]

- More recent European studies report ranges of 0.3% – 0.7% and 0.9% – 1.3% for 30-day mortality following endovascular repair and open surgery respectively.[549,550] Neither study explicitly states the mean age of patients receiving surgery, but

[540] Jacomelli J, Summers L, Stevenson A et al. Impact of the first 5 years of a national abdominal aortic aneurysm screening programme. *British Journal of Surgery*. 2016; 103(9): 1125-31.
[541] Wanhainen A, Hultgren R, Linné A et al. Outcome of the Swedish nationwide abdominal aortic aneurysm screening program. *Circulation*. 2016; 134(16): 1141-8.
[542] Guirguis-Blake JM, Beil TL, Senger CA et al. Ultrasonography screening for abdominal aortic aneurysms: a systematic evidence review for the US Preventive Services Task Force. *Annals of Internal Medicine.* 2014; 160(5): 321-9.
[543] Greenhalgh R, Brady A, Brown L et al. Mortality results for randomised controlled trial of early elective surgery or ultrasonographic surveillance for small abdominal aortic aneurysms. The UK Small Aneurysm Trial Participants. *The Lancet.* 1998; 352: 1649-55.
[544] Lederle FA, Wilson SE, Johnson GR et al. Immediate repair compared with surveillance of small abdominal aortic aneurysms. *New England Journal of Medicine*. 2002; 346(19): 1437-44.
[545] Greenhalgh R, Brady A, Brown L et al. Mortality results for randomised controlled trial of early elective surgery or ultrasonographic surveillance for small abdominal aortic aneurysms. The UK Small Aneurysm Trial Participants. *The Lancet.* 1998; 352: 1649-55.
[546] Lederle FA, Wilson SE, Johnson GR et al. Immediate repair compared with surveillance of small abdominal aortic aneurysms. *New England Journal of Medicine*. 2002; 346(19): 1437-44.
[547] Thompson S, Ashton H, Gao L et al. Final follow-up of the Multicentre Aneurysm Screening Study (MASS) randomized trial of abdominal aortic aneurysm screening. *British Journal of Surgery*. 2012; 99(12): 1649-56.
[548] Schermerhorn ML, Buck DB, O'malley AJ et al. Long-term outcomes of abdominal aortic aneurysm in the Medicare population. *New England Journal of Medicine*. 2015; 373(4): 328-38.
[549] Jacomelli J, Summers L, Stevenson A et al. Impact of the first 5 years of a national abdominal aortic aneurysm screening programme. *British Journal of Surgery*. 2016; 103(9): 1125-31.
[550] Wanhainen A, Hultgren R, Linné A et al. Outcome of the Swedish nationwide abdominal aortic aneurysm screening program. *Circulation*. 2016; 134(16): 1141-8.

Jacomelli et al.[551] report on screening of 65 year-old men and Wanhainen et al.[552] on 65 – 74 year old men, so it can be inferred that their results are taken from a younger cohort than is reported by Schermerhorn and colleagues.[553]

- In a report using Ontario data de Mestral and colleagues report a 90-day mortality rate following endovascular repair of 1.6%.[554]
- Reporting on outcomes of open repair of AAA in Ontario, Dubois and colleagues report a 30-day mortality for open repair of 3%.[555]

- We model a 30-day mortality of 1.0% and 3.0% for elective endovascular and open surgery respectively (Table 5, rows *z* & *aa* and *ar* & *as*).

- In their evidence synthesis for the USPSTF, Guirguis-Blake and colleagues report an estimate of 41% mortality (either in hospital or 30-day) associated with emergency surgery for AAA.[556]

- We model an emergency surgery 30-day mortality of 41% (Table 5, row *ae* & *ax*).

Based on these assumptions, the CPB associated with screening for abdominal aortic aneurysms in males aged 65 who have ever smoked is 340 QALYs (see Table 5, row *bk*).

Comparison to Actual BC Data

Analysis from the discharge abstract database in BC from 2013/14 – 2017/18 indicates that 77.8 / 100,000 men over 65 years old had elective AAA surgery and 24.8 / 100,000 men over 65 years old had emergency and / or ruptured AAA surgery, a ratio of 3.14.[557] Our model calculates these rates at 88.4 /100,000 and 21.4 / 100,000 respectively, a difference of approximately 14% from the actuals in both cases. With no screening (i.e. in the control group), the Viborg study reported the same rates of elective and emergency surgery (see Table 4). If there was no screening in BC, we might expect a similar ratio as the unscreened population in the Viborg study. The fact that there are more than three times as many elective as emergency surgeries in BC suggests that BC physicians are already opportunistically screening their patients in the province. In the fully screened population analysed by the USPSTF,[558] the ratio of elective to emergency surgeries was 4.13, indicating that while

[551] Jacomelli J, Summers L, Stevenson A et al. Impact of the first 5 years of a national abdominal aortic aneurysm screening programme. *British Journal of Surgery*. 2016; 103(9): 1125-31.

[552] Wanhainen A, Hultgren R, Linné A et al. Outcome of the Swedish nationwide abdominal aortic aneurysm screening program. *Circulation*. 2016; 134(16): 1141-8.

[553] Schermerhorn ML, Buck DB, O'malley AJ et al. Long-term outcomes of abdominal aortic aneurysm in the Medicare population. *New England Journal of Medicine*. 2015; 373(4): 328-38.

[554] de Mestral C, Croxford R, Eisenberg N et al. The impact of compliance with imaging follow-up on mortality after endovascular abdominal aortic aneurysm repair: a population based cohort study. *European Journal of Vascular and Endovascular Surgery*. 2017; 54(3): 315-23.

[555] Dubois L, Shariff S, Jenkyn KB et al. PC010 Higher Surgeon Annual Volume, but Not Years of Experience, Leads to Reduced Rates of Perioperative Complications and Reoperations Following Open AAA Repair. *Journal of Vascular Surgery.* 2017; 65(6): 143S-4S.

[556] Guirguis-Blake J, Beil T, Sun X et al. Primary Care Screening for Abdominal Aortic Aneurysm: A Systematic Evidence Review for the US Preventive Services Task Force. Evidence Synthesis No. 109. 2014: Available at https://www.ncbi.nlm.nih.gov/books/NBK184793/. Accessed January 2019.

[557] Aciemme (Sam) Ospan, Senior Manager, Lifetime Prevention Schedule, Healthy Living and Health Promotion Branch, BC Ministry of Health. June 3, 2019. Personal communication.

[558] Guirguis-Blake J, Beil T, Sun X et al. Primary Care Screening for Abdominal Aortic Aneurysm: A Systematic Evidence Review for the US Preventive Services Task Force. Evidence Synthesis No. 109. 2014: Available at https://www.ncbi.nlm.nih.gov/books/NBK184793/. Accessed January 2019.

opportunistic screening is occurring in BC, it has not yet reached a level in which the majority of eligible males (we model a 'best-in-the –world' rate of 85.8%[559]) are screened.

Table 5: CPB of Abdominal Aortic Aneurysm Screening in Ever-Smoking Men 65+
In a BC Birth Cohort of 40,000

Row Label	Variable	Base Case	Data Source
	Deaths and Life-Years Lost due to AAA in an Unscreened Cohort		
a	Number of 65-year old men in cohort	17,559	BC Life Table
b	Proportion of population, *never-smokers*	47.0%	√
c	Proportion of population, *former smokers*	40.1%	√
d	Proportion of population, *current smokers*	12.9%	√
e	Prevalence of AAA in population	2.35%	√
f	Prevalence of AAA in *never-smokers*	1.21%	Table 2
g	Prevalence of AAA in *former smokers*	2.54%	Table 2
h	Prevalence of AAA in *current smokers*	5.90%	Table 2
i	Life years for cohort from 65 - 84	289,017	Table 3
j	Life years, ever-smokers for cohort from 65 - 84	153,179	= i * (c + d)
k	Number with AAA in cohort at age 65, *never-smokers*	100	=a * b * f
l	Number with AAA in cohort at age 65, *former smokers*	179	=a * c * g
m	Number with AAA in cohort at age 65, *current smokers*	134	=a * d * h
n	Number of AAA-related deaths over cohort lifetime	149	Table 3
o	Fraction of those with AAA dying over cohort lifetime, total population	36.2%	= n / (k + l + m)
p	Number of deaths over cohort lifetime, **never-smokers**	**36**	= k * o
q	Number of deaths over cohort lifetime, **former smokers**	**65**	= l * o
r	Number of deaths over cohort lifetime, **current smokers**	**48**	= m * o
s	Life years lost over cohort lifetime, **never-smokers**	**259**	Table 3
t	Life years lost over cohort lifetime, **former smokers**	**464**	Table 3
u	Life years lost over cohort lifetime, **current smokers**	**346**	Table 3
	AAA-related deaths in an Unscreened Cohort of *Ever-Smokers*		
v	Rate of elective surgery per 100,000, unscreened population	41	Table 4
w	Number of elective surgeries in cohort	63	= (v / 100,000) * j
x	Proportion of elective surgeries that are endovascular	58%	√
y	Proportion of elective surgeries that are open	42%	= (1 - ag)
z	30-day mortality for elective endovascular AAA surgery	1.0%	√
aa	30-day mortality for elective open AAA surgery	3.0%	√
ab	Number of deaths associated with **elective surgeries**	**1.2**	= w * ((x * z) + (y * aa))
ac	Rate of emergency surgery per 100,000, unscreened population	41	Table 4
ad	Number of emergency surgeries in cohort	63	= (ac / 100,000) * j
ae	Death rate, emergency surgery	41%	√
af	Number of deaths associated with **emergency surgeries**	**25.8**	= ad * ae
ag	Number of deaths **prior to arriving at hospital for surgery**	**86.2**	= (q + r) - ab - af

[559] Jacomelli J, Summers L, Stevenson A et al. Impact of the first 5 years of a national abdominal aortic aneurysm screening programme. *British Journal of Surgery*. 2016; 103(9): 1125-31.

Table 5: CPB of Abdominal Aortic Aneurysm Screening in Ever-Smoking Men 65+ In a BC Birth Cohort of 40,000			
Row Label	**Variable**	**Base Case**	**Data Source**
	AAA-related deaths in a Screened Cohort of *Ever-Smokers*		
ah	Number targeted for screening, base case: **ever-smokers** (current + former)	9,306	= a * (c + d)
ai	Screening Rate	85.8%	√
aj	Total Number screened	7,985	= v * w
ak	Proportion of AAA opportunistically detected without screening	13%	√
al	Relative risk of elective surgery, screened vs. unscreened population	2.15	√
am	Rate of elective surgery per 100,000, screened population	88.4	= al * v
an	Number of elective surgeries in cohort	135	= ((am / 100,000) * j)
ao	Number of elective surgeries in cohort, due to screening alone	63	= an * (1 - ak)
ap	Proportion of elective surgeries that are endovascular	58%	= x
aq	Proportion of elective surgeries that are open	42%	= y
ar	30-day mortality for elective endovascular AAA surgery	1.0%	= z
as	30-day mortality for elective open AAA surgery	3.0%	= aa
at	Number of deaths associated with **elective surgeries**	**2.5**	= an * ((ap * ar) + (aq * as))
au	Relative risk of emergency surgery, screened vs. unscreened population	0.52	√
av	Rate of emergency surgery per 100,000, unscreened population	21.4	= au *ac
aw	Number of emergency surgeries in cohort	33	= (au / 100,000) * j
ax	Death rate, emergency surgery	41%	√
ay	Number of deaths associated with **emergency surgeries**	**13.4**	= aw * ax
az	Relative risk of AAA-related death, overall, screened vs. unscreened population	0.58	√
ba	AAA-related deaths in screened cohort	66	= (q + r) * az
bb	Number of deaths **prior to arriving at hospital for surgery**	**49.7**	= ba - ay - at
	Difference in AAA-related deaths in a Screened vs. Unscreened Cohort of *Ever-Smokers*		
bc	Deaths due to elective surgeries, screened vs. unscreened	1.3	= at - ab
bd	Deaths due to emergency surgeries, screened vs. unscreened	-12.4	= ay - af
bf	Deaths prior to hospital arrival, screened vs. unscreened	-36.5	= bb - ag
bg	**Difference in total AAA-related deaths, screened vs. unscreened**	**-47.6**	= bc + bd + bf
bh	Total AAA-related deaths in unscreened cohort	113	= q + r
bi	Fraction of deaths avoided as a result of screening	42%	= (-bg) / bh
	Difference in Life Years, Screened vs. Unscreened Cohort of *Ever-Smokers*		
bj	Life years lost due to **death from** AAA in unscreened ever-smoking group	810	Table 3
bk	QALYs saved by screening	340	= bi * bj

v = Estimates from the literature

For the sensitivity analysis, we modified the relative risk assumptions and recalculated the CPB as follows:

- Assume that the relative risk of overall death is increased from 0.58 to 0.88 (Table 5, row *az*), the relative risk of elective surgery in screened individuals is *decreased* from 2.15 to 1.89 (Table 5, row *al*) and the relative risk of emergency surgery is increased from 0.52 to 0.66 (Table 5, row *au)*: CPB = 97
- Assume that the relative risk of overall death is decreased from 0.58 to 0.39 (Table 5, row az), the relative risk of elective surgery in screened individuals is *increased* from 2.15 to 2.44 (Table 5, row al) and the relative risk of emergency surgery is decreased from 0.52 to 0.40 (Table 5, row au): CPB = 494
- Offer screening to all 65 year old males, rather than to just 65 year old male ever-smokers (Table 5, rows *b*, *c* and *d*): CPB = 449
- Assume vital statistics death rate of 0.74% in population 65 and older due to abdominal aortic aneurysm, rather than the 1.90% calculated in the model: CPB = 133

Modelling Cost-Effectiveness

In this section, we will calculate the CE associated with screening for abdominal aortic aneurysms in males ages 65 to 75 who have ever smoked

In modelling CE, we made the following assumptions:

- The single screen recommended by the USPSTF is conducted at age 65.
- The screen targets only the population of ever-smokers (i.e. current and former smokers). We assess the benefits of screening the whole population in our sensitivity analysis.
- For modelling purposes, we assume that 12.9% of men 65 years of age are current smokers (Table 6, row *d*) and 40.1% are former smokers (Table 6, row *c*).
- We assume that all 65 year old males will have at least one visit to their GP each year.
- We model a best-in-world screening acceptance rate of 85.8% (Table 6, row *e*).[560]
- The cost of each 10 minute primary care provider office visit is $34.85 (Reference Document) (Table 6, row *g)*
- The value of patient time (based on 2 hours, including travel time) for each visit to a primary care office and for abdominal ultrasound screening is $59.38 (Reference Document) (Table 6, row *h*).
- The proportion of each office visit attributable to recommending screening is 50% (Reference Document) (Table 8, row *i*).
- The average service fee cost of an abdominal B-scan (ultrasound – fee item 8648) in BC between 2012 and 2016 was $106.81 (Table 6, row *k*).[561]
- Visser reported elective endovascular surgery costs at €20,767 (2003) or $38,084 (2017 CAD), with those costs rising to €23,588 (2003) or $43,257 (2017 CAD) if one-year follow-up costs were included.[562]
- Matsumura and colleagues reported elective endovascular surgery costs between $34,800 – 38,900 USD (2008) or $33,750 – 37,726 (2017 CAD), depending on which device was used in the surgery.[563]
- Similarly, in their cost-effectiveness analysis, Svensjo and colleagues use an elective endovascular surgery cost of €24,493 (2012), with that cost rising to €29,758 if post-

[560] Jacomelli J, Summers L, Stevenson A et al. Impact of the first 5 years of a national abdominal aortic aneurysm screening programme. *British Journal of Surgery*. 2016; 103(9): 1125-31.
[561] B.C. Ministry of Health, Health Sector Information, Analysis & Reporting Division. *MSP Fee-For-Service Payment Analysis 2012/2013 - 2016/2017*. 2017. Available at https://www2.gov.bc.ca/assets/gov/health/practitioner-pro/medical-services-plan/ffs_complete.pdf. Accessed November 2018.
[562] Visser JJ, van Sambeek MR, Hunink MM et al. Acute abdominal aortic aneurysms: cost analysis of endovascular repair and open surgery in hemodynamically stable patients with 1-year follow-up. *Radiology*. 2006; 240(3): 681-9.
[563] Matsumura JS, Stroupe KT, Lederle FA et al. Costs of repair of abdominal aortic aneurysm with different devices in a multicenter randomized trial. *Journal of Vascular Surgery*. 2015; 61(1): 59-65.

operative costs were included as well.[564] Converted to 2017 CAD the amounts are $40,778 and $49,544 respectively.

- For elective endovascular surgery, Burgers and colleagues reported surgery costs of €14,690 (2013) or $22,534 (2017 CAD).[565]

- Elective endovascular surgery costs, adjusted to 2017 CAD, range between $22,534 (Burgers et al.) and $49,544 (Svensjö et al.). We model elective endovascular AAA-repair surgery costs at $36,039 (the mid-point of this) and vary this to $22,534 and $49,544 in our sensitivity analysis (Table 6, row *s*).

- We noted previously that we assume a 30-day mortality of 1.0% and 3.0% for elective endovascular and open surgery respectively. This early mortality advantage associated with EVAR erodes over time, with no survival advantage after 4 to 5 years of follow-up.[566,567,568]

- Based on 15 years of follow-up results from the UK EVAR trial, graft-related re-interventions remained higher in patients with endovascular repair compared with open repair. Overall, any graft-related re-intervention occurred in 26% of EVAR vs. 12% of open patients. Serious graft-related re-interventions occurred in 22% of EVAR vs. 9% of open patients while life-threatening re-interventions occurred in 14% of EVAR vs. 7% of open patients. The authors note that "there is no time to assume that it is safe to discontinue surveillance in patients who have had EVAR".[569]

- Studies assessing the long-term cost-effectiveness of EVAR vs. open surgery that take into account the changing survival profile following EVAR and open surgery, as well as differential graft-related intervention rates, have found no differences in cost-effectiveness. Epstein and colleagues "did not find that EVAR is cost-effective compared with open repair in the long term in trials conducted in European centres."[570] Lederle and co-authors conclude that, based on follow-up of 9 years, "survival, quality of life, costs and cost-effectiveness did not differ between elective open and endovascular repair of AAA."[571] Cost-effectiveness studies with a follow-up period of less than 4 years, on the other hand, find EVAR to be cost-effective

[564] Svensjö S, Mani K, Björck M et al. Screening for abdominal aortic aneurysm in 65-year-old men remains cost-effective with contemporary epidemiology and management. *European Journal of Vascular and Endovascular Surgery*. 2014; 47(4): 357-65.
[565] Burgers L, Vahl A, Severens J et al. Cost-effectiveness of elective endovascular aneurysm repair versus open surgical repair of abdominal aortic aneurysms. *European Journal of Vascular and Endovascular Surgery*. 2016; 52(1): 29-40.
[566] Patel R, Sweeting MJ, Powell JT et al. Endovascular versus open repair of abdominal aortic aneurysm in 15-years' follow-up of the UK endovascular aneurysm repair trial 1 (EVAR trial 1): a randomised controlled trial. *The Lancet*. 2016; 388(10058): 2366-74.
[567] Deery SE and Schermerhorn ML. Open versus endovascular abdominal aortic aneurysm repair in Medicare beneficiaries. *Surgery*. 2017; 162(4): 721-31.
[568] Powell JT, Sweeting MJ, Ulug P et al. Meta-analysis of individual-patient data from EVAR-1, DREAM, OVER and ACE trials comparing outcomes of endovascular or open repair for abdominal aortic aneurysm over 5 years. *British Journal of Surgery*. 2017; 104(3): 166-78.
[569] Patel R, Sweeting MJ, Powell JT et al. Endovascular versus open repair of abdominal aortic aneurysm in 15-years' follow-up of the UK endovascular aneurysm repair trial 1 (EVAR trial 1): a randomised controlled trial. *The Lancet*. 2016; 388(10058): 2366-74.
[570] Epstein D, Sculpher M, Powell J et al. Long-term cost-effectiveness analysis of endovascular versus open repair for abdominal aortic aneurysm based on four randomized clinical trials. *British Journal of Surgery*. 2014; 101(6): 623-31.
[571] Lederle FA, Stroupe KT, Kyriakides TC et al. Long-term cost-effectiveness in the veterans affairs open vs endovascular repair study of aortic abdominal aneurysm: A randomized clinical trial. *JAMA Surgery.* 2016; 151(12): 1139-44.

compared with open surgery, largely due to the early survival advantages associated with EVAR.[572]

- Because of this long term convergence in the benefits and costs between EVAR and open surgery, we have not taken into account the longer-term benefits or costs of EVAR or open surgery in our modelling.
- Visser reported elective open surgery costs at €35,470 (2003) or $65,047 (2017 CAD), with those costs rising to €36,448 (2003) or $66,840 (2017 CAD) if one-year follow-up costs were included.[573]
- Matsumura and colleagues reported elective open surgery costs between $38,900 – 45,100 USD (2008) or $37,726 – 43,739 (2017 CAD), depending on which device was used in the surgery.[574]
- Similarly, in their cost-effectiveness analysis, Svensjo and colleagues use an elective open surgery cost of €30,099 (2012), with that cost rising to €35,615 if post-operative costs were included as well.[575] Converted to 2017 CAD the amounts are $50,112 and $59,295 respectively.
- For elective open surgery, Burgers and colleagues reported surgery costs of €16,399 (2013) or $25,156 (2017 CAD).[576]
- In papers not reporting on the specific type of elective surgery, the elective surgery costs ranged from $14,075 - $44,388 (2017 CAD).[577,578,579,580,581,582,583,584]

[572] IMPROVE Trial Investigators. Comparative clinical effectiveness and cost-effectiveness of endovascular strategy v open repair for ruptured abdominal aortic aneurysm: three year results of the IMPROVE randomised trial. *British Medical Journal.* 2017; 359: j4859.
[573] Visser JJ, van Sambeek MR, Hunink MM et al. Acute abdominal aortic aneurysms: cost analysis of endovascular repair and open surgery in hemodynamically stable patients with 1-year follow-up. *Radiology*. 2006; 240(3): 681-9.
[574] Matsumura JS, Stroupe KT, Lederle FA et al. Costs of repair of abdominal aortic aneurysm with different devices in a multicenter randomized trial. *Journal of Vascular Surgery.* 2015; 61(1): 59-65.
[575] Svensjö S, Mani K, Björck M et al. Screening for abdominal aortic aneurysm in 65-year-old men remains cost-effective with contemporary epidemiology and management. *European Journal of Vascular and Endovascular Surgery*. 2014; 47(4): 357-65.
[576] Burgers L, Vahl A, Severens J et al. Cost-effectiveness of elective endovascular aneurysm repair versus open surgical repair of abdominal aortic aneurysms. *European Journal of Vascular and Endovascular Surgery*. 2016; 52(1): 29-40.
[577] Lindholt JS, Sørensen J, Søgaard R et al. Long-term benefit and cost-effectiveness analysis of screening for abdominal aortic aneurysms from a randomized controlled trial. *British Journal of Surgery*. 2010; 97(6): 826-34.
[578] Thompson S, Ashton H, Gao L et al. Screening men for abdominal aortic aneurysm: 10 year mortality and cost-effectiveness results from the randomised Multicentre Aneurysm Screening Study. *British Medical Journal.* 2009; 338: b2307.
[579] Chew HF, You C, Brown MG et al. Mortality, morbidity, and costs of ruptured and elective abdominal aortic aneurysm repairs in Nova Scotia, Canada. *Annals of Vascular Surgery.* 2003; 17(2): 171-9.
[580] Brox AC, Filion KB, Zhang X et al. In-hospital cost of abdominal aortic aneurysm repair in Canada and the United States. *Archives of Internal Medicine.* 2003; 163(20): 2500-4.
[581] Wanhainen A, Lundkvist J, Bergqvist D et al. Cost-effectiveness of different screening strategies for abdominal aortic aneurysm. *Journal of Vascular Surgery.* 2005; 41(5): 741-51.
[582] Silverstein MD, Pitts SR, Chaikof EL et al. Abdominal aortic aneurysm (AAA): cost-effectiveness of screening, surveillance of intermediate-sized AAA, and management of symptomatic AAA. *Baylor University Medical Center Proceedings*. 2005; 18(4): 345-67.
[583] Montreuil B and Brophy J. Screening for abdominal aortic aneurysms in men: a Canadian perspective using Monte Carlo–based estimates. *Canadian Journal of Surgery*. 2008; 51(1): 23.
[584] Giardina S, Pane B, Spinella G et al. An economic evaluation of an abdominal aortic aneurysm screening program in Italy. *Journal of Vascular Surgery.* 2011; 54(4): 938-46.

- Elective open surgery costs, adjusted to 2017 CAD, range between $25,156 (Burgers et al.) and $66,840 (Visser et al.). We model elective open AAA-repair surgery costs at $45,998 (open surgery mid-point) and vary this to $25,156 and $66,840 in our sensitivity analysis (Table 6, row *t*).

- Chew and colleagues reported that emergency AAA-repair surgery costs in Nova Scotia were $18,899 (1998 CAD), including overhead. This is equivalent to $27,500 (2017 CAD).[585]
- In a Swedish cost analysis, Wanhainen and colleagues used €32,183 (2003) for emergency AAA-repair with rupture or $50,301 (2017 CAD).[586]
- In a model of US costs, Silverstein and colleagues used $60,000 (2003) USD to account for emergency surgery and emergency care costs. Adjusted to 2017 CAD, this comes to $66,582.[587]
- Montreuil and colleagues conducted a Monte Carlo analysis of screening Canadian men for AAA and used $35,982 (2005 CAD) for emergency AAA-repair surgery costs, equivalent to $43,494 (2017 CAD).[588]
- Lindholt and colleagues reported an emergency AAA-repair surgery cost of €35,928 (2007) in Denmark or $63,497 (2017 CAD).[589]
- Reporting on the cost-effectiveness of screening using the MASS results, Thompson and colleagues used an emergency AAA-repair cost of £14,825 (2008) or $29,935 (2017 CAD).[590]
- Giardina and colleagues report an emergency AAA-repair cost of €15,602 (2009) in Italy, or $27,123 (2017 CAD).[591]

- Emergency AAA-repair surgery costs, adjusted to 2017 CAD, range between $27,123 (Giardina et al.) and $66,582 (Silverstein et al.). We model the cost of emergency surgery as $46,853 (mid-point of emergency surgery range) and vary this from $27,123 to $66,582 in our sensitivity analysis (Table 6, row *ao*).

- Chew et al. reported a mean length of stay in Nova Scotia of 19.57 days in hospital for emergency surgery survivors and 9.22 days in hospital for emergency surgery patients who died.[592] We model accordingly (Table 6, rows *aq* & *ar*)

[585] Chew HF, You C, Brown MG et al. Mortality, morbidity, and costs of ruptured and elective abdominal aortic aneurysm repairs in Nova Scotia, Canada. *Annals of Vascular Surgery.* 2003; 17(2): 171-9.
[586] Wanhainen A, Lundkvist J, Bergqvist D et al. Cost-effectiveness of different screening strategies for abdominal aortic aneurysm. *Journal of Vascular Surgery.* 2005; 41(5): 741-51.
[587] Silverstein MD, Pitts SR, Chaikof EL et al. Abdominal aortic aneurysm (AAA): cost-effectiveness of screening, surveillance of intermediate-sized AAA, and management of symptomatic AAA. *Baylor University Medical Center Proceedings*. 2005; 18(4): 345-67.
[588] Montreuil B and Brophy J. Screening for abdominal aortic aneurysms in men: a Canadian perspective using Monte Carlo–based estimates. *Canadian Journal of Surgery*. 2008; 51(1): 23.
[589] Lindholt JS, Sørensen J, Søgaard R et al. Long-term benefit and cost-effectiveness analysis of screening for abdominal aortic aneurysms from a randomized controlled trial. *British Journal of Surgery*. 2010; 97(6): 826-34.
[590] Thompson S, Ashton H, Gao L et al. Screening men for abdominal aortic aneurysm: 10 year mortality and cost-effectiveness results from the randomised Multicentre Aneurysm Screening Study. *British Medical Journal.* 2009; 338: b2307.
[591] Giardina S, Pane B, Spinella G et al. An economic evaluation of an abdominal aortic aneurysm screening program in Italy. *Journal of Vascular Surgery.* 2011; 54(4): 938-46.
[592] Chew HF, You C, Brown MG et al. Mortality, morbidity, and costs of ruptured and elective abdominal aortic aneurysm repairs in Nova Scotia, Canada. *Annals of Vascular Surgery.* 2003; 17(2): 171-9.

- The Canadian Society for Vascular Surgery (CSVS) and HealthLinkBC agree that hospital stays for elective endovascular AAA-repair surgery will range between 1 – 3 days.[593,594]
- The Canadian Society for Vascular Surgery suggests that elective open AAA-repair surgery will require 5 – 7 days in hospital.[595]
- Analysis from the discharge abstract database in BC from 2013/14 – 2017/18 indicates the average length of stay for elective endovascular AAA repair in BC is no less than 4 days, while the average length of stay for elective open AAA repair is 10 days.[596]
- HealthLinkBC states that patients will typically fully recover 4 weeks after *endovascular* AAA-repair surgery and suggests planning to take 1 - 2 weeks off work.[597] The CSVS reports a full recovery time between 2 – 4 weeks.[598]
- HealthLinkBC states that patients will typically resume "usual activities" 4 – 6 weeks after *open* AAA-repair surgery and that full recovery will take 2 – 3 months.[599] The CSVS reports a full recovery time between 1 – 3 months.[600]

- For the purposes of calculating patient time costs, we model 4 days and 10 days in hospital for elective endovascular and open AAA-repair surgeries respectively (Table 6, rows *v* & *w*). We model time off work at 10 days (midpoint of 1 – 2 weeks) and 35 days (midpoint of 4 – 6 weeks) for endovascular and open AAA-repair surgeries respectively (Table 6, rows *x* & *y*). In our sensitivity analysis we range the days off work between 7 – 14 for endovascular and 28 – 42 for open surgery.

- Emergency ground transport in BC costs $530 for non-MSP beneficiaries.[601] This can be considered the unsubsidized cost of emergency ground transportation.

- We model that the difference in the sum of emergency surgeries and deaths prior to hospitalization for AAA between the unscreened and screened cohort is equivalent to the number of avoided emergency transports (Table 6, row *ay*). These emergency transports each cost $530 (Table 6, row *az*).

Based on these assumptions, the CE associated with screening for abdominal aortic aneurysms in males ages 65 to 75 who have ever smoked is $11,995 / QALY (see Table 6, row *bg*).

[593] Canadian Society for Vascular Surgery. *Abdominal Aortic Aneurysm.* 2018. Available at https://canadianvascular.ca/Abdominal-Aortic-Aneurysms. Accessed February 2019.
[594] HealthLinkBC. *Endovascular Repair for Abdominal Aortic Aneurysm.* 2018. Available at https://www.healthlinkbc.ca/health-topics/abn3549#abn3550. Accessed February 2019.
[595] Canadian Society for Vascular Surgery. *Abdominal Aortic Aneurysm.* 2018. Available at https://canadianvascular.ca/Abdominal-Aortic-Aneurysms. Accessed February 2019.
[596] Aciemme (Sam) Ospan, Senior Manager, Lifetime Prevention Schedule, Healthy Living and Health Promotion Branch, BC Ministry of Health. June 3, 2019. Personal communication.
[597] HealthLinkBC. *Endovascular Repair for Abdominal Aortic Aneurysm.* 2018. Available at https://www.healthlinkbc.ca/health-topics/abn3549#abn3550. Accessed February 2019.
[598] Canadian Society for Vascular Surgery. *Abdominal Aortic Aneurysm.* 2018. Available at https://canadianvascular.ca/Abdominal-Aortic-Aneurysms. Accessed February 2019.
[599] HealthLinkBC. *Open Repair Surgery for Abdominal Aortic Aneurysm.* 2018. Available at https://www.healthlinkbc.ca/health-topics/abn3540. Accessed February 2019
[600] Canadian Society for Vascular Surgery. *Abdominal Aortic Aneurysm.* 2018. Available at https://canadianvascular.ca/Abdominal-Aortic-Aneurysms. Accessed February 2019.
[601] BC Emergency Health Services. *Fees*. 2019. Available at http://www.bcehs.ca/about/billing/fees. Accessed March 2019.

Table 6: Cost Effectiveness of Abdominal Aortic Aneurysm Screening in Ever-Smoking Men 65+ In a BC Birth Cohort of 40,000			
Row Label	Variable	Base case	Data Source
a	Number of 65-year old men in cohort	17,559	BC Life Table
b	Proportion who are former smokers	40.1%	√
c	Proportion who are current smokers	12.9%	√
d	Number targeted for screening	9,306	= a * (d + e)
e	Screening Rate	85.8%	√
f	Total Number screened	7,985	= f * g
g	Cost of 10 minute office visit	$34.85	Ref Doc
h	Value of patient time and travel for office visit	$59.38	Ref Doc
i	Portion of 10-minute office visit for screening	50%	Ref Doc
j	Cost of initial primary care visit for cohort	$376,207	= f * (g + h) * i
k	Cost of ultrasonic screening session	$107	√
l	Cost of ultrasonic screening for cohort	$1,327,006	= f * (h + k)
m	Number of elective surgeries in ever-smokers, unscreened	63	Table 5, row w
n	Number of elective surgeries in ever-smokers, screened	135	Table 5, row an
o	Rate of opportunistically detected AAA	13%	Table 5, row ak
p	Number of additional elective surgeries attributable to screening alone	63	= ((n - m) * (1 - o))
q	Proportion of surgeries that are endoscopic surgeries	58%	Table 5, row ap
r	Proportion of surgeries that are open surgeries	42%	= 1 - q
s	Cost per elective surgery, endoscopic AAA repair	$36,039	√
t	Cost per elective surgery, open AAA repair	$45,998	√
u	Cost of additional elective surgery due to screening	$2,533,146	= p * ((q * s) + (r * t))
v	Time in hospital, days, endovascular AAA repair	4	√
w	Time in hospital, days, open AAA repair	10	√
x	Recovery time, days, endovascular AAA repair	10	√
y	Recovery time, days, open AAA repair	35	√
z	Cost per day of patient time in hospital	$223	Ref Doc
aa	Patient time cost for additional elective AAA surgeries	$377,903.66	= p * ((q * (v + x)) + (r * (w + y)) * z
ab	Number of elective surgeries, endoscopic	37	= p * q
ac	Cost of CT Scan	$223.50	√
ad	Cost of office visit, 100% for AAA follow-up	$94	= g + h
ae	Average life expectancy of 65-year old man	20	BC Life Table
af	Estimated compliance with annual follow-up protocol	70%	√
ag	Cost of CT Scans	$114,973	= ab * ac * ae * af
ah	Cost of follow-up office visits	$48,474	= ab * ad * ae * af
ai	Lifetime failure rates of EVAR	10%	√
aj	Cost to correct EVAR failure with open surgery	$169,017	= ab * ai * t
ak	Total cost due to additional elective AAA surgery in cohort	$3,243,513	= u + aa + ag + ah + aj
al	Number of emergency surgeries in ever-smokers, unscreened	63.0	Table 5, row ad
am	Number of emergency surgeries in ever-smokers, screened	32.8	Table 5, row aw
an	Reduction in emergency surgeries in screened population	30.2	= al - am
ao	Cost of emergency surgery, AAA rupture repair	$46,853	√
ap	Cost reduction due to avoided surgery	$1,416,717	= an * ao
aq	Time in hospital, emergency AAA repair, survivors	19.57	√
ar	Time in hospital, emergency AAA repair, patients who die	9.22	√
as	Death rate, emergency surgery	41%	√
at	Average time in hospital, emergency AAA repair	15.3	= ((aq * (1 - as)) + (ar * as))
au	Patient time cost avoided due to avoided emergency surgery	$103,195	an * at * z
av	Total cost reduction due to avoided surgeries	$1,519,913	= ap + av
aw	Number of emergency surgeries and pre-hospital deaths, unscreened cohort	149	Table 5, row ad + Table 5, row ag
ax	Number of emergency surgeries and pre-hospital deaths, screened cohort	83	Table 5, row aw + Table 5, row bb
ay	Number of avoided emergency transports due to screening	67	= aw - ax
az	Average cost of emergency transport	$530	√
ba	Avoided emergency transportation cost	$35,361	= ay * az
bb	Net cost of intervention	$3,391,452	= j + l + ak - av - ba
bc	QALYs saved	340	Table 5, row bk
bd	Cost effectiveness (CE) of intervention, $/QALY	$9,973	= bb / bc
be	Net Cost of Intervention (1.5% Discount)	$3,512,843	Calculated
bf	Net QALYs Gained (1.5% Discount)	293	Calculated
bg	Cost Effectiveness (CE) of Intervention, $/QALY (1.5% Discount)	$11,995	= be / bf

For the sensitivity analysis, we modified a number of major assumptions and recalculated the CE as follows:

- Assume that the relative risk of overall death moves from 0.58 to 0.88 (Table 5, row *az*), the relative risk of elective surgery in screened individuals is *decreased* from 2.15 to 1.89 (Table 5, row *al*) and the relative risk of emergency surgery moves from 0.52 to 0.66 (Table 5, row *au)*: CE = $38,251
- Assume that the relative risk of overall death moves from 0.58 to 0.39 (Table 5, row *az*), the relative risk of elective surgery in screened individuals is *increased* from 2.15 to 2.44 (Table 5, row *al*) and the relative risk of emergency surgery moves from 0.52 to 0.40 (Table 5, row *au)*: CE = $9,328
- Assume the rate of opportunistically detected AAA in the population increases from 13% to 25% (Table 5, row *ak*): CE = $10,512
- Assume the rate of opportunistically detected AAA in the population decreases from 13% to 7% (Table 5, row *ak*): CE = $12,736
- Assume the cost of elective endovascular surgery increases from $36,039 to $49,544 (Table 6, row *s*), the cost of elective open endovascular surgery increases from $45,998 to $66,840 (Table 6, row *t*), and the cost of emergency AAA-repair surgery increases from $46,853 to $66,582 (Table 6, row *af*): CE = $13,955
- Assume the cost of elective endovascular surgery decreases from $36,039 to $22,534 (Table 6, row *s*), the cost of elective open endovascular surgery decreases from $45,998 to $25,156 (Table 6, row *t*), and the cost of emergency AAA-repair surgery decreases from $46,853 to $27,123 (Table 6, row *af*): CE = $10,034
- Assume that the time off work for elective endovascular surgery increases from 10 to 14 days (Table 6, row *x*) and the time off work for elective open surgery increases from 35 to 42 days (Table 6, row *y*): CE = $12,239
- Assume that the time off work for elective endovascular surgery decreases from 10 to 7 days (Table 6, row *x*) and the time off work for elective open surgery increases from 35 to 28 days (Table 6, row *y*): CE = $11,778
- Assume vital statistics death rate of 0.74% in population 65 and older due to abdominal aortic aneurysm, rather than the 1.90% calculated in the model: CE = $21,015
- Offer screening to all 65 year old males, rather than to just 65 year old male ever-smokers (Table 5, rows *b*, *c* and *d*): CE = $17,293

Summary

Ever-Smoking Males Ages 65 and Older

Applying a 1.5% discount rate, the clinically preventable burden (CPB) associated with screening for, and treatment of, abdominal aortic aneurysm in ever-smoking males ages 65 and older is estimated to be 293 quality-adjusted life years (QALYs) while the cost-effectiveness (CE) is estimated to be $11,995 per QALY (see Table 7).

Table 7: Abdominal Aortic Aneurysm Screening in Ever-Smoking Men 65+ in a BC Birth Cohort of 40,000

Summary

	Base Case	Range	
CPB (Potential QALYs Gained)			
Assume No Current Service			
1.5% Discount Rate	**293**	84	425
3% Discount Rate	254	73	369
0% Discount Rate	340	97	494
CE ($/QALY) ***including*** patient time costs			
1.5% Discount Rate	**$11,995**	$9,328	$38,251
3% Discount Rate	$14,175	$11,053	$44,859
0% Discount Rate	$9,973	$7,725	$32,136
CE ($/QALY) ***excluding*** patient time costs			
1.5% Discount Rate	$8,516	$6,750	$26,836
3% Discount Rate	$10,162	$8,079	$31,705
0% Discount Rate	$6,984	$5,511	$22,315

All Males Ages 65 and Older

Applying a 1.5% discount rate, the clinically preventable burden (CPB) associated with screening for, and treatment of, abdominal aortic aneurysm in in all males ages 65 and older is estimated to be 386 quality-adjusted life years (QALYs) while the cost-effectiveness (CE) is estimated to be $17,293 per QALY (see Table 8).

Table 8: Abdominal Aortic Aneurysm Screening in Men 65+ in a BC Birth Cohort of 40,000

Summary

	Base Case	Range	
CPB (Potential QALYs Gained)			
Assume No Current Service			
1.5% Discount Rate	**386**	110	561
3% Discount Rate	335	96	487
0% Discount Rate	449	128	652
CE ($/QALY) ***including*** patient time costs			
1.5% Discount Rate	**$17,293**	$13,475	$54,894
3% Discount Rate	$20,409	$15,941	$64,341
0% Discount Rate	$14,403	$11,184	$46,152
CE ($/QALY) ***excluding*** patient time costs			
1.5% Discount Rate	$12,319	$9,788	$38,573
3% Discount Rate	$14,672	$11,689	$45,534
0% Discount Rate	$10,130	$8,018	$32,111

Screening for Sexually Transmitted Infections and Blood Borne Pathogens

Human Immunodeficiency Virus

United States Preventive Services Task Force Recommendations (2013)

> *An estimated 1.2 million persons in the United States are currently living with HIV infection, and the annual incidence of the disease is approximately 50 000 cases. Since the first cases of AIDS were reported in 1981, more than 1.1 million persons have been diagnosed and nearly 595 000 have died from the condition.*
>
> *Approximately 20% to 25% of individuals living with HIV infection are unaware of their positive status.*
>
> *The USPSTF recommends that clinicians screen adolescents and adults aged 15 to 65 years for HIV infection. Younger adolescents and older adults who are at increased risk should also be screened. (A recommendation)*
>
> *The USPSTF recommends that clinicians screen all pregnant women for HIV, including those who present in labor who are untested and whose HIV status is unknown. (A recommendation)*[602]

Canadian Task Force on Preventive Health Care Recommendations (2016)

The CTFPHC has reviewed the USPSTF guideline on screening for HIV infection and conclude that it "is a high-quality guideline, but the CTFPHC does not recommend its use in Canada. In the opinion of the CTFPHC, available evidence does not justify routinely screening all adult Canadians for HIV." Instead, the focus should be on screening high-risk groups and pregnant women.[603]

Modelling the Clinically Preventable Burden

In this section, we will calculate the CPB associated with screening adolescents and adults aged 15 to 65 years for HIV infection in a BC birth cohort of 40,000.

In modelling CPB, we made the following assumptions:

- The total number of individuals living with HIV infections in BC is estimated to be 12,100 (with a range from 9,700 to 14,500) (see Table 1).[604]

[602] Moyer VA. Screening for HIV: U.S. Preventive Services Task Force Recommendation Statement. *Annals of Internal Medicine*. 2013; 159(1): 51-60.
[603] Canadian Task Force on Preventive Health Care. *HIV 2013 Critical Appraisal Report.* Available online at https://canadiantaskforce.ca/wp-content/uploads/2016/05/2013-hiv-en-ca-final.pdf. Accessed February 2018.
[604] BC Centre for Disease Control. *HIV in British Columbia: Annual Surveillance Report 2015*. 2017. Available online at http://www.bccdc.ca/resource-gallery/Documents/Statistics%20and%20Research/Statistics%20and%20Reports/STI/HIV_Annual_Report_2015-FINAL.pdf. Accesed February 2018.

Table 1: Estimated Number of Prevalent HIV Infections In British Columbia by Exposure Category
2014

Exposure Category	Number	Range		% of Total
MSM	5,500	4,400	6,600	45%
MSM-PWID	385	270	500	3%
PWID	3,400	2,700	4,100	28%
HET (non-endemic)	2,220	1,740	2,700	18%
HET (endemic)	470	340	600	4%
Other	125	80	170	1%
All	12,100	9,700	14,500	

MSM - Men who have sex with men
PWID - People who inject drugs
HET (non-endemic) - Heterosexual contact with a person who is either HIV-infected or at risk for HIV or heterosexual as the only identified risk
HET (endemic) - Heterosexual contact and origin from a country where HIV is endemic
Other - Recipients of blood transfusion or clotting factor, perinatal, and occupational transmission

- 20% of HIV-infected men who have sex with men (MSM), 24% of HIV-infected injection drug users (IDU) and 34% of HIV-infected heterosexuals (HET) are unaware of their HIV status (Table 2, rows *c*, *f* & *i*).[605]
- Adherence with universal screening was assumed to be 83% for MSM, 45% for HET and 60% for IDU (Table 2, rows *u*, *v* & *w*) (see Reference Document).
- 4.56% of HIV infected individuals die prematurely without early initiation of antiretroviral therapy (ART) (deferring initiation of ART to CD4 levels of 200 cells/µL). This can be reduced to 1.11% with early initiation of ART (Table 2, rows *y* & *z*).[606]
- The average age at which undiagnosed HIV is detected is 40 (Table 2, row *bb*).[607]
- The gain in quality of life associated with early detection and treatment of an HIV infection is 0.11 (Table 2, row *ee*).[608]
- Antiretroviral therapy is a potent intervention for prevention of HIV in discordant couples. The RCT by Cohen, et al. found that just 1 of 28 transmissions occurred in a serodiscordant couple in which the infected partner received early initiation of antiretroviral therapy (a hazard ratio of 0.04; 95% CI from 0.01 to 0.27).[609] The 2013 Cochrane review by Anglemyer and colleagues noted the RCT study by Cohen, et al. as well as nine observational studies. Results from the observational studies suggested that treating the HIV-infected partner in a serodiscordant couple reduces the risk of transmission by 64% (a relative risk of 0.36; 95% CI from 0.17 to

[605] Public Health Agency of Canada. *Summary: Estimates of HIV Prevalence and Incidence in Canada, 2011*. 2011. Available at http://www.phac-aspc.gc.ca/aids-sida/publication/survreport/assets/pdf/estimat2011-eng.pdf. Accessed May 2014.
[606] Siegfried N, Uthman OA and Rutherford GW. Optimal time for initiation of antiretroviral therapy in asymptomatic, HIV-infected, treatment-naive adults. *Cochrane Database of Systematic Reviews.* 2011.
[607] Ibid.
[608] Long EF, Brandeau ML and Owens DK. The cost-effectiveness and population outcomes of expanded HIV screening and antiretroviral treatment in the United States. *Annals of Internal Medicine*. 2010; 153(12): 778-89.
[609] Cohen MS, Chen YQ, McCauley M et al. Prevention of HIV-1 infection with early antiretroviral therapy. *New England Journal of Medicine*. 2011; 365(6): 493-505.

0.75).[610,611] In BC, the expanded utilization of highly active antiretroviral therapy (HAART) between 1996 and 2012 is associated with a 66% decrease in new diagnoses of HIV.[612] To incorporate this information into our model, we first calculated the rate per person year of HIV transmission in HIV-discordant couples if the HIV-positive partner is not treated with ART. This is based on the results from the control arms of the 1 RCT and 9 observational studies included in the Cochrane review by Anglemyer et al. (1,094 transmissions during 42,917 person-years, a transmission rate of 0.0255 per person-year, Table 2, row *gg*). We then assumed a 64% reduction in the transmission rate per person-year if the HIV-positive partner is treated with ART. This results in an annual transmission rate of 0.0092 per person-year (Table 2, row *hh*). In the sensitivity analysis we used results from the Cohen et al study (96% reduction) as the upper bounds and the 95% CI from the 9 observational studies reviewed by Anglemyer et al (RR of 0.75 or a 25% reduction) as the lower bounds.

- We assumed that the 16.58 infections avoided associated with screening and the early treatment with ART (Table 2, row *kk*) would lead to an additional 11.91 infections avoided (Table 2, row *nn*), due to second order transmission benefits.
- The difference in quality of life between avoided infection and symptomatic HIV treated with ART is 0.17 (Table 2, row *oo*).[613]
- Other assumptions used in assessing the clinically preventable burden are detailed in the Reference Document.

Based on these assumptions, the calculation of CPB (Table 2, row *qq*) is 360 QALYs. This represents the potential CPB of moving from no screening to 45% in the heterosexual population, 60% in people who inject drugs and 83% in men who have sex with men.

[610] Anglemyer A, Rutherford GW, Horvath T et al. Antiretroviral therapy for prevention of HIV transmission in HIV-discordant couples. *Cochrane Database of Systematic Reviews.* 2013.
[611] Anglemyer A, Horvath T and Rutherford G. Antiretroviral therapy for prevention of HIV transmission in HIV-discordant couples. *Journal of the American Medical Association*. 2013; 310(15): 1619-20.
[612] Montaner JS, Lima VD, Harrigan PR et al. Expansion of HAART coverage is associated with sustained decreases in HIV/AIDS morbidity, mortality and HIV transmission: the "HIV Treatment as Prevention" experience in a Canadian setting. *PLoS One*. 2014; 9(2): e87872.
[613] Long EF, Brandeau ML and Owens DK. The cost-effectiveness and population outcomes of expanded HIV screening and antiretroviral treatment in the United States. *Annals of Internal Medicine*. 2010; 153(12): 778-89.

Table 2: CPB of Screening to Detect and Treat HIV in a BC Birth Cohort of 40,000			
Row Label	**Variable**	**Base Case**	**Data Source**
a	Prevalence of HIV Infections in B.C.	12,100	Table 1
b	Prevalence of HIV Infections in MSM	5,500	√
c	% Undiagnosed in MSM	20%	√
d	Undiagnosed HIV in MSM	1,100	= b*c
e	Prevalence of HIV Infections in PWID	3,785	√
f	% Undiagnosed in PWID	24%	√
g	Undiagnosed HIV in PWID	908	= e*f
h	Prevalence of HIV Infections in HET	2,690	√
i	% Undiagnosed in HET	34%	√
j	Undiagnosed HIV in HET	915	= h*i
k	Undiagnosed HIV in BC	2,923	= d+g+j
l	Diagnosed HIV in BC	9,177	= a-k
m	BC Population Ages 15-65	3,239,000	√
n	Prevalence / 100,000 Diagnosed HIV	283	=l/(m/100,000)
o	Prevalence / 100,000 Undiagnosed HIV	90	=k/(m/100,000)
p	Est. diagnosed HIV in BC birth cohort of 40,000	113	= n*0.4
q	Est. undiagnosed HIV in BC birth cohort of 40,000	36	= o*0.4
r	Est. undiagnosed HIV in BC birth cohort of 40,000 - MSM	14	= (d/k)*q
s	Est. undiagnosed HIV in BC birth cohort of 40,000 - PWID	11	= (g/k)*q
t	Est. undiagnosed HIV in BC birth cohort of 40,000 - HET	11	= (j/k)*q
u	Adherence with screening - MSM	83.0%	Ref Doc
v	Adherence with screening - PWID	60.0%	√
w	Adherence with screening - HET	45.0%	Ref Doc
x	Previously undiagnosed HIV infections detected by universal screening	23.09	=r*u+s*v+t*w
y	% early death without early initiation of antiretroviral therapy (ART)	4.56%	√
z	% early death with early initiation of ART	1.11%	√
aa	Early deaths avoided with early initiation of ART	0.80	=(x*y)-(x*z)
bb	Average age at which undiagnosed HIV infection detected	40	√
cc	Life expectancy of a 40 year-old	44	√
dd	QALYs gained - premature death avoided	35.0	=aa*cc
ee	Gain in QoL associated with early detection and treatment of HIV	0.11	√
ff	QALYs gained - early detection and treatment	112	=x*cc*ee
gg	HIV transmission in HIV-discordant couples, HIV positive partner **untreated** with ART - rate/person year	0.0255	√
hh	HIV transmission in HIV-discordant couples, HIV positive partner **treated** with ART - rate/person year	0.0092	√
ii	Potential HIV transmissions, HIV positive partner **untreated** with ART	25.91	=x*cc*gg
jj	Potential HIV transmissions, HIV positive partner **treated** with ART	9.33	=x*cc*hh
kk	Infections avoided per early detection associated with ART-first order	16.58	=ii-jj
ll	Potential HIV transmissions, HIV positive partner **untreated** with ART	18.60	=kk*gg*cc
mm	Potential HIV transmissions, HIV positive partner **treated** with ART	6.70	=kk*hh*cc
nn	Infections avoided per early detection associated with ART-second order	11.91	=ll-mm
oo	Difference in QoL associated with no infection vs. symptomatic infection treated with ART	0.17	√
pp	QALYs gained - infections avoided due to ART	213	=(kk+nn)*cc*oo
qq	Total QALYs gained, Utilization increasing from 0% to 45% for HET, 60% for PWID and 83% for MSM	360	=dd+ff+pp

√ = Estimates from the literature

We also modified several major assumptions and recalculated the CPB as follows:

- Assume the prevalence of individuals living with HIV infections in BC is decreased from 12,100 to 9,700 (Table 2, row *a*): CPB = 288.
- Assume the prevalence of individuals living with HIV infections in BC is increased from 12,100 to 14,500 (Table 2, row *a*): CPB = 431.
- Assume that the early initiation of antiretroviral therapy is associated with a 96% reduction (from 64%) in the transmission rate per person-year (Table 2, row *hh*): CPB = 533.
- Assume that the early initiation of antiretroviral therapy is associated with a 25% reduction (from 64%) in the transmission rate per person-year (Table 2, row *hh*): CPB = 209.

Modelling Cost-Effectiveness

In this section, we will calculate the CE associated with screening adolescents and adults aged 15 to 65 years for HIV infection in a BC birth cohort of 40,000.

In modelling CE, we made the following assumptions:

- **Number of screens** – We have assumed screening between the ages of 15-65 would occur every year in high risk populations and once every 5 years in low-risk populations.[614] Long and colleagues estimated the high-risk population to be 2.85% of the total population ages 15-65 in the US[615] and 1.62% in the UK.[616] We assumed 2.85% for BC (Table 3, row *a*). In the sensitivity analysis, we adjusted screening once every five years in the low-risk population to once every 10 years and once per lifetime.
- **True / false positive screens** – The ratio of true to false positive test results is 1:1 (Table 3, row *i*).[617]
- **Laboratory cost per screen** – The estimated cost per screen is $7 (with a range from $5 to $9). The estimated cost of confirming true / false positive results is $400 (with a range from $300 to $500) (Table 3, rows *m* & *n*).[618]
- **Cost of a counselling session** - We estimated the average cost of a counselling session associated with a true / false positive result to be $84.45, based on MSP fee item 13015 (*HIV/AIDS Primary Care Management – in or out of office – per half hour or major portion thereof*) (Table 3, row *o*).[619]

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[614] Office of the Provincial Health Officer. *HIV Testing Guidelines for the Province of British Columbia* 2014. Available at http://www.bccdc.ca/NR/rdonlyres/B35EDEBD-98CA-48BB-AB7C-B18A357AC19D/0/HIV_GUIDE_051114.pdf. Accessed May 2014.

[615] Long EF, Brandeau ML and Owens DK. The cost-effectiveness and population outcomes of expanded HIV screening and antiretroviral treatment in the United States. *Annals of Internal Medicine*. 2010; 153(12): 778-89.

[616] Long EF, Mandalia R, Mandalia S et al. Expanded HIV testing in low-prevalence, high-income countries: a cost-effectiveness analysis for the United Kingdom. *PLoS One*. 2014; 9(4): e95735.

[617] Dr. Mel Krajden, Associate Medical Director, BCCDC Public Health Microbiology and Reference Laboratory, BC Centre for Disease Control. Personal communication, March, 2014.

[618] Ibid.

[619] Medical Services Commission. *Payment Schedule: Section 7 General Practice*. 2017. Available online at https://www2.gov.bc.ca/assets/gov/health/practitioner-pro/medical-services-plan/msc-payment-schedule-july-2017.pdf. Accesed February 2018.

- **Average annual cost of antiretrovirals for HIV** – Calculated based on an estimated average cost per day of treatment in Canada of $26.00[620] (Table 3, row *s*). Costs in BC may be as high as $47.00 per day.[621] We have used this higher estimate in our sensitivity analysis.
- **Direct medical costs avoided** – The annual direct medical costs (excluding medications) associated with HIV/AIDS in Canada have been estimated by stage of infection at $1,684 for asymptomatic HIV, $2,534 for symptomatic HIV and $9,715 for AIDS (in 2009 CAD).[622] We modelled avoided cost using the annual direct medical costs associated with symptomatic HIV, updated to 2017 CAD of $2,843 (Table 3, row *w*).
- Other costs and assumptions used in assessing cost-effectiveness are detailed in the Reference Document.
- Discount rate of 1.5%, varied from 0% to 3% in the sensitivity analysis.

Based on these assumptions, the estimated cost per QALY would be $16,434 (see Table 3, row *gg*).

[620] Centre for Health Services and Policy Research. *The Canadian Rx Atlas: Third Edition*. 2013. Available at http://www.chspr.ubc.ca/sites/default/files/file_upload/publications/2013/RxAtlas/canadianrxatlas2013.pdf. Accessed January 2014.
[621] Johnston KM, Levy AR, Lima VD et al. Expanding access to HAART: a cost-effective approach for treating and preventing HIV. *AIDS*. 2010; 24(12): 1929-35.
[622] Kingston-Riechers, J. *The Economic Cost of HIV/AIDS in Canada*. Canadian AIDS Society, 2011. Available online at http://www.cdnaids.ca/files.nsf/pages/economiccostofhiv-aidsincanada/$file/Economic%20Cost%20of%20HIV-AIDS%20in%20Canada.pdf. Accessed July, 2014.

Table 3: CE of Screening to Detect and Treat HIV in a BC Birth Cohort of 40,000			
Row Label	**Variable**	**Base Case**	**Data Source**
a	Proportion of population high risk	2.85%	√
b	Proportion of population low risk	97.15%	=1-a
c	Screening rate in high risk populations	Annual	√
d	Screening rate in low risk populations	Every 5 years	√
e	Lifetime screens in high risk populations	45,583	Calculated
f	Lifetime screens in low risk populations	170,778	Calculated
g	Total screens	216,361	=e+f
h	# of true positive screens	23.09	Table 2, row x
i	Estimated # of false positive screens	23.09	=h
	Costs of screening and counseling		
j	Cost of 10-minute office visit	$34.85	Ref Doc
k	Value of patient time and travel for office visit	$59.38	Ref Doc
l	Proportion of office visit required	0.50	Assumed
m	Cost per screen	$7	√
n	Cost per true/false positive screen	$400	√
o	Cost per counselling session	$84.45	√
p	Cost of screening	$5,303,081	=(g*j*l)+(g*m)+(h+i)*n
q	Cost of counselling	$3,900	=(h+i)*o
r	Patient time costs	$6,423,750	= g*k*l
	Costs of antiretrovirals		
s	Cost per day of treatment	$26	√
t	Cost of antiretrovirals	$9,640,931	=Table 2, row x * Table 2, row cc *365 * s
	Costs avoided		
u	HIV infections avoided - treatment with ART	28.49	Table 2, row kk + Table 2, row nn
v	Cost of antiretrovirals avoided	-$11,894,198	= -u * Table 2, row cc*365*s
w	Annual direct medical costs (excluding medications) associated with symptomatic HIV	$2,843	√
x	Direct medical costs avoided	-$3,563,246	= -u * Table 2, row cc*w
	CE calculation		
y	Cost of screening and counseling (undiscounted)	$11,730,731	= p+q+r
z	Cost of antiretrovirals (undiscounted)	$9,640,931	= t
aa	Costs avoided (undiscounted)	-$15,457,444	= v+x
bb	QALYs saved (undiscounted)	360	Table 2, row qq
cc	Cost of screening and counseling (1.5% discount rate)	$8,603,838	Calculated
dd	Cost of antiretrovirals (1.5% discount rate)	$7,071,086	Calculated
ee	Costs avoided (1.5% discount rate)	-$11,337,175	Calculated
ff	QALYs saved (1.5% discount rate)	264	Calculated
gg	**CE ($/QALY saved)**	**$16,434**	=(cc+dd+ee)/ff

√ = Estimates from the literature

We also modified several major assumptions and recalculated the cost per QALY as follows:

- Assume the prevalence of individuals living with HIV infections in BC is decreased from 12,100 to 9,700 (Table 2, row *a*): CE = $24,483.
- Assume the prevalence of individuals living with HIV infections in BC is increased from 12,100 to 14,500 (Table 2, row *a*): CE = $11,049.
- Assume that the early initiation of antiretroviral therapy is associated with a 96% reduction (from 64%) in the transmission rate per person-year (Table 2, row *hh*): CE = -$12,463.
- Assume that the early initiation of antiretroviral therapy is associated with a 25% reduction (from 64%) in the transmission rate per person-year (Table 2, row *hh*): CE = $80,739.

- Assume screening once every 10 years rather than once every 5 years in the low-risk population (Table 3, row *d*): CE = $3,521.
- Assume screening once per lifetime rather than once every 5 years in the low-risk population (Table 3, row *d*): CE = -$6,669.
- Assume the cost of screening is reduced from $7 and $400 to $5 and $300 (Table 3, rows *m* & *n*): CE = $15,218.
- Assume the cost of screening is increased from $7 and $400 to $9 and $500 (Table 3, rows *m* & *n*): CE = $17,649.
- Assume the proportion of an office visit required is reduced from 0.50 to 0.33 (Table 3, row *l*): CE = $6,803.
- Assume the proportion of an office visit required is increased from 0.50 to 0.67 (Table 3, row *l*): CE = $26,084.
- Assume the average annual cost of antiretrovirals for HIV is increased from $26 to $47 per day (Table 3, row *s*): CE = $11,377.

Summary

Applying a 1.5% discount rate, the clinically preventable burden (CPB) associated with screening adolescents and adults aged 15 to 65 years for HIV infection is estimated to be 264 quality-adjusted life years (QALYs) while the cost-effectiveness (CE) is estimated to be $16,434 per QALY (see Table 4).

Table 4: Screening to Diagnose and Treat HIV Infections in a Birth Cohort of 40,000

Summary

	Base Case	Range	
CPB (Potential QALYs Gained)			
1.5% Discount Rate	**264**	153	391
3% Discount Rate	198	115	294
0% Discount Rate	360	209	533
CE ($/QALY) **including** patient time costs			
1.5% Discount Rate	**$16,434**	-$12,463	$80,739
3% Discount Rate	$16,434	-$12,463	$80,739
0% Discount Rate	$16,434	-$12,463	$80,739
CE ($/QALY) **excluding** patient time costs			
1.5% Discount Rate	-$1,416	-$24,516	$49,990
3% Discount Rate	-$1,416	-$24,516	$49,990
0% Discount Rate	-$1,416	-$24,516	$49,990

Chlamydia / Gonorrhea

There is a strong overlap in the at-risk populations for chlamydia and gonorrhea with both STIs often seen in the same individual. Indeed, the USPSTF recommends "chlamydia and gonorrhea screening for all sexually active women younger than 25 years (including adolescents), even if they are not engaging in high-risk sexual behaviours."[623] They further note that younger women tend to be at higher risk as they tend to have more new sex partners, their immune system tends to be relatively immature and the presence of "columnar epithelium on the adolescent exocervix."[624]

Following are the specific recommendations from the USPSTF and the CTFPHC with respect to screening for chlamydia and gonorrhea.

USPSTF Recommendations (2014)

> *The USPSTF recommends screening for chlamydia in sexually active females aged 24 years or younger and in older women who are at increased risk for infection. (B recommendation)*
>
> *The USPSTF recommends screening for gonorrhea in sexually active females aged 24 years or younger and in older women who are at increased risk for infection. (B recommendation)*[625]

CTFPHC Recommendations (1994)

The CTFPHC recommendations have not been updated since 1994.

> *Although there is sufficient evidence linking chlamydial infections to many complications, there is currently insufficient evidence in males and non-pregnant females to show that screening is effective in preventing these complications. Thus routine screening is not recommended in the general population (D Recommendation).* [626]
>
> *The low prevalence rate of infection with N. gonorrheae would make mass screening of the general population an inefficient intervention (D Recommendation). However, screening should be performed in certain populations: 1) individuals under 30 years, particularly adolescents, with at least 2 sexual partners in the previous year; 2) prostitutes; 3) sexual contacts of individuals known to have a sexually transmitted disease; and 4) age ≤16 years at first intercourse (A Recommendation).* [627]

Modelling the Clinically Preventable Burden

In this section, we will calculate the CPB associated with screening females less than 30 years of age at increased risk for infection with chlamydia and gonorrhea.

The USPSTF recommends that screening be performed in all sexually active females younger than 25. The CTFPHC also recommends screening in individuals under 30 years with at least

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[623] Meyers D, Wolff T, Gregory K et al. USPSTF recommendations for STI screening. *American Family Physician*. 2008; 77(6): 819-24.
[624] Ibid.
[625] LeFevre ML. Screening for chlamydia and gonorrhea: US Preventive Services Task Force recommendation statement. *Annals of Internal Medicine*. 2014; 161(12): 902-10.
[626] Canadian Task Force on Preventive Health Care. *Canadian Guide to Clinical Preventive Health Care: Chapter 60: Screening for Chlamydial Infection*. 1994. Available at http://canadiantaskforce.ca/wp-content/uploads/2013/03/Chapter60_chlamydia94.pdf?0136ff. Accessed November 2013.
[627] Beagan BL and Wang EEL. *Canadian Guide to Clinical Preventive Health Care: Chapter 59: Prevention of Gonorrhea*. 1994. Available at http://canadiantaskforce.ca/wp-content/uploads/2013/03/Chapter59_gonorrhea94.pdf?0136ff. Accessed November 2013.

2 sexual partners in the previous year. This means that approximately 189,099 females would be eligible for screening in BC in 2017 (see Table 1).

Table 1: Relevant Female Population for Chlamydia/Gonorrhea Screening in B.C.

Age	% Sexual Intercourse*	% Multiple Partners in Past Year**	2017 B.C. Female Population	Eligible for Screening
12-14	8.2%		68,283	5,599
15-17	17.5%		79,417	13,898
18-19	58.5%		52,944	30,966
20-24	82.3%		158,416	130,381
25-29	85.2%	6.0%	161,437	8,254
		Total	520,497	**189,099**

* Age 12-14 - Statistics Canada. *Table 1: Number and Percentage of 15- to 24-year-olds who had First Sexual Intercourse before Age 17, by Sex, Household Population, Canada, 2003 and 2009/2010.* 2013. Available at http://www.statcan.gc.ca/pub/82-003-x/2012001/article/11632/tbl/tbl1-eng.htm. Accessed January 2014.

* Age 15-29 "This analysis is based on the Statistics Canada's **Canadian Community Health Survey 1.1 Public Use Microdata File** and the **Canadian Community Health Survey 2010 Public Use Microdata File**. All computations, use and interpretation of these data are entirely that of **H. Krueger & Associates Inc**."

** Centre for Infectious Disease Prevention and Control. *Sexual Risk Behaviours of Canadians - HIV/AIDS Epi Updates.* 1999. Available at http://www.phac-aspc.gc.ca/publicat/epiu-aepi/hiv-vih/epi0599/sexbe-eng.php. Accessed January 2014.

In estimating CPB, we used the results based on a state transition simulation model developed by Hu and colleagues.[628] They found the most cost-effective approach to screening included annual screening in at-risk women ages 15 to 29 years of age followed by semi-annual screening for those with a history of infection. Our analysis is based on the assumption that this screening approach would be followed. Unless otherwise noted, the following assumptions are based on their analysis.

- In the absence of screening, the lifetime risk of chronic pelvic pain, infertility and ectopic pregnancy is 3.44%, 3.88% and 1.74%, respectively (Table 2, rows *d*, *e* & *f*).
- With the screening protocol noted above, the lifetime risk of chronic pelvic pain, infertility and ectopic pregnancy is reduced by 41% (Table 2, row *g)*.
- The quality of life impact estimates for chronic pelvic pain, infertility and ectopic pregnancy can have a significant impact on model results.[629]
- Hu and colleagues suggest that chronic pelvic pain is associated with a 0.40 reduction in quality of life for a period of 5 years.[630] The GBD study, however, found that moderate pelvic pain is associated a disability weight of 0.114 (95% CI of 0.078 to

[628] Hu D, Hook EW and Goldie SJ. Screening for Chlamydia trachomatis in women 15 to 29 years of age: a cost-effectiveness analysis. *Annals of Internal Medicine*. 2004; 141(7): 501-13.
[629] Jackson L, Auguste P, Low N et al. Valuing the health states associated with Chlamydia trachomatis infections and their sequelae: A systematic review of economic evaluations and primary studies. *Value in Health*. 2014; 17: 116-30.
[630] Hu D, Hook EW and Goldie SJ. Screening for Chlamydia trachomatis in women 15 to 29 years of age: a cost-effectiveness analysis. *Annals of Internal Medicine*. 2004; 141(7): 501-13.

0.159).[631] Given the average QoL of women ages less than 30 of 0.914 (see Reference Document), the 0.114 disability weight results in a reduced QoL of 12.5% (95% CI of 8.5% to 17.4%) (Table 2, row *n)*.

- Hu and colleagues suggest that infertility is associated with a 0.18 reduction in quality of life up until age 50.[632] The GBD study, however, found that primary infertility ("wants to have a child and has a fertile partner but the couple cannot conceive") is associated with a disability weight of just 0.008 (95% CI of 0.003 to 0.015).[633] Given the average QoL of women ages less than 50 of approximately 0.886 (see Reference Document), the 0.008 disability weight results in a reduced QoL of 0.9% (95% CI of 0.3% to 1.7%). We assumed the average infection would occur at age 21[634] with 29 potential years of infertility (Table 2, rows *o)*.
- Hu and colleagues suggest that ectopic pregnancy is associated with a 0.42 reduction in quality of life for a period of 4 weeks.[635] The GBD study, however, found that an ectopic pregnancy is associated a disability weight of 0.114 (95% CI of 0.078 to 0.159).[636] Given the average QoL of women ages less than 30 of 0.914 (see Reference Document), the 0.114 disability weight results in a reduced QoL of 12.5% (95% CI of 8.5% to 17.4%) (Table 2, rows *p)*.
- Other assumptions used in assessing the clinically preventable burden are detailed in the Reference Document.

Based on these assumptions, the calculation of CPB (Table 2, row *t*) is 143 QALYs. This represents the potential CPB moving from no screening to approximately 55% screening uptake.

[631] Institute for Health Metrics and Evaluation. *GBD 2016 sequelae, health states, health state lay descriptions, and disability weights*. Available online at http://ghdx.healthdata.org/record/global-burden-disease-study-2016-gbd-2016-disability-weights. Accessed January 2018.
[632] Hu D, Hook EW and Goldie SJ. Screening for Chlamydia trachomatis in women 15 to 29 years of age: a cost-effectiveness analysis. *Annals of Internal Medicine*. 2004; 141(7): 501-13.
[633] Institute for Health Metrics and Evaluation. *GBD 2016 sequelae, health states, health state lay descriptions, and disability weights*. Available online at http://ghdx.healthdata.org/record/global-burden-disease-study-2016-gbd-2016-disability-weights. Accessed January 2018.
[634] Oakeshott P, Kerry S, Aghaizu A et al. Randomised controlled trial of screening for Chlamydia trachomatis to prevent pelvic inflammatory disease: the POPI (prevention of pelvic infection) trial. *British Medical Journal*. 2010; 340(340): c1642.
[635] Hu D, Hook EW and Goldie SJ. Screening for Chlamydia trachomatis in women 15 to 29 years of age: a cost-effectiveness analysis. *Annals of Internal Medicine*. 2004; 141(7): 501-13.
[636] Institute for Health Metrics and Evaluation. *GBD 2016 sequelae, health states, health state lay descriptions, and disability weights*. Available online at http://ghdx.healthdata.org/record/global-burden-disease-study-2016-gbd-2016-disability-weights. Accessed January 2018.

Table 2: CPB of Screening to Detect and Treat Chlamydia/Gonorrhea in a Birth Cohort of 40,000 (B.C.)			
Row Label	Variable	Base Case	Data Source
a	At-risk population in B.C. birth cohort of 40,000	20,000	√
b	Potential adherence with screening	55%	Ref Doc
c	At-risk population screened	11,000	= a*b
d	Lifetime risk of chronic pelvic pain (CPP) without screening	3.44%	√
e	Lifetime risk of infertility without screening	3.88%	√
f	Lifetime risk of ectopic pregnancy (EP) without screening	1.74%	√
g	Effectiveness of screening in reducing CPP, infertility and EP	41%	√
h	Lifetime risk of chronic pelvic pain with screening	2.03%	= (1-g)*d
i	Lifetime risk of infertility with screening	2.29%	= (1-g)*e
j	Lifetime risk of ectopic pregnancy with screening	1.03%	= (1-g)*f
k	Cases of chronic pelvic pain avoided with screening	155	=(c*d)-(c*h)
l	Cases of infertility avoided with screening	175	=(c*e)-(c*i)
m	Cases of ectopic pregnancy avoided with screening	79	=(c*f)-(c*j)
n	QALYs parameters - chronic pelvic pain (5 years)	0.125	√
o	QALYs parameters - infertility (to age 50)	0.009	√
p	QALYs parameters - ectopic pregnancy (4 weeks)	0.125	√
q	QALYs gained with screening - chronic pelvic pain	97	=k*n*5
r	QALYs gained with screening - infertility	46	=l*o*29
s	QALYs gained with screening - ectopic pregnancy	0.8	=m*p*0.077
t	Total QALYs gained, 55% adherence with screening	143	=q+r+s

√ = Estimates from the literature

As noted by Hu and colleagues, the effectiveness and cost-effectiveness associated with their modelling is highly sensitive to a number of key assumptions.[637] Furthermore, there is significant debate about these key assumptions. For example, Hu and colleagues assumed that 30% of infections with chlamydia would lead to acute pelvic inflammatory disease (PID), with a range from 10-40%. Subsequent research suggests that the rate might be much lower, resulting in a change in the lower end of the range from 10% to just 0.43%.[638,639] Others indicate that we simply do not know very much about the natural progression from infection with either chlamydia or gonorrhea to PID.[640]

There is also significant debate about whether screening is associated with any significant reduction in PID and its sequelae. In a seminal article published in the *New England Journal of Medicine* in 1996, Scholes et al. present the results of a randomized controlled clinical trial in which they observed a significant reduction in PID in women screened for chlamydia (relative risk of 0.44; 95% CI of 0.20 to 0.90).[641] Subsequent research, however, has not been able to replicate these results. The Prevention of Pelvic Infection (POPI) trial in the UK, also

[637] Hu D, Hook III EW and Goldie SJ. The impact of natural history parameters on the cost-effectiveness of Chlamydia trachomatis screening strategies. *Sexually Transmitted Diseases*. 2006; 33(7): 428-36.
[638] van Valkengoed IG, Morré SA, van den Brule AJ et al. Overestimation of complication rates in evaluations of Chlamydia trachomatis screening programmes - implications for cost-effectiveness analyses. *International Journal of Epidemiology*. 2004; 33(2): 416-25.
[639] Hu D, Hook III EW and Goldie SJ. The impact of natural history parameters on the cost-effectiveness of Chlamydia trachomatis screening strategies. *Sexually Transmitted Diseases*. 2006; 33(7): 428-36.
[640] Herzog SA, Heijne JC, Althaus CL et al. Describing the progression from Chlamydia trachomatis and Neisseria gonorrhoeae to pelvic inflammatory disease: systematic review of mathematical modelling studies. *Sexually Transmitted Diseases*. 2012; 39(8): 628-37.
[641] Scholes D, Stergachis A, Heidrich FE et al. Prevention of pelvic inflammatory disease by screening for cervical chlamydial infection. *New England Journal of Medicine*. 1996; 334(21): 1362-6.

a randomized controlled trail, found a non-significant reduction in PID associated with screening (relative risk of 0.65; 95% CI of 0.34 to 1.22).[642]

Assumptions about the proportion of women with an infection that progresses to PID and the effectiveness of screening (and early treatment) in reducing the proportion of women with an infection who progress to PID are critical to any analysis about the effectiveness and cost-effectiveness of screening. In fact, Low notes that "under realistic assumptions, introducing a chlamydia screening programme is likely to be an expensive intervention".[643] She further notes that many chlamydia screening programs have been uncritically accepted as being effective.

With these caveats in mind, we modified the following major assumptions and recalculated the CPB as follows:

- Assume the potential adherence rate with screening is reduced from 55% to 45% (Table 2, row *b)*: CPB = 117.
- Assume the potential adherence rate with screening is increased from 55% to 65% (Table 2, row *b)*: CPB = 169.
- Assume the effectiveness of screening in reducing chronic pelvic pain, infertility and ectopic pregnancies is reduced from 41% to 10% (Table 2, rows *g)*: CPB = 35.
- Assume that the QoL reduction associated with chronic pelvic pain is reduced from 12.5% to 8.5% (Table 2 – row *n*), the QoL reduction associated with infertility is reduced from 0.9% to 0.3% (Table 2 – row *o*) and the QoL reduction associated with ectopic pregnancy is reduced from 12.5% to 8.5% (Table 2 – row *p*): CPB = 84.
- Assume that the QoL reduction associated with chronic pelvic pain is increased from 12.5% to 17.4% (Table 2 – row *n*), the QoL reduction associated with infertility is increased from 0.9% to 1.7% (Table 2 – row *o*) and the QoL reduction associated with ectopic pregnancy is increased from 12.5% to 17.4% (Table 2 – row *p*): CPB = 222.

Modelling Cost-Effectiveness

In this section, we will calculate the CE associated with screening females less than 30 years of age at increased risk for infection with chlamydia and gonorrhea.

In modelling CE, we made the following assumptions:

- **Proportion of at-risk population with infection** – We assumed that 5.68% of the at-risk population would test positive for either chlamydia or gonorrhea (Table 3, row *f*).[644] This assumption was varied between 2% and 33% in the sensitivity analysis.[645]

[642] Oakeshott P, Kerry S, Aghaizu A et al. Randomised controlled trial of screening for Chlamydia trachomatis to prevent pelvic inflammatory disease: the POPI (prevention of pelvic infection) trial. *British Medical Journal*. 2010; 340(340): c1642.
[643] Low N. Screening programmes for chlamydial infection: when will we ever learn? *British Medical Journal*. 2007; 334(7596): 725-8.
[644] Oakeshott P, Kerry S, Aghaizu A et al. Randomised controlled trial of screening for Chlamydia trachomatis to prevent pelvic inflammatory disease: the POPI (prevention of pelvic infection) trial. *British Medical Journal*. 2010; 340(340): c1642.
[645] Hu D, Hook III EW and Goldie SJ. The impact of natural history parameters on the cost-effectiveness of Chlamydia trachomatis screening strategies. *Sexually Transmitted Diseases*. 2006; 33(7): 428-36.

- **Screening protocol** – We assumed that screening included annual screening in at-risk women ages 15 to 29 years of age followed by semi-annual screening for those with a history of infection (Table 3, rows *g*, *h* and *i*).[646]
- **Costs of screening tests** – Hu et al. estimated the cost of a urine nucleic acid amplification test to be $13 (2000 USD)[647] or $15.28 in 2017 CAD. Robinson et al. estimated the costs to be £7.35 (in 2005)[648] or $16.17 in 2017 CAD. We used an estimate of $15.73 (the midpoint between the two estimates) per screening test in the model (Table 3, row *m*).
- **Average cost of antibiotic treatment –** The recommended drug regimen for chlamydia is doxycycline 100 mg PO bid for 7 days (estimated cost of $22.18 including dispensing fee[649]) or azithromycin 1g PO in a single dose (estimated cost of $18.10 including dispensing fee[650]) while the recommended drug regimen for gonorrhea is cefixime 800mg PO in a single dose (estimated cost of $19.04 including dispensing fee[651]) or ceftriaxone 250mg in a single dose plus azithromycin 1 g PO in a single dose.[652] We used an average cost of $19.77 (Table 3, row *p*) with a range from $18.10 to $22.18.
- Other costs and assumptions used in assessing cost-effectiveness are detailed in the Reference Document.
- Discount rate of 1.5%, varied from 0% to 3% in the sensitivity analysis.

Based on these assumptions, the estimated cost per QALY would be $57,174 (see Table 3, row *v*).

[646] Hu D, Hook EW and Goldie SJ. Screening for Chlamydia trachomatis in women 15 to 29 years of age: a cost-effectiveness analysis. *Annals of Internal Medicine*. 2004; 141(7): 501-13.
[647] Ibid.
[648] Robinson S, Roberts T, Barton P et al. Healthcare and patient costs of a proactive chlamydia screening programme: the Chlamydia Screening Studies project. *Sexually Transmitted Infections*. 2007; 83(4): 276-81.
[649] Pacific Blue Cross. *Pharmacy Compass*. 2018. Available at http://pharmacycompass.ca/BestPrice. Accessed February 2018.
[650] Ibid.
[651] Ibid.
[652] BC Centre for Disease Control. *British Columbia Treatment Guidelines: Sexually Transmitted Infections in Adolescents and Adults*. 2014. Available at http://www.bccdc.ca/resource-gallery/Documents/Communicable-Disease-Manual/Chapter%205%20-%20STI/CPS_BC_STI_Treatment_Guidelines_20112014.pdf. Accessed February 2018.

Table 3: CE of Screening to Detect and Treat Chlamydia/Gonorrhea in a Birth Cohort of 40,000 (B.C.)			
Label	**Variable**	**Base Case**	**Data Source**
a	At-risk population screened	11,000	Table 2, row c
b	# of annual screens between age 15 and 24	10	√
c	Total # of screens, 15 - 24	110,000	=a*b
d	% Population at-risk between 25-29	6%	√
e	Total # of screens, 25 - 29	3,300	=d*a*5
f	% with chlamydia/gonorrhea infection	5.68%	√
g	Total screens - positive	6,435	= (c+e)*d
h	Total screens - negative	106,865	= c+e-g
i	Additional follow-up screens in positive women	6,435	= g
	Costs of screening		
j	Cost of 10-minute office visit	$34.85	Ref Doc
k	Cost of patient time and travel for office visit	$59.38	Ref Doc
l	Portion of office visit needed	50%	Ref Doc
m	Cost per screening test	$15.73	√
n	Costs of screening	$7,524,774	= (g+h+i)*(((j+k)*l)*m)
o	**Costs of antibiotics**		
p	Cost per treatment	$19.77	√
q	Cost of antibiotics	$127,218	= g*p
	CE calculation		
r	Costs (undiscounted)	$7,651,992	= n+q
s	QALYs saved (undiscounted)	143	Table 2, row t
t	Costs (1.5% discount rate)	$6,813,920	Calculated
u	QALYs saved (1.5% discount rate)	119	Calculated
v	**CE ($/QALY saved)**	**$57,174**	= t/u

√ = Estimates from the literature

We also modified several major assumptions and recalculated the cost per QALY as follows:

- Assume the effectiveness of screening in reducing chronic pelvic pain, infertility and ectopic pregnancies is reduced from 41% to 10% (Table 2, row *b)*: CE = $234,414.
- Assume that the QoL reduction associated with chronic pelvic pain is reduced from 12.5% to 8.5% (Table 2 – row *n*), the QoL reduction associated with infertility is reduced from 0.9% to 0.3% (Table 2 – row *o*) and the QoL reduction associated with ectopic pregnancy is reduced from 12.5% to 8.5% (Table 2, row *p*): CE = $96,519.
- Assume that the QoL reduction associated with chronic pelvic pain is increased from 12.5% to 17.4% (Table 2 – row *n*), the QoL reduction associated with infertility is increased from 0.9% to 1.7% (Table 2 – row *o*) and the QoL reduction associated with ectopic pregnancy is increased from 12.5% to 17.4% (Table 2, row *p*): CE = $37,189.
- Assume that the proportion of the at-risk population who would test positive for either chlamydia or gonorrhea is reduced from 5.68% to 2.0% (Table 3, row *f*): CE = $54,601.
- Assume that the proportion of the at-risk population who would test positive for either chlamydia or gonorrhea is increased from 5.68% to 33.0% (Table 3, row *f*): CE = $76,281.
- Assume the portion of an office visit required is decreased from 50 to 33% (Table 3, row *l*): CE = $42,843.

- Assume the portion of an office visit required is increased from 50% to 67% (Table 3, row *l*): CE = $71,506.
- Assume the cost for antibiotic treatment is decreased from $19.77 to $18.10 (Table 3, row *p*): CE = $57,094.
- Assume the cost for antibiotic treatment is increased from $19.77 to $22.18 (Table 3, row *p*): CE = $57,290.

Summary

Applying a 1.5% discount rate, the clinically preventable burden (CPB) associated with screening females less than 30 years of age at increased risk for infection with chlamydia and gonorrhea is estimated to be 119 quality-adjusted life years (QALYs) while the cost-effectiveness (CE) is estimated to be $57,174 per QALY (see Table 4).

Table 4: Screening to Diagnose and Treat Chlamydia/Gonorrhea Infections in a Birth Cohort of 40,000
Summary

	Base Case	Range	
CPB (Potential QALYs Gained)			
1.5% Discount Rate	**119**	29	183
3% Discount Rate	100	24	153
0% Discount Rate	143	35	222
CE ($/QALY) **including** patient time costs			
1.5% Discount Rate	**$57,174**	$37,189	$234,414
3% Discount Rate	$60,733	$39,750	$249,007
0% Discount Rate	$53,410	$34,494	$218,983
CE ($/QALY) **excluding** patient time costs			
1.5% Discount Rate	$30,612	$19,912	$125,511
3% Discount Rate	$32,518	$21,283	$133,324
0% Discount Rate	$28,597	$18,469	$117,248

Hepatitis C Virus

United States Preventive Services Task Force Recommendations (2013)

Hepatitis C virus is the most common chronic bloodborne pathogen in the United States and a leading cause of complications from chronic liver disease. The prevalence of the anti-HCV antibody in the United States is approximately 1.6% in noninstitutionalized persons. According to data from 1999 to 2008, about three fourths of patients in the United States living with HCV infection were born between 1945 and 1965, with a peak prevalence of 4.3% in persons aged 40 to 49 years from 1999 to 2002. The most important risk factor for HCV infection is past or current injection drug use, with most studies reporting a prevalence of 50% or more. The incidence of HCV infection was more than 200 000 cases per year in the 1980s but decreased to 25 000 cases per year by 2001. According to the Centers for Disease Control and Prevention (CDC), there were an estimated 16 000 new cases of HCV infection in 2009 and an estimated 15 000 deaths in 2007. Hepatitis C–related end-stage liver disease is the most common indication for liver transplants among U.S. adults, accounting for more than 30% of cases. Studies suggest that about one half of the recently observed 3-fold increase in incidence of hepatocellular carcinoma is related to acquisition of HCV infection 2 to 4 decades earlier.

The USPSTF recommends screening for HCV infection in persons at high risk for infection. The USPSTF also recommends offering 1-time screening for HCV infection to adults born between 1945 and 1965. (B recommendation)[653]

United States Preventive Services Task Force Recommendations – (2019 DRAFT)

HCV is the most common chronic bloodborne pathogen in the United States and a leading cause of complications from chronic liver disease. HCV infection is associated with more deaths than the top 60 other reportable infectious diseases combined, including HIV. The most important risk factor for HCV infection is past or current injection drug use. In the United States, an estimated 4.1 million persons have past or current HCV infection (i.e., tests positive for the anti-HCV antibody). Of these persons with antibodies, approximately 2.4 million have current infections based on testing with molecular assays for HCV RNA. The estimated prevalence of chronic HCV infection is approximately 1.0% (2013 to 2016). An estimated 41,200 new HCV infections occurred in the United States in 2016. Cases of acute HCV infection have increased approximately 3.5-fold (2010 to 2016) over the last decade. The increase in acute HCV incidence has mostly affected young, white persons who inject drugs (PWID), especially those living in rural areas. There has also been an increase in the number of women ages 15 to 44 years with HCV infection.

The USPSTF recommends screening for hepatitis C virus (HCV) infection in adults ages 18 to 79 years. (B recommendation.)[654]

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[653] Moyer VA. Screening for hepatitis C virus infection in adults: U.S. Preventive Services Task Force recommendation statement. *Annals of Internal Medicine*. 2013; 159(5): 349-57.

[654] U.S. Preventive Services Task Force. *Draft Recommendation Statement Hepatitis C Virus Infection in Adolescents and Adults: Screening.* 2019. Available at https://www.uspreventiveservicestaskforce.org/Page/Document/draft-recommendation-statement/hepatitis-c-screening1. Accessed October 2019.

Canadian Task Force on Preventive Health Care Recommendations (2017)

> *The task force recommends against screening for HCV in asymptomatic Canadian adults (including baby boomers) who are not at elevated risk of HCV infection. Strong recommendation based on very low-quality evidence.*
>
> *A strong recommendation against screening is warranted given its uncertain benefits but the certainty that it would lead to high levels of resource consumption. Referring individuals with screen-detected HCV for assessment would reduce access to assessment and treatment for people with clinically evident HCV.*[655]

Background

In 2014, the BC Lifetime Prevention Schedule Expert Committee (LPSEC) requested that the CPB and CE of "offering 1-time screening for HCV infection to adults born between 1945 and 1965" in BC be modelled, based on the 2013 USPSTF recommendation.

In 2018, the LPSEC requested that all 26 CPS modelled to date be updated using 2017 data (or the most recently available data) and that all modelling assumptions be consistently applied in each of the individual models. At the time of this update, the CTFPHC recommendation "against screening for HCV in asymptomatic Canadian adults (including baby boomers)" had been published. In considering the divergent recommendations of the USPSTF and the CTFPHC, the LPSEC recommended that the analysis of CPB and CE be updated following the USPSTF recommendation to offer one-time screening for HCV infection to adults born between 1945 and 1965 due to the higher HCV infection rate in BC compared with the rest of Canada.

In 2019, the LPSEC became aware of a significant error in the calculation of CPB in the existing model. In addition, a substantial amount of new and updated data is currently available to allow for a more thorough model of CPB and CE.

Modelling the Clinically Preventable Burden

In this section, we will update and recalculate the CPB associated with one-time screening for HCV infection in BC adults born between 1945 and 1964.

In modelling CPB, we made the following assumptions:

- Hepatitis C infections tend to occur as "twin epidemics". ***New infections*** occur in younger birth cohorts who are commonly co-infected with HIV and/or the hepatitis B virus (HBV), socioeconomically marginalized, and living with mental health and addictions. ***Prevalent infections*** tend to be acquired in the distant past (prevalent infections are currently highest in the 1945 - 1964 birth cohort) and do not usually involve ongoing risk activities.[656]
- The hepatitis C virus has multiple genotypes. A genotype is a way of categorizing HCV based on similar genes. Until recently, HCV was categorized into six genotypes[657], which could be split into sub-types, but as genome sequencing

[655] Canadian Task Force on Preventive Health Care. Recommendations on hepatitis C screening for adults. *Canadian Medical Association Journal*. 2017; 189(16): E594-E604.
[656] Janjua N, Yu A, Kuo M, et al. Twin epidemics of new and prevalent hepatitis C infections in Canada: BC Hepatitis Testers Cohort. *BMC Infectious Diseases*. 2016; 16(334):
[657] Hajarizadeh B, Grebely J and Dore GJ. Epidemiology and natural history of HCV infection. *Nature Reviews Gastroenterology & Hepatology*. 2013; 10(9): 553.

technology has improved, as many as eight distinct genotypes have been discovered.[658]

- HCV genotypes are important because different genotypes respond differently to some medication used to treat and cure HCV.[659] The BC Centre for Disease Control routinely performs HCV genotyping after confirming an HCV infection "as it will inform the type and length of treatment."[660]
- Recent treatment advances for HCV include direct-acting antivirals (DAA). Some of the most recent DAA are "pangenotypic" meaning that cure rates are similar regardless of genotype.[661,662]
- HCV Genotype 1 is the most common genotype in North America.[663] Genotypes 1, 2 and 3 are the most common in BC.[664]
- The presence of an HCV infection is verified by the presence of HCV antibodies in the blood. A person thus infected is termed anti-HCV positive, meaning that HCV antibodies have been detected. The majority of HCV infections are asymptomatic.[665]
- An HCV infection is considered active if the HCV virus is replicating itself. This is determined by testing for the presence of HCV RNA (ribonucleic acid), the virus' genetic material.[666]
- Approximately 25% of persons infected with HCV spontaneously clear the infection (i.e. without medication).[667,668,669] In these individuals, the hepatitis C virus stops replicating and they are considered cured.

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[658] Borgia SM, Hedskog C, Parhy B et al. Identification of a novel hepatitis C virus genotype from Punjab, India: expanding classification of hepatitis C virus into 8 genotypes. *The Journal of Infectious Diseases.* 2018; 218(11): 1722-9.
[659] Treatment Action Group. *HCV Genotypes.*2016. Available at http://www.treatmentactiongroup.org/sites/default/files/Genotypes.pdf. Accessed October 2019.
[660] BC Centre for Disease Control. *Communicable Disease Control. Hepatitis C.* 2016. Available at http://www.bccdc.ca/health-professionals/clinical-resources/communicable-disease-control-manual/communicable-disease-control. Accessed October 2019.
[661] Treatment Action Group. *HCV Genotypes.*2016. Available at http://www.treatmentactiongroup.org/sites/default/files/Genotypes.pdf. Accessed October 2019.
[662] Ponziani FR, Miele L, Tortora A et al. Treatment of early stage chronic hepatitis C virus infection. *Expert Review of Clinical Pharmacology.* 2018; 11(5): 519-24.
[663] Hajarizadeh B, Grebely J and Dore GJ. Epidemiology and natural history of HCV infection. *Nature Reviews Gastroenterology & Hepatology.* 2013; 10(9): 553.
[664] BC Centre for Disease Control. *Communicable Disease Control. Hepatitis C.* 2016. Available at http://www.bccdc.ca/health-professionals/clinical-resources/communicable-disease-control-manual/communicable-disease-control. Accessed October 2019.
[665] Hajarizadeh B, Grebely J and Dore GJ. Epidemiology and natural history of HCV infection. *Nature Reviews Gastroenterology & Hepatology.* 2013; 10(9): 553.
[666] BC Centre for Disease Control. *Communicable Disease Control. Hepatitis C.* 2016. Available at http://www.bccdc.ca/health-professionals/clinical-resources/communicable-disease-control-manual/communicable-disease-control. Accessed October 2019.
[667] Government of Canada. *For Health Professionals: Hepatitis C*. 2019. Available at https://www.canada.ca/en/public-health/services/diseases/hepatitis-c/health-professionals-hepatitis-c.html. Accessed October 2019.
[668] Hajarizadeh B, Grebely J and Dore GJ. Epidemiology and natural history of HCV infection. *Nature Reviews Gastroenterology & Hepatology.* 2013; 10(9): 553.
[669] Hajarizadeh B, Grebely J and Dore GJ. Epidemiology and natural history of HCV infection. *Nature Reviews Gastroenterology & Hepatology.* 2013; 10(9): 553.

- Individuals who do not spontaneously clear the infection continue to have HCV RNA present and are considered HCV RNA positive.
- Successful treatment of HCV interferes with the replication of the hepatitis C virus.[670] Removal of the virus and an absence of HCV RNA after 12 weeks indicates having achieved a sustained virologic response (SVR), or a cure.[671]
- Individuals who have not either spontaneously cleared HCV or achieved SVR are considered to be actively infected. We use the term *chronic* HCV infection to identify these individuals.
- An active HCV infection kills liver cells (mostly through the body's response to the inflammation caused by HCV). Part of the body's natural defence against infection involves placing fibrous collagen[672] in the area around damaged cells. The collagen is normally then dissolved as part of the completed healing process. When infected with hepatitis C however, the body is producing collagen at a faster rate than it can be dissolved leading to an accumulation of scar tissue in the liver that is termed fibrosis. Eventually, this accumulation of scar tissue (i.e. fibrosis progression), reduces the liver's ability to function since healthy cells are being cut off from nutrients and oxygen provided by the blood.[673]
- Fibrosis generally progresses slowly and is classified in stages. One commonly used classification system is the METAVIR system (see Table 1).[674,675]

Table 1: Liver Fibrosis Stages (METAVIR Scoring)

Stage	Technical Definition	Common Definition	Liver Damage and Liver Function
F0	No Fibrosis	Mild fibrosis	No liver damage.
F1	Portal fibrosis without septa*	Mild fibrosis	Very mild liver damage.
F2	Portal fibrosis with few septa*	Significant fibrosis	Scarring has built up around the blood supply to the liver.
F3	Numerous septa* without cirrhosis	Severe fibrosis	The scars around different blood vessels in the liver are joined but liver function is unaffected.
F4	Cirrhosis	Compensated cirrhosis	The scarring is beginning to build up in the tissues of the liver and it's function is impaired.
		Decompensated cirrhosis	The liver can no longer maintain its function due to the extent of the scarring.

** A septum is a partition separating two chambers. Septa is the plural of septum.*

[670] Treatment Action Group. *HCV Genotypes.*2016. Available at http://www.treatmentactiongroup.org/sites/default/files/Genotypes.pdf. Accessed October 2019.
[671] BC Centre for Disease Control. *Communicable Disease Control. Hepatitis C.* 2016. Available at http://www.bccdc.ca/health-professionals/clinical-resources/communicable-disease-control-manual/communicable-disease-control. Accessed October 2019.
[672] Scar tissue
[673] The Hepatitis C Trust. *How Hepatitis C Damages the Liver*. 2019. Available at http://www.hepctrust.org.uk/information/impact-hepatitis-c-liver/hepatitis-c-and-liver-damage. Accessed October 2019.
[674] Poynard T, Bedossa P and Opolon P. Natural history of liver fibrosis progression in patients with chronic hepatitis C. *The Lancet*. 1997; 349(9055): 825-32.
[675] The Hepatitis C Trust. *Hepatitis C Liver Damage Progression*. 2019. Available at http://www.hepctrust.org.uk/information/impact-hepatitis-c-liver/progression-hepatitis-c. Accessed October 2019.

- After progressing through the stages of fibrosis, individuals with *chronic* HCV can further progress to hepatic decompensation (decompensated cirrhosis) and / or hepatocellular carcinoma.[676]
- There is not any conclusive evidence linking genotype and the rate of fibrosis progression.[677]

- We model HCV infection overall, rather than on a genotype level, since current treatment success rates and disease progression are largely genotype-independent.

- In their analysis of the burden of disease of HCV in Canada, Myers and colleagues back-calculated HCV progression rates by sex and 10-year age band.[678] We use these data and apply a weighting to the Myers et al. numbers based on the proportion of each sex who have HCV in BC.[679] The results are shown in Table 2.

Table 2: Disease Progression through to Cirrhosis and Hepatocellular Carcinoma (HCC)
Annual Rate of Progression to Next Stage, by Age

	Current Stage (From) / Future Stage (To)	f0 to f1	f1 to f2	f2 to f3	f3 to Cirrhosis	f3 to HCC	Cirrhosis to HCC
Male	20 - 29	5.2%	3.8%	5.3%	2.5%	0.0%	0.3%
	30 - 39	3.8%	2.7%	3.9%	5.7%	0.0%	0.5%
	40 - 49	13.9%	10.1%	14.3%	8.8%	0.1%	0.9%
	50 - 59	17.1%	12.4%	17.5%	4.8%	0.1%	1.4%
	60 - 69	19.4%	14.1%	19.9%	9.9%	0.2%	2.4%
	70 - 79	21.8%	15.8%	22.4%	19.1%	0.3%	3.9%
	80+	17.9%	13.0%	18.3%	19.1%	0.3%	3.9%
Female	20 - 29	4.3%	3.1%	4.4%	2.1%	0.0%	0.3%
	30 - 39	3.1%	2.3%	3.2%	4.7%	0.0%	0.4%
	40 - 49	11.6%	8.4%	11.9%	7.4%	0.0%	0.7%
	50 - 59	14.3%	10.4%	14.6%	4.0%	0.1%	1.2%
	60 - 69	16.2%	11.7%	16.6%	8.3%	0.1%	2.0%
	70 - 79	18.2%	13.2%	18.6%	15.9%	0.2%	3.3%
	80+	14.9%	10.8%	15.3%	1.6%	0.2%	3.3%
Weighted Total	20 - 29	4.9%	3.5%	5.0%	2.4%	0.0%	0.3%
	30 - 39	3.5%	2.6%	3.6%	5.3%	0.0%	0.5%
	40 - 49	13.1%	9.5%	13.4%	8.3%	0.1%	0.8%
	50 - 59	16.1%	11.7%	16.4%	4.5%	0.1%	1.3%
	60 - 69	18.2%	13.2%	18.7%	9.3%	0.2%	2.3%
	70 - 79	20.5%	14.8%	21.0%	17.9%	0.3%	3.7%
	80+	16.8%	12.2%	17.2%	12.6%	0.3%	3.7%

BC HCV Diagnosed who are Male	**63.1%**
BC HCV Diagnosed who are Female	**36.9%**

[676] Xu F, Moorman AC, Tong X et al. All-cause mortality and progression risks to hepatic decompensation and hepatocellular carcinoma in patients infected with hepatitis C virus. *Clinical Infectious Diseases*. 2015; 62(3): 289-97.
[677] Hajarizadeh B, Grebely J and Dore GJ. Epidemiology and natural history of HCV infection. *Nature Reviews Gastroenterology & Hepatology*. 2013; 10(9): 553.
[678] Myers RP, Krajden M, Bilodeau M et al. Burden of disease and cost of chronic hepatitis C virus infection in Canada. *Canadian Journal of Gastroenterology and Hepatology*. 2014; 28(5): 243-50.
[679] Bartlett S, Yu A, Chapinal N, et al. The population level care cascade for hepatitis C in British Columbia, Canada as of 2018: Impact of direct acting antivirals. *Liver International*. 2019; DOI: 10.1111/liv.14227.

- In addition to the annual progression probabilities outlined in Table 2, we have assumed that, once cirrhosis has developed, there is an annual risk of 3 – 6% of **hepatic decompensation**.[680,681] We model an annual risk of hepatic decompensation after cirrhosis of 4.5% (the mid-point of 3% and 6%) and vary this between 3% and 6% in our sensitivity analysis.

- The annual probability of death due to hepatic decompensation ranges from 13.5% to 21.6%.[682,683,684] We model an annual risk of death following hepatic decompensation of 17.6% (the mid-point of 13.5% and 21.6%) and vary this between 13.5% and 21.6% in our sensitivity analysis.

- Once cirrhosis has developed, there is an annual risk of 1 – 5% of developing hepatocellular carcinoma (HCC).[685,686,687,688] Our model values fall within this range (see Table 2).

- We model the annual probability of death due to **HCC** at 70.7% (43.0% to 77.0%) in the first year and 16.2% (11.0% – 23.0%) each subsequent year.[689]

- We model the annual probability of a **liver transplant** following decompensated cirrhosis or liver cancer is 3.2%.[690,691]

- Myers and colleagues report an annual probability of death after liver transplant of between 10.7% and 33.1% in the first year and between 3.9% and 4.8% each subsequent year.[692]

[680] Rein DB, Smith BD, Wittenborn JS et al. The cost-effectiveness of birth-cohort screening for hepatitis C antibody in U.S. primary care settings. *Annals of Internal Medicine*. 2012; 156(4): 263-70.
[681] Westbrook RH and Dusheiko G. Natural history of hepatitis C. *Journal of Hepatology.* 2014; 61(1): S58-S68.
[682] Rein DB, Smith BD, Wittenborn JS et al. The cost-effectiveness of birth-cohort screening for hepatitis C antibody in U.S. primary care settings. *Annals of Internal Medicine*. 2012; 156(4): 263-70.
[683] Westbrook RH and Dusheiko G. Natural history of hepatitis C. *Journal of Hepatology.* 2014; 61(1): S58-S68.
[684] Wong WW, Erman A, Feld JJ et al. Model-based projection of health and economic effects of screening for hepatitis C in Canada. *CMAJ Open.* 2017; 5(3): E662.
[685] Rein DB, Smith BD, Wittenborn JS et al. The cost-effectiveness of birth-cohort screening for hepatitis C antibody in U.S. primary care settings. *Annals of Internal Medicine*. 2012; 156(4): 263-70.
[686] Hajarizadeh B, Grebely J and Dore GJ. Epidemiology and natural history of HCV infection. *Nature Reviews Gastroenterology & Hepatology.* 2013; 10(9): 553.
[687] Westbrook RH and Dusheiko G. Natural history of hepatitis C. *Journal of Hepatology.* 2014; 61(1): S58-S68.
[688] Wong WW, Erman A, Feld JJ et al. Model-based projection of health and economic effects of screening for hepatitis C in Canada. *CMAJ Open.* 2017; 5(3): E662.
[689] Myers RP, Krajden M, Bilodeau M et al. Burden of disease and cost of chronic hepatitis C virus infection in Canada. *Canadian Journal of Gastroenterology and Hepatology*. 2014; 28(5): 243-50.
[690] Rein DB, Smith BD, Wittenborn JS et al. The cost-effectiveness of birth-cohort screening for hepatitis C antibody in U.S. primary care settings. *Annals of Internal Medicine*. 2012; 156(4): 263-70.
[691] Wong WW, Erman A, Feld JJ et al. Model-based projection of health and economic effects of screening for hepatitis C in Canada. *CMAJ Open.* 2017; 5(3): E662.
[692] Myers RP, Krajden M, Bilodeau M et al. Burden of disease and cost of chronic hepatitis C virus infection in Canada. *Canadian Journal of Gastroenterology and Hepatology*. 2014; 28(5): 243-50.

- Wong et al. use a 14.2% annual probability of death within the first year of a liver transplant and 3.4% each subsequent year.[693]

- We model annual probability of death after **liver transplant** after Myers et al.[694] and use the midpoint of the ranges for liver transplant deaths (21.9% in the first year and 4.4% in each subsequent year.)

- In 2019, an individual born in 1964 would be approximately 55 years of age while an individual born in 1945 would be approximately 74 years of age. The average age of the cohort is 65 (average of 55 and 74 rounded up). The average life expectancy of a 65 year old in BC is 20.8 years.

- For the 65-year-old cohort representative of the 1945 – 1964 birth cohort we assume that any HCV infected individual whose disease had progressed beyond cirrhosis (i.e. fibrosis stage f4) by age 65 had been detected and identified as HCV infected.

- In their modelling, Wong et al. estimate treatment naïve patients with a mean age of 50 years old to be distributed into the following stages of fibrosis: f0 – 8%, f1 – 20%, f2 – 35%, f3 – 21% and f4 (cirrhosis) – 16%.[695]

- In a different model, Wong et al. assumed the following distribution in 55 – 79 year olds based on intake data from a tertiary treatment facility: f0 – 5%, f1 – 10%, f2 – 15%, f3 – 45% and f4 (cirrhosis) – 25%.[696]

- We model the distribution of cases detected by screening after the treatment naïve patients and use the tertiary intake data in our sensitivity analysis.

- The BC Hepatitis Testers Cohort (BC-HTC) consists of over 1.7 million individuals in British Columbia tested for HCV or human immunodeficiency virus (HIV) or those reported as a case of hepatitis B virus (HBV), HCV, HIV or active tuberculosis (TB) since 1990.[697]

- Based on data from the BC-HTC, in the BC 1945-64 birth cohort, there are an estimated 37,056 individuals in BC who are HCV antibody positive; 30,574 have been diagnosed[698] and an estimated 6,482 are undiagnosed.[699] In 2018, there are an estimated 1,278,177 individuals in the BC 1945-64 birth cohort, suggesting that 2.392% (Table 11, row *f*) of the cohort are diagnosed HCV antibody positive and 0.507% (6,482 / 1,278,177) are undiagnosed (Table 11, row *g*).

[693] Wong WW, Erman A, Feld JJ et al. Model-based projection of health and economic effects of screening for hepatitis C in Canada. *CMAJ Open*. 2017; 5(3): E662.
[694] Myers RP, Krajden M, Bilodeau M et al. Burden of disease and cost of chronic hepatitis C virus infection in Canada. *Canadian Journal of Gastroenterology and Hepatology*. 2014; 28(5): 243-50.
[695] Wong WW, Lee KM, Singh S et al. Drug therapies for chronic hepatitis C infection: a cost-effectiveness analysis. *CMAJ Open.* 2017; 5(1): E97.
[696] Wong WW, Erman A, Feld JJ et al. Model-based projection of health and economic effects of screening for hepatitis C in Canada. *CMAJ Open*. 2017; 5(3): E662.
[697] Bartlett S, Yu A, Chapinal N, et al. The population level care cascade for hepatitis C in British Columbia, Canada as of 2018: Impact of direct acting antivirals. *Liver International*. 2019; DOI: 10.1111/liv.14227.
[698] Bartlett S, Yu A, Chapinal N, et al. The population level care cascade for hepatitis C in British Columbia, Canada as of 2018: Impact of direct acting antivirals. *Liver International*. 2019; DOI: 10.1111/liv.14227.
[699] Dr. Mel Krajden. Medical Head, Hepatitis, BC Centre for Disease Control. Personal Communication. November 2019.

- Using the estimated 0.507% of undiagnosed cases in the BC 1945-64 birth cohort, we calculated the number of cases of HCV that would be detected by screening within our birth cohort of 40,000 at 113.3 (Table 11, row *m*). We proceed to model these 113.3 previously undiagnosed cases detected through screening within our birth cohort based on the assumption of no universal screening (they would ***not*** be detected). That is, we modelled changes in their disease states assuming no intervention with DAA for the 20.8 years of life remaining for the average 65 year old British Columbian (see Table 3).

Table 3: Undetected Individuals with RNA+ HCV in BC 1945 - 64 Birth Cohort within BC Birth Cohort of 40,000

Number of Indivduals in Each Disease State at the Start of the Year - In the ***Absence*** of Screening and Treatment

Age	f0	f1	f2	f3	Cirrhosis	Decomp. Cirr	1st Year HCC	HCC	1st Year Liver Transplant	Liver Transplant	HCV-Related Death	Total
65	***9.1***	***22.7***	***39.7***	***23.8***	***18.1***	0.0	0.0	0.0	0.0	0.0	0.0	113.3
66	7.4	21.3	35.2	29.0	19.1	0.8	0.4	0.0	0.0	0.0	0.0	113.3
67	6.1	19.9	31.5	32.8	20.5	1.5	0.5	0.1	0.0	0.0	0.5	113.3
68	5.0	18.3	28.2	35.6	22.2	2.1	0.5	0.2	0.1	0.0	1.1	113.3
69	4.1	16.8	25.4	37.5	24.0	2.7	0.6	0.3	0.1	0.1	1.9	113.3
70	3.3	15.3	22.9	38.7	25.9	3.2	0.6	0.4	0.1	0.2	2.8	113.3
71	2.6	13.7	20.3	36.4	30.7	3.7	1.1	0.5	0.1	0.2	3.9	113.3
72	2.1	12.2	18.1	34.1	34.7	4.3	1.2	0.7	0.2	0.3	5.4	113.3
73	1.7	10.8	16.1	31.7	38.0	5.0	1.4	0.9	0.2	0.4	7.2	113.3
74	1.3	9.6	14.3	29.3	40.5	5.7	1.5	1.0	0.2	0.6	9.2	113.3
75	1.1	8.4	12.8	27.0	42.5	6.3	1.6	1.2	0.3	0.7	11.5	113.3
76	0.8	7.4	11.3	24.8	43.8	6.9	1.6	1.4	0.3	0.9	14.0	113.3
77	0.7	6.5	10.0	22.6	44.7	7.5	1.7	1.6	0.3	1.1	16.7	113.3
78	0.5	5.6	8.9	20.6	45.1	7.9	1.7	1.7	0.3	1.3	19.6	113.3
79	0.4	4.9	7.9	18.7	45.1	8.3	1.7	1.8	0.4	1.5	22.6	113.3
80	0.3	4.3	6.9	17.0	44.8	8.6	1.7	1.9	0.4	1.7	25.7	113.3
81	0.3	3.8	6.3	16.0	43.3	8.9	1.7	2.0	0.4	1.9	28.9	113.3
82	0.2	3.4	5.7	15.0	41.7	9.0	1.6	2.0	0.4	2.2	32.1	113.3
83	0.2	3.0	5.1	14.0	40.2	9.0	1.6	2.1	0.4	2.4	35.3	113.3
84	0.2	2.7	4.6	13.1	38.7	8.9	1.5	2.1	0.4	2.6	38.5	113.3
85	0.1	2.4	4.1	12.2	37.2	8.8	1.5	2.1	0.4	2.8	41.7	113.3
86	0.1	2.1	3.7	11.3	35.7	8.7	1.4	2.0	0.4	3.0	44.8	113.3

- Transition data from Table 2 was then used to estimate how many of the 113.3 individuals in the cohort would enter a given disease state (e.g. cirrhosis, decompensated cirrhosis, HCC, liver transplant recipient and death) by year / age in the absence of any screening / treatment program (see Table 4). That is, of the 113.3 individuals, 96.2 either already had or would eventually get cirrhosis and 34.9 of these would move to decompensated cirrhosis. Of the 113.3 individuals, 28.4 (1.27 + 27.08) would move to HCC and 5.8 (4.09 + 1.69) would get a liver transplant. Finally, a total of 47.9 HCV-related deaths would occur in the cohort, 23.3 due to HCC, 22.4 due to decompensated cirrhosis and 2.2 following a liver transplant (see Table 4).

Table 4: Undetected Individuals with RNA+ HCV in BC 1945 - 64 Birth Cohort within BC Birth Cohort of 40,000

Number of Incident Cases in each Disease State by Year - In the ***Absence*** of Screening and Treatment

						HCC Originating From		Liver Tx Originating From		Deaths Resulting From					
Age	f1	f2	f3	Cirrhosis	Decomp Cirrhosis	f3	Cirrhosis	Decomp Cirrhosis	HCC	Decomp Cirrhosis	Liver Tx (Within the 1st Yr)	Liver Tx (*After* the 1st Yr)	HCC (Within the 1st Yr)	HCC (*After* the 1st Yr)	Total HCV-Related Deaths
65	1.65	2.99	7.41	2.22	0.82	0.04	0.41	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
66	1.35	2.82	6.58	2.70	0.86	0.05	0.43	0.03	0.01	0.14	0.00	0.00	0.32	0.00	0.46
67	1.10	2.62	5.88	3.05	0.92	0.05	0.46	0.05	0.02	0.26	0.01	0.00	0.34	0.02	0.63
68	0.90	2.42	5.27	3.31	1.00	0.06	0.50	0.07	0.02	0.37	0.01	0.00	0.36	0.04	0.79
69	0.74	2.22	4.74	3.49	1.08	0.06	0.54	0.09	0.03	0.47	0.02	0.00	0.39	0.05	0.94
70	0.68	2.28	4.80	6.93	1.16	0.10	0.95	0.10	0.03	0.56	0.02	0.01	0.43	0.06	1.08
71	0.54	2.04	4.27	6.53	1.38	0.10	1.13	0.12	0.05	0.65	0.03	0.01	0.74	0.08	1.51
72	0.43	1.82	3.80	6.11	1.56	0.09	1.28	0.14	0.06	0.76	0.04	0.01	0.87	0.11	1.78
73	0.34	1.61	3.38	5.68	1.71	0.08	1.40	0.16	0.07	0.87	0.04	0.02	0.97	0.14	2.04
74	0.27	1.42	3.01	5.25	1.82	0.08	1.49	0.18	0.08	0.99	0.05	0.03	1.05	0.17	2.28
75	0.22	1.25	2.68	4.84	1.91	0.07	1.56	0.20	0.09	1.11	0.06	0.03	1.11	0.20	2.50
76	0.17	1.10	2.38	4.44	1.97	0.07	1.61	0.22	0.10	1.21	0.06	0.04	1.15	0.23	2.70
77	0.14	0.96	2.11	4.06	2.01	0.06	1.64	0.24	0.10	1.31	0.07	0.05	1.19	0.25	2.86
78	0.11	0.84	1.87	3.70	2.03	0.05	1.66	0.25	0.11	1.39	0.07	0.06	1.20	0.27	3.00
79	0.09	0.73	1.65	3.36	2.03	0.05	1.66	0.27	0.11	1.46	0.08	0.07	1.21	0.29	3.10
80	0.06	0.52	1.19	2.15	2.01	0.04	1.65	0.28	0.12	1.51	0.08	0.08	1.21	0.31	3.18
81	0.05	0.46	1.08	2.02	1.95	0.04	1.59	0.28	0.12	1.55	0.09	0.09	1.20	0.32	3.24
82	0.04	0.41	0.97	1.90	1.88	0.04	1.54	0.29	0.12	1.57	0.09	0.10	1.15	0.33	3.24
83	0.03	0.37	0.88	1.78	1.81	0.04	1.48	0.29	0.12	1.57	0.09	0.10	1.11	0.34	3.21
84	0.03	0.33	0.79	1.66	1.74	0.03	1.42	0.29	0.12	1.56	0.09	0.11	1.07	0.34	3.18
85	0.02	0.29	0.71	1.54	1.67	0.03	1.37	0.28	0.11	1.55	0.09	0.12	1.03	0.34	3.12
86	0.02	0.26	0.64	1.43	1.61	0.03	1.31	0.28	0.11	1.52	0.09	0.13	0.99	0.33	3.06
Total	**8.97**	**29.76**	**66.09**	**78.11**	**34.94**	**1.27**	**27.08**	**4.09**	**1.69**	**22.37**	**1.18**	**1.05**	**19.09**	**4.20**	**47.90**

- HCV testing data from the BC-HTC is summarized on Table 5.[700] A total of 1,235,457 British Columbians had been tested for HCV by December 31, 2015. Of these, 55,568 (4.5%) tested positive and were still alive. A total of 3,459,242 British Columbians had not yet been tested, or 74% of the population.
- For the 1,325,760 individuals born between 1945 and 1965, 416,669 (31.4%, see Table 11, row *c*) had been tested for HCV by December 31, 2015 (see Table 5). Of 416,669 that had been tested, 34,511 (8.3%) tested positive and were still alive. A total of 909,091 (or 68.6%) of this cohort had not yet been tested.

Table 5: Testing for HCV Positive Individuals in BC

As of December 31, 2015, Adjusted for Deaths

Birth Year Cohort	2015 Population BC	Ever Tested for HCV	% of Cohort Tested	HCV Positive	% of Tested HCV Positive
<1945	504,792	104,771	20.8%	2,677	2.6%
1945-65	1,325,760	416,669	31.4%	34,511	8.3%
1966-75	635,543	252,364	39.7%	11,187	4.4%
>1975	2,228,604	461,653	20.7%	7,193	1.6%
Total	**4,694,699**	**1,235,457**	**26.3%**	**55,568**	**4.5%**

- Based on the data in Table 5, we assumed that 31.4% (Table 11, row *c*) of the BC 1945-64 birth cohort in our model has been screened.

- Using data from the BC-HTC, Bartlett and colleagues provide details on the population level care cascade for Hep C in BC based on all individuals ever tested between 1990 and 2015, with linkage to the data on medical visits, hospitalizations,

[700] Dr. Mel Krajden. Medical Head, Hepatitis, BC Centre for Disease Control. Personal Communication. September, 2019.

cancers, prescription drugs and deaths through to December 31, 2018. We use this data in Table 6.[701]

- A total of 44,507 individuals who are HCV antibody positive have had HCV RNA testing. 32,031 of these 44,507 (72.0%) tested RNA positive. For the 1945-64 birth cohort, 19,060 of the 25,577 (74.5%) tested RNA positive (Table 6 and Table 11, row *j*).
- Of the 17,441 individuals who have had HCV treatment initiated, an estimated 15,672 (89.9%) achieved a sustained virologic response (SVR). For the 1945-64 birth cohort, an estimated 10,895 of 12,030 (90.6%) achieved SVR.

Table 6: The Care Cascade for Hepatitis C in BC

As of December 31, 2018, Adjusted for Deaths

Birth Year Cohort	Tested HCV Antibody #	Tested HCV Antibody %	2018 Population BC	HCV Antibody % +ve	HCV RNA Tested	HCV RNA Positive	HCV RNA % +ve	HCV Treatment Initiated	SVR Achieved / Unknown	% Achieving SVR[1]
<1945	2,249	4.2%	426,050	0.53%	1,770	1,315	74.3%	697	616	88.4%
1945-64	30,574	57.2%	1,278,177	2.39%	25,577	19,060	74.5%	12,030	10,895	90.6%
1965-74	11,679	21.9%	680,687	1.72%	9,472	6,680	70.5%	2,981	2,641	88.6%
>1974	8,939	16.7%	2,605,235	0.34%	7,688	4,976	64.7%	1,733	1,520	87.7%
Total	**53,441**	**100.0%**	**4,990,150**	**1.07%**	**44,507**	**32,031**	**72.0%**	**17,441**	**15,672**	**89.9%**

[1] Patients who were treated, but who did not have an HCV RNA negative test on record (unknown) were assumed to achieve SVR at the same rate as those had an HCV RNA negative test recorded.

- In their modelling work, Wong and colleagues assumed an uptake of screening ranging from 76.6% to 90.0% based on the cohort's risk of infection and age range, using clinical expert's opinions.[702] We have assumed that 83.3% (the mid-point of the Wong et al estimates) of the unscreened population within the 1945-64 birth cohort would accept screening (see Table 11, row *l*) and varied this from 76.6% to 90.0% in the sensitivity analysis.

- In their modelling work, Wong and colleagues assumed an uptake of treatment ranging from 80.0% to 95.0% based on the cohort's risk of infection and age range, using clinical expert's opinions.[703] We have assumed that, in the absence of personal financial barriers, the proportion of the population that is HCV RNA+ that is eligible for and will accept treatment is estimated at 87.5% % (the mid-point of the Wong et al estimates) (see Table 11, row *n*), and varied this from 80.0% to 95.0% in the sensitivity analysis.

[701] Bartlett S, Yu A, Chapinal N, et al. The population level care cascade for hepatitis C in British Columbia, Canada as of 2018: Impact of direct acting antivirals. *Liver International*. 2019; DOI: 10.1111/liv.14227.
[702] Wong WW, Erman A, Feld JJ et al. Model-based projection of health and economic effects of screening for hepatitis C in Canada. *CMAJ Open*. 2017; 5(3): E662.
[703] Wong WW, Erman A, Feld JJ et al. Model-based projection of health and economic effects of screening for hepatitis C in Canada. *CMAJ Open*. 2017; 5(3): E662.

- The efficacy of Direct Acting Antiviral (DAA) treatment in producing a sustained viral response (i.e. a cure) in *clinical trials* is 95%.[704,705,706,707]
- As noted above, the effectiveness of DAA treatment in BC in the 1945-64 birth cohort appears to be 90.6% (see Table 6).[708]
- Newer types of DAA treatment continue to come on to the market. Some of these treatments are more efficacious for specific genotypes, but pangenomic treatments are now available where the efficacy is similar for all genotypes. Since 2017 in BC, 66.9% of DAA treatment for HCV has been by Epclusa, a pangenomic treatment. In 2018 and 2019, 91.1% of HCV treatment in BC was with Epclusa, Maviret and Zepatier.[709] Epclusa and Maviret are both pangenomic, while Zepatier is indicated for genotypes 1 and 4.
- **Epclusa** (sofosbuvir 400 mg – velpatasvir 100 mg) results in an SVR in 98.2% of HCV infected individuals of all genotypes, with or without cirrhosis (except genotype 3 with cirrhosis). For individuals with genotype 3 HCV and cirrhosis, 96.3% achieved SVR.[710] Overall, Epclusa achieved SVR rates of 95 – 99% in clinical trials.[711,712]
- In clinical trials of **Zepatie**r, overall SVR rates of 95% were reported for treatment-naïve participants with HCV genotypes 1, 4 and 6.[713]
- In clinical trials of **Maviret** (glecaprevir 300 mg – pibrentasvir 120 mg), SVR rates in excess of 99% for all genotypes without cirrhosis were achieved, except genotype 3 for which SVR rates were 95%.[714,715]

[704] Kowdley KV, Gordon SC, Reddy KR et al. Ledipasvir and sofosbuvir for 8 or 12 weeks for chronic HCV without cirrhosis. *New England Journal of Medicine*. 2014; 370(20): 1879-88.
[705] Afdhal N, Zeuzem S, Kwo P et al. Ledipasvir and sofosbuvir for untreated HCV genotype 1 infection. *New England Journal of Medicine*. 2014; 370(20): 1889-98.
[706] Afdhal N, Reddy KR, Nelson DR et al. Ledipasvir and sofosbuvir for previously treated HCV genotype 1 infection. *New England Journal of Medicine*. 2014; 370(16): 1483-93.
[707] Zeuzem S, Dusheiko GM, Salupere R et al. Sofosbuvir and ribavirin in HCV genotypes 2 and 3. *New England Journal of Medicine*. 2014; 370(21): 1993-2001.
[708] Bartlett SR, Yu A, Chapinal N et al. The population level care cascade for hepatitis C in British Columbia, Canada as of 2018: Impact of Direct Acting Antivirals. *Liver International*. 2019; 00: 1-12.
[709] Tijana Fazlagic. A/Executive Director, Pharmacare Benefits, Pharmaceutical Therapies & Pharmacare Division, BC Ministry of Health. Personal Communication. October 30, 2019.
[710] Jacobson IM, Lawitz E, Gane EJ et al. Efficacy of 8 weeks of sofosbuvir, velpatasvir, and voxilaprevir in patients with chronic HCV infection: 2 phase 3 randomized trials. *Gastroenterology*. 2017; 153(1): 113-22.
[711] Feld JJ, Jacobson IM, Hézode C et al. Sofosbuvir and velpatasvir for HCV genotype 1, 2, 4, 5, and 6 infection. *New England Journal of Medicine*. 2015; 373(27): 2599-607.
[712] Foster GR, Afdhal N, Roberts SK et al. Sofosbuvir and velpatasvir for HCV genotype 2 and 3 infection. *New England Journal of Medicine*. 2015; 373(27): 2608-17.
[713] Zeuzem S, Ghalib R, Reddy KR et al. Grazoprevir–elbasvir combination therapy for treatment-naive cirrhotic and noncirrhotic patients with chronic hepatitis C virus genotype 1, 4, or 6 infection: a randomized trial. *Annals of Internal Medicine.* 2015; 163(1): 1-13.
[714] Asselah T, Kowdley KV, Zadeikis N et al. Efficacy of glecaprevir/pibrentasvir for 8 or 12 weeks in patients with hepatitis C virus genotype 2, 4, 5, or 6 infection without cirrhosis. *Clinical Gastroenterology and Hepatology*. 2018; 16(3): 417-26.
[715] Zeuzem S, Foster GR, Wang S et al. Glecaprevir–pibrentasvir for 8 or 12 weeks in HCV genotype 1 or 3 infection. *New England Journal of Medicine*. 2018; 378(4): 354-69.

- We model the effectiveness of DAA treatment in the 1945-64 birth cohort at 97% (midpoint of 95% and 99% for Epclusa, the most common type of DAA currently prescribed) and vary this between 95% - 99% in the sensitivity analysis (Table 11, row *p*).

- We assume that a salvage treatment using a combination of sofosbuvir / velpatasvir / voxilaprevir is attempted for individuals who do not respond to the first treatment. We model the effectiveness of the salvage DAA treatment at a rate of 97%, varied between 95% - 99% in the sensitivity analysis (Table 11, row *p*).[716]

- We then updated our model assuming that 87.5% (Table 11, row *n*) of the 113.3 individuals with undiagnosed RNA+ HCV infection detected through screening would accept treatment and that the overall effectiveness of DAA treatment, including salvage treatment, in achieving SVR would be 99.9% (Table 11, row *q*). We assume that disease progression stops once SVR is achieved. Using this approach means that 14.3 of the 113.3 individuals with undiagnosed RNA+ HCV infection detected through screening would either not accept treatment or would not achieve SVR if treated. Using only these 14.3 individuals beginning at age 65, we allowed the disease to progress without any intervention for the 20.8 years of life remaining for the average 65 year old British Columbian (see Table 7).

Table 7: Undetected Individuals with RNA+ HCV in BC 1945 - 64 Birth Cohort within BC Birth Cohort of 40,000

Number of Indivduals in Each Disease State at the Start of the Year - Untreated or Failed Treatment

Age	f0	f1	f2	f3	Cirrhosis	Decomp. Cirr	1st Year HCC	HCC	1st Year Liver Transplant	Liver Transplant	HCV-Related Death	Total
65	1.14	2.85	4.99	2.99	2.28	0.00	0.00	0.00	0.00	0.00	0.00	14.3
66	0.93	2.68	4.43	3.64	2.41	0.10	0.06	0.00	0.00	0.00	0.00	14.3
67	0.76	2.50	3.96	4.13	2.58	0.19	0.06	0.01	0.01	0.00	0.06	14.3
68	0.62	2.31	3.55	4.47	2.79	0.27	0.06	0.03	0.01	0.00	0.14	14.3
69	0.51	2.12	3.19	4.71	3.02	0.34	0.07	0.04	0.01	0.01	0.24	14.3
70	0.42	1.93	2.87	4.86	3.25	0.40	0.08	0.05	0.01	0.02	0.35	14.3
71	0.33	1.73	2.56	4.58	3.86	0.47	0.13	0.06	0.02	0.03	0.49	14.3
72	0.26	1.54	2.28	4.29	4.37	0.54	0.15	0.08	0.02	0.04	0.68	14.3
73	0.21	1.36	2.03	3.98	4.78	0.63	0.17	0.11	0.02	0.06	0.90	14.3
74	0.17	1.21	1.80	3.69	5.10	0.71	0.19	0.13	0.03	0.07	1.16	14.3
75	0.13	1.06	1.60	3.39	5.34	0.79	0.20	0.15	0.03	0.09	1.45	14.3
76	0.11	0.93	1.42	3.11	5.51	0.87	0.21	0.18	0.04	0.11	1.76	14.3
77	0.08	0.81	1.26	2.85	5.62	0.94	0.21	0.20	0.04	0.14	2.10	14.3
78	0.07	0.71	1.12	2.59	5.67	1.00	0.21	0.21	0.04	0.16	2.46	14.3
79	0.05	0.62	0.99	2.36	5.67	1.05	0.22	0.23	0.05	0.19	2.84	14.3
80	0.04	0.54	0.87	2.14	5.63	1.08	0.21	0.24	0.05	0.22	3.23	14.3
81	0.04	0.48	0.79	2.01	5.44	1.11	0.21	0.25	0.05	0.24	3.63	14.3
82	0.03	0.43	0.71	1.89	5.25	1.13	0.21	0.26	0.05	0.27	4.04	14.3
83	0.02	0.38	0.64	1.77	5.06	1.13	0.20	0.26	0.05	0.30	4.44	14.3
84	0.02	0.34	0.58	1.65	4.87	1.12	0.19	0.26	0.05	0.33	4.85	14.3
85	0.02	0.30	0.52	1.53	4.68	1.11	0.18	0.26	0.05	0.35	5.25	14.3
86	0.01	0.27	0.47	1.43	4.49	1.09	0.18	0.26	0.05	0.38	5.64	14.3

[716] Dr. Naveed Janjua, Epidemiologist and Senior Scientists, Hepatitis, BC Centre for Disease Control. Personal Communication. November 2019.

- Transition data from Table 2 was then used to estimate how many of the 14.3 individuals in the cohort would enter a given disease state (e.g. cirrhosis, decompensated cirrhosis, HCC, liver transplant recipient and death) by year / age in the absence of any screening / treatment program (see Table 8). That is, of the 14.3 individuals, 12.1 either already had or would eventually get cirrhosis and 4.40 of these would move to decompensated cirrhosis. Of the 14.3 individuals, 3.6 (0.16 + 3.41) would move to HCC and 0.73 (0.51 + 0.21) would get a liver transplant. Finally, a total of 6.02 HCV-related deaths would occur in the cohort, 2.93 due to HCC, 2.81 due to decompensated cirrhosis and 0.28 following a liver transplant (see Table 8).

Table 8: Undetected Individuals with RNA+ HCV in BC 1945 - 64 Birth Cohort within BC Birth Cohort of 40,000

Number of Incident Cases in each Disease State by Year - In the *Presence* of Screening and Treatment

						HCC Originating From		Liver Tx Originating From		Deaths Resulting From					
Age	f1	f2	f3	Cirrhosis	Decomp Cirrhosis	f3	Cirrhosis	Decomp Cirrhosis	HCC	Decomp Cirrhosis	Liver Tx (Within the 1st Yr)	Liver Tx (*After* the 1st Yr)	HCC (Within the 1st Yr)	HCC (*After* the 1st Yr)	Total HCV-Related Deaths
65	0.21	0.38	0.93	0.28	0.10	0.00	0.05	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
66	0.17	0.35	0.83	0.34	0.11	0.01	0.05	0.00	0.00	0.02	0.00	0.00	0.04	0.00	0.06
67	0.14	0.33	0.74	0.38	0.12	0.01	0.06	0.01	0.00	0.03	0.00	0.00	0.04	0.00	0.08
68	0.11	0.30	0.66	0.42	0.13	0.01	0.06	0.01	0.00	0.05	0.00	0.00	0.05	0.00	0.10
69	0.09	0.28	0.60	0.44	0.14	0.01	0.07	0.01	0.00	0.06	0.00	0.00	0.05	0.01	0.12
70	0.09	0.29	0.60	0.87	0.15	0.01	0.12	0.01	0.00	0.07	0.00	0.00	0.05	0.01	0.14
71	0.07	0.26	0.54	0.82	0.17	0.01	0.14	0.01	0.01	0.08	0.00	0.00	0.09	0.01	0.19
72	0.05	0.23	0.48	0.77	0.20	0.01	0.16	0.02	0.01	0.10	0.00	0.00	0.11	0.01	0.22
73	0.04	0.20	0.43	0.71	0.21	0.01	0.18	0.02	0.01	0.11	0.01	0.00	0.12	0.02	0.26
74	0.03	0.18	0.38	0.66	0.23	0.01	0.19	0.02	0.01	0.12	0.01	0.00	0.13	0.02	0.29
75	0.03	0.16	0.34	0.61	0.24	0.01	0.20	0.03	0.01	0.14	0.01	0.00	0.14	0.02	0.31
76	0.02	0.14	0.30	0.56	0.25	0.01	0.20	0.03	0.01	0.15	0.01	0.01	0.15	0.03	0.34
77	0.02	0.12	0.27	0.51	0.25	0.01	0.21	0.03	0.01	0.16	0.01	0.01	0.15	0.03	0.36
78	0.01	0.11	0.23	0.46	0.26	0.01	0.21	0.03	0.01	0.17	0.01	0.01	0.15	0.03	0.38
79	0.01	0.09	0.21	0.42	0.26	0.01	0.21	0.03	0.01	0.18	0.01	0.01	0.15	0.04	0.39
80	0.01	0.07	0.15	0.27	0.25	0.01	0.21	0.03	0.01	0.19	0.01	0.01	0.15	0.04	0.40
81	0.01	0.06	0.14	0.25	0.24	0.01	0.20	0.04	0.01	0.19	0.01	0.01	0.15	0.04	0.41
82	0.00	0.05	0.12	0.24	0.24	0.00	0.19	0.04	0.01	0.20	0.01	0.01	0.15	0.04	0.41
83	0.00	0.05	0.11	0.22	0.23	0.00	0.19	0.04	0.01	0.20	0.01	0.01	0.14	0.04	0.40
84	0.00	0.04	0.10	0.21	0.22	0.00	0.18	0.04	0.01	0.20	0.01	0.01	0.13	0.04	0.40
85	0.00	0.04	0.09	0.19	0.21	0.00	0.17	0.04	0.01	0.19	0.01	0.02	0.13	0.04	0.39
86	0.00	0.03	0.08	0.18	0.20	0.00	0.17	0.03	0.01	0.19	0.01	0.02	0.12	0.04	0.38
Total	**1.13**	**3.74**	**8.31**	**9.83**	**4.40**	**0.16**	**3.41**	**0.51**	**0.21**	**2.81**	**0.15**	**0.13**	**2.40**	**0.53**	**6.02**

- A comparison of the results between Table 4 and Table 8 suggest that screening and treatment in the birth cohort would result in the following:
    - The number of new cases of cirrhosis would be reduced by 68.3 (see Table 11, row *u*), from 78.1 in the *absence* of screening and treatment (see Table 4) to 9.8 in the *presence* of screening and treatment (see Table 8).
    - The number of cases of decompensated cirrhosis would be reduced by 30.6 (see Table 11, row *v*), from 34.9 in the *absence* of screening and treatment (see Table 4) to 4.4 in the *presence* of screening and treatment (see Table 8).
    - The number of cases of HCC would be reduced by 24.8 (see Table 11, row *w*), from 28.4 in the *absence* of screening and treatment (see Table 4) to 3.6 in the *presence* of screening and treatment (see Table 8).
    - The number of liver transplants would be reduced by 5.1 (see Table 11, row *x*), from 5.8 in the *absence* of screening and treatment (see Table 4) to 0.7 in the *presence* of screening and treatment (see Table 8).

- The number of HCV-related deaths would be reduced by 41.9 (see Table 11, row *y*), from 47.9 in the *absence* of screening and treatment (see Table 4) to 6.0 in the *presence* of screening and treatment (see Table 8).

- Impairment in health-related quality of life (QoL) associated with various HCV-related disease states is based on a study of 751 HCV patients recruited from several tertiary care settings in Vancouver, Canada[717] and utilized in Canadian modelling studies.[718,719,720] Impairment in QoL following a liver transplant are from Ratcliffe and colleagues[721] as calculated by Williams et al.[722]
- We have assumed an average QoL for a 65 year old in BC to be 0.80 (see Reference Document) and calculated the impairment in QoL accordingly, as follows:
  - Non-cirrhosis (fibrosis stage 0-3): -8.8% (ranging from -3.8% to -13.8%)
  - Compensated cirrhosis (fibrosis stage 4): -13.8% (ranging from -8.8% to -18.8%)
  - Decompensated cirrhosis: -18.8% (ranging from -8.8% to -18.8%)
  - HCC: -10.0% (ranging from -6.3% to -15.0%)
  - Liver transplant (1st year): -43.8%
  - Liver transplant (subsequent years): -16.3%
  - On-treatment: -11.3% (ranging from -6.3% to -16.3%) (Table 11, row *af*)
  - Viral clearance: No change in QoL
- We then calculated the number of QALYs lost by individuals in the cohort who would be in a given disease state by year / age in the ***absence*** of any screening / treatment program (see Table 9) as well as the number of QALYs lost by individuals in the cohort who would be in a given disease state by year / age in the ***presence*** of a screening / treatment program (see Table 10).
- Based on this approach, the QALYs gained because of disease states avoided due to screening and treatment are as follows:
  - Non-cirrhosis – 69.9 QALYs gained (Table 11, row *z*)
  - Compensated cirrhosis – 74.7 QALYs gained (Table 11, row *aa*)
  - Decompensated cirrhosis – 16.8 QALYs gained (Table 11, row *ab*)
  - HCC – 3.7 QALYs gained (Table 11, row *ac*)
  - Liver transplant – 4.4 QALYs gained (Table 11, row *ad*)

[717] Hsu PC, Federico CA, Krajden M et al. Health utilities and psychometric quality of life in patients with early- and late-stage hepatitis C virus infection. *Journal of Gastroenterology and Hepatology.* 2012; 27(1): 149-57.
[718] Wong WW, Tu H-A, Feld JJ et al. Cost-effectiveness of screening for hepatitis C in Canada. *Canadian Medical Association Journal.* 2015; 187(3): E110-E21.
[719] Wong WW, Erman A, Feld JJ et al. Model-based projection of health and economic effects of screening for hepatitis C in Canada. *CMAJ Open.* 2017; 5(3): E662.
[720] Wong WW, Lee KM, Singh S et al. Drug therapies for chronic hepatitis C infection: a cost-effectiveness analysis. *CMAJ Open.* 2017; 5(1): E97.
[721] Ratcliffe J, Longworth L, Young T et al. Assessing health-related quality of life pre- and post-liver transplantation: a prospective multicenter study. *Liver Transplantation*. 2002; 8(3): 263-270.
[722] Williams J, Miners A, Harris R et al. The Cost-Effectiveness of One-Time Birth Cohort Screening for Hepatitis C as Part of the National Health Service Health Check Programme in England. *Value in Health*. 2019:

- HCV – related death – 387.1 QALYs gained (Table 11, row *ag*)

Table 9: QALYs Lost by Disease State and Age
In the ***Absence*** of Screening and Treatment

Age	Non-Cirrhosis	Cirrhosis	Decomp. Cirrhosis	HCC	Liver Transplant	HCV-Related Death	Total
65	6.7	1.99	0.00	0.00	0.00	0.0	**8.7**
66	6.5	2.10	0.12	0.04	0.00	0.0	**8.8**
67	6.3	2.26	0.23	0.05	0.01	8.2	**17.1**
68	6.1	2.44	0.32	0.06	0.03	10.8	**19.7**
69	5.9	2.64	0.40	0.07	0.04	12.9	**21.9**
70	5.6	2.85	0.48	0.08	0.06	14.6	**23.7**
71	5.1	3.38	0.56	0.12	0.08	16.1	**25.4**
72	4.7	3.82	0.65	0.15	0.10	21.4	**30.8**
73	4.2	4.18	0.75	0.18	0.13	24.0	**33.5**
74	3.8	4.46	0.85	0.20	0.16	26.1	**35.6**
75	3.4	4.67	0.95	0.22	0.19	27.6	**37.1**
76	3.1	4.82	1.04	0.24	0.22	28.8	**38.2**
77	2.8	4.92	1.12	0.26	0.25	29.1	**38.5**
78	2.5	4.96	1.19	0.27	0.29	29.2	**38.4**
79	2.2	4.96	1.25	0.28	0.32	28.8	**37.8**
80	2.0	4.92	1.29	0.29	0.36	27.9	**36.8**
81	1.8	4.76	1.33	0.29	0.39	26.7	**35.4**
82	1.7	4.59	1.35	0.29	0.42	25.6	**33.9**
83	1.6	4.42	1.35	0.29	0.45	24.0	**32.0**
84	1.4	4.26	1.34	0.29	0.48	22.2	**30.0**
85	1.3	4.09	1.32	0.28	0.50	20.3	**27.8**
86	1.2	3.93	1.30	0.28	0.53	18.4	**25.7**
Total	**80.0**	**85.42**	**19.17**	**4.24**	**5.00**	**442.8**	**636.7**

Table 10: QALYs Lost by Disease State and Age
In the ***Presence*** of Screening and Treatment

Age	Non-Cirrhosis	Cirrhosis	Decomp. Cirrhosis	HCC	Liver Transplant	HCV-Related Death	Total
65	0.8	0.25	0.00	0.00	0.00	0.0	**1.1**
66	0.8	0.26	0.02	0.00	0.00	0.0	**1.1**
67	0.8	0.28	0.03	0.01	0.00	1.0	**2.1**
68	0.8	0.31	0.04	0.01	0.00	1.4	**2.5**
69	0.7	0.33	0.05	0.01	0.01	1.6	**2.8**
70	0.7	0.36	0.06	0.01	0.01	1.8	**3.0**
71	0.6	0.42	0.07	0.02	0.01	2.0	**3.2**
72	0.6	0.48	0.08	0.02	0.01	2.7	**3.9**
73	0.5	0.53	0.09	0.02	0.02	3.0	**4.2**
74	0.5	0.56	0.11	0.03	0.02	3.3	**4.5**
75	0.4	0.59	0.12	0.03	0.02	3.5	**4.7**
76	0.4	0.61	0.13	0.03	0.03	3.6	**4.8**
77	0.4	0.62	0.14	0.03	0.03	3.7	**4.8**
78	0.3	0.62	0.15	0.03	0.04	3.7	**4.8**
79	0.3	0.62	0.16	0.04	0.04	3.6	**4.8**
80	0.3	0.62	0.16	0.04	0.04	3.5	**4.6**
81	0.2	0.60	0.17	0.04	0.05	3.4	**4.4**
82	0.2	0.58	0.17	0.04	0.05	3.2	**4.3**
83	0.2	0.56	0.17	0.04	0.06	3.0	**4.0**
84	0.2	0.54	0.17	0.04	0.06	2.8	**3.8**
85	0.2	0.51	0.17	0.04	0.06	2.6	**3.5**
86	0.2	0.49	0.16	0.03	0.07	2.3	**3.2**
Total	**10.1**	**10.74**	**2.41**	**0.53**	**0.63**	**55.7**	**80.1**

- Treatment based cures of HCV infection have a positive effect on extrahepatic disease states such as type 2 diabetes, chronic kidney disease and mood and anxiety disorders.[723] We have assumed that the impairment in QoL associated with being in a state of non-cirrhosis in HCV positive individuals noted above takes into account the potential change in QoL associated with extrahepatic manifestations.
- Although highly effective and well tolerated, each DAA has its own metabolism and presents an important potential for drug–drug interactions.[724,725] The model does not take into account any additional resources that might be required in managing drug–drug interactions or the potential harms associated with drug–drug interactions.
- Other assumptions used in assessing the CPB are detailed in the Reference Document.

Based on these assumptions, the calculation of CPB is 555 QALYs (Table 11, row *aj*). This represents the potential CPB of one-time screening for 83% of the previously unscreened BC birth cohort born between 1945 and 1964 and treating 88% of individuals detected with RNA+ HCV with direct acting antiviral (DAA) treatment.

[723] Rossi C, Jeong D, Wong S, et al. Sustained virological response from interferon-based hepatitis C regimens is associated with reduced risk of extrahepatic manifestations. *Journal of Hepatology*. 2019; 71: 1116-1125.
[724] Pons S, Boyer A, Lamblin G et al. Managing drug–drug interactions with new direct-acting antiviral agents in chronic hepatitis C. *British Journal of Clinical Pharmacology*. 2017; 83(2): 269-93.
[725] Néant N & Solas C. Drug-drug interactions potential of direct-acting antivirals for the treatment of chronic hepatitis C virus infection. *International Journal of Antimicrobial Agents*. 2018; https://doi.org/10.1016/j.ijantimicag.2018.10.014.

Table 11: CPB of Screening to Detect and Treat Hepatitis C Infection in a Birth Cohort of 40,000 (B.C.) For Individuals Born Between 1945 - 64			
Row Label	**Variable**	**Base Case**	**Data Source**
a	Median age of Birth Cohort (2019)	65	√
b	Birth Cohort population of 65 year olds	35,996	BC Life Table
c	% of Birth Cohort screened	31.4%	Table 5
d	Estimated # of individuals in Birth Cohort **screened**	11,313	b * c
e	Estimated # of individuals in Birth Cohort **unscreened**	24,683	b - d
f	Estimated % of individuals in Birth Cohort living with **diagnosed** HVC	2.392%	√
g	Estimated % of individuals in Birth Cohort living with **undiagnosed** HVC	0.507%	√
h	Estimated # of individuals in Birth Cohort living with **diagnosed** HVC	861	b * f
i	Estimated # of individuals in Birth Cohort living with **undiagnosed** HVC	183	b * g
j	% of individuals with undiagnosed HCV expected to be RNA+	74.5%	Table 6
k	# of individuals with undiagnosed HCV expected to be RNA+	136.0	i * j
l	Adherence with screening	83.3%	√
m	Cases of undiagnosed RNA+ HCV infection detected through screening	113.3	k * l
n	% eligible for and accepting treatment	87.5%	√
o	Cases of undiagnosed RNA+ HCV infection detected through screening receiving treatment	99.2	m * n
p	Effectiveness of antiviral therapy in producing a sustained viral response (i.e. a cure) in BC Birth Cohort	97.0%	√
q	Total SVR rate, including salvage treatment	99.9%	= 1 - (1 - p)^2
r	Cases of undiagnosed RNA+ HCV infection detected through screening receiving treatment and achieving a SVR (i.e. are 'cured')	99.1	o * q
s	Cases of undiagnosed RNA+ HCV infection that are detected through screening but are untreated or fail to achieve SVR	14.3	m - r
	Disease states avoided due to screening and treatment		
t	- Non-cirrhosis	91.6	Table 4 - Table 8
u	- Cirrhosis	68.3	Table 4 - Table 8
v	- Decompensated cirrhosis	30.5	Table 4 - Table 8
w	- HCC	24.8	Table 4 - Table 8
x	- Liver transplant	5.1	Table 4 - Table 8
y	- HCV-related death	41.9	Table 4 - Table 8
	QALYs gained because of disease states avoided due to screening and treatment		
z	- Non-cirrhosis	69.9	Table 9 - Table 10
aa	- Cirrhosis	74.7	Table 9 - Table 10
ab	- Decompensated cirrhosis	16.8	Table 9 - Table 10
ac	- HCC	3.7	Table 9 - Table 10
ad	- Liver transplant	4.4	Table 9 - Table 10
ae	- HCV-related death	387.1	Table 9 - Table 10
af	QALYs gained	556.6	z + aa + ab + ac + ad + ae
ag	QALY decrement associated with treatment	11.3%	√
ah	Length of time on treatment (12 weeks) - in years	0.23	12 / 52
ai	QALYs lost due to treatment	2.1	o * (ag * 0.8) * ah
aj	Total (net) QALYs gained	554.5	af - ai

√ = Estimates from the literature

We also modified several major assumptions and recalculated the CPB as follows:

- Assume the annual progression probabilities are **reduced** as follows:
    - From cirrhosis to hepatic decomposition is reduced from 4.5% to 3.0%
    - From hepatic decomposition to death is reduced from 17.6% to 13.5%
    - From hepatocellular carcinoma to death is reduced from 70.7% to 43.0% in Year 1 and from 16.2% to 11.0% in subsequent years.
    - CPB = 463
- Assume the annual progression probabilities are **increased** as follows:
    - From cirrhosis to hepatic decomposition is reduced from 4.5% to 6.0%
    - From hepatic decomposition to death is reduced from 17.6% to 21.6%
    - From hepatocellular carcinoma to death is reduced from 70.7% to 77.0% in Year 1 and from 16.2% to 23.0% in subsequent years.
    - CPB = 614
- Assume that the proportion of the unscreened population within the 1945-64 birth cohort that would accept screening is **reduced** from 83.3% to 76.6% (Table 11, row l). CPB = 510
- Assume that the proportion of the unscreened population within the 1945-64 birth cohort that would accept screening is **increased** from 83.3% to 90.0% (Table 11, row l). CPB = 599
- Assume that the uptake of treatment is **reduced** from 87.5% to 80.0% (Table 11, row n). CPB = 507
- Assume that the uptake of treatment is **increased** from 87.5% to 95.0% (Table 11, row n). CPB = 602
- Assume there is **more** of an annual QoL decrement associated with various disease states follows:
    - Non-cirrhosis from -8.8% to -13.8%
    - Compensated cirrhosis from -13.8% to -18.8%
    - HCC from -10.0% to -15.0%
    - Treatment from -11.3% to -6.3%
    - CPB = 623
- Assume there is **less** of an annual QoL decrement associated with various disease states follows:
    - Non-cirrhosis from -8.8% to -3.8%
    - Compensated cirrhosis from -13.8% to -8.8%
    - Decompensated cirrhosis from -18.8% to -8.8%
    - HCC from -10.0% to -6.3%
    - Treatment from -11.3% to -16.3%

- CPB = 478

- Assume the rate of sustained virologic response (SVR) **increases** from 97% to 99% (Table 11, row *p*). CPB = 555
- Assume the rate of sustained virologic response (SVR) **decreases** from 97% to 95% (Table 11, row *p*). CPB = 554

Modelling Cost-Effectiveness

In this section, we will calculate the CE associated with one-time screening for HCV infection in BC adults born between 1945 and 1965.

In modelling CE, we made the following assumptions:

- **Screening for HCV** – We assumed that there would be two office visits associated with screening, one to initiate screening and one to discuss lab results and follow-up treatment, if necessary (Table 12, row *l*). Furthermore, we have assumed that 50% of the office visit would be required (as per the Reference Document) but that the entire office visit to discuss lab results would be required if the lab test is positive.
- An HCV antibody test is used to determine if HCV antibodies are present in the serum. HCV antibodies are produced when an individual is exposed to HCV and usually remain present for life. Anti-HCV becomes detectable 5-10 weeks after infection, and confirms that the individual has been infected at some time. Nucleic Acid Testing (NAT) is required to confirm if active infection is present by detecting hepatitis C RNA. If HCV RNA is detected, a repeat HCV RNA test would be performed after 6 months to establish chronic infection.[726]
- In BC, the majority (95%) of HCV antibody tests and all HCV RNA tests are performed at the BC Center for Disease Control (BCCDC) Public Health Laboratory.[727]
- We estimated the cost of a hepatitis C antibody EIA test to be $24.28 (Table 12, row *n*).[728] A positive screening test would be followed by a hepatitis C RNA amp probe and a hepatitis C RNA quant test to confirm RNA detection and quantify RNA for a total cost per positive screening test of $234.62.[729] Total lab costs associated with a positive screening test of $469.24 (Tale 12, row *o*) include a repeat HCV RNA test after 6 months to establish chronic infection.
- **Cost of Direct-Acting Antivirals** (DAA) – As noted previously, the majority of current HCV treatment in BC is with Epclusa, Maviret and Zepatier.
- **Epclusa** is made by Gilead Sciences and contains the following medicines: sofosbuvir – 400 mg and velpatasvir – 100 mg. The wholesale price of Epclusa in

[726] BC Centre for Disease Control. *Communicable Disease Control: Hepatitis C*. August 2016. Available online at http://www.bccdc.ca/resource-gallery/Documents/Guidelines%20and%20Forms/Guidelines%20and%20Manuals/Epid/CD%20Manual/Chapter%201%20-%20CDC/HepC_Guidelines.pdf. Accessed November 2019.
[727] BC Centre for Disease Control. *Communicable Disease Control: Hepatitis C*. August 2016. Available online at http://www.bccdc.ca/resource-gallery/Documents/Guidelines%20and%20Forms/Guidelines%20and%20Manuals/Epid/CD%20Manual/Chapter%201%20-%20CDC/HepC_Guidelines.pdf. Accessed November 2019.
[728] Leggett L, Coward S, Soril L, et al. *Hepatitis C Screening in Alberta: A Health Technology Assessment*. Government of Alberta. 2016. Available at https://open.alberta.ca/publications/hepatitis-c-screening-in-alberta. Accessed November 2019.
[729] Ibid.

Canada is reported as $60,000 per treatment (1 pill per day x 12 weeks).[730] Using the Pacific Blue Cross Pharmacy Compass[731] and searching for "Epclusa, 400 mg-100 mg. DIN: 02456370" results in prices per pill ranging from $728.72 - $837.85 excluding a $10 - $13 dispensing fee. We calculate a treatment cost of $61,222 - $70,392 CAD per treatment (12 weeks of daily pills).

- **Zepatier,** made by Merck, is a fixed-dose formulation (one pill) containing the following two medicines: elbasvir – 50 mg and grazoprevir – 100 mg. The wholesale price of Zepatier in Canada is reported as $60,300 per 12 week treatment.[732]
- **Maviret**, made by Abbvie, consists of a combination of two DAAs (glecaprevir and pibrentasvir). The wholesale price of Maviret in Canada is reported as $40,000 per 8-week treatment.[733] The Government of BC lists three treatment lengths with Maviret; 8, 12 and 16 weeks.[734] Using the midpoint (12 weeks) results in an estimated cost of $60,000 for a 12-week course of treatment. Using the Pacific Blue Cross Pharmacy Compass[735] and searching for "Maviret, 100 mg-40 mg. DIN: 02467550" results in prices per pill ranging from $242.85 - $260.28 excluding a $10.25 - $12.95 dispensing fee. We calculate a treatment cost of $61,210 - $65,600 CAD per treatment (12 weeks of pills three times a day).
- While the listed prices for current DAAs are approximately $60,000 per course of treatment, a number of countries have been able to negotiate substantial price discounts. While details of these contractual arrangements are confidential they do suggest a steep price discount, particularly if governments "present plans (to the pharmaceutical companies) that ensure a greater number of patients undertake treatment."[736]
- Available evidence suggests that Australia, Italy, Spain and Portugal have all negotiated DAA course prices of between $10,000 and $16,000.[737] DAA prices in the UK have also recently been "slashed"[738] leading Williams et al to use a cost of approximately $17,000 in their recent UK-based cost-effectiveness modelling.[739]
- BC has also negotiated a confidential price reduction for DAA. For modelling purposes, we have assumed a cost per treatment for DAA in BC of $13,500 (the

[730] CATIE. *Hepatitis C treatment Epclusa approved in Canada—key information*. 2016 Available at https://www.catie.ca/en/catienews/2016-07-20/hepatitis-c-treatment-epclusa-approved-canada-key-information. Accessed November 2019.
[731] Pacific Blue Cross. *Pharmacy Compass.* 2019. Available at https://www.pac.bluecross.ca/pharmacycompass. Accessed November 2019.
[732] CATIE. *Zepatier for hepatitis C approved in Canada*. 2016 Available at https://www.catie.ca/en/catienews/2016-01-29/zepatier-hepatitis-c-approved-canada. Accessed November 2019.
[733] ClaimSecure. *MAVIRET™ - Short Course Antiviral Therapy for All Genotypes of Hepatitis C Virus.* 2018. Available at https://www.claimsecure.com/drug-reviews-blog/2018/february/maviret-short-course-antiviral-therapy-for-all-genotypes-of-hepatitis-c-virus/. Accessed November 2019.
[734] Government of BC. *Limited Coverage Drugs – glecaprevir-pibrentasvir.* Available at https://www2.gov.bc.ca/gov/content/health/practitioner-professional-resources/pharmacare/prescribers/limited-coverage-drug-program/limited-coverage-drugs-glecaprevir-pibrentasvir. Accessed November 2019.
[735] Pacific Blue Cross. *Pharmacy Compass.* 2019. Available at https://www.pac.bluecross.ca/pharmacycompass. Accessed November 2019.
[736] Douglass CH, Pedrana A, Lazarus JV et al. Pathways to ensure universal and affordable access to hepatitis C treatment. *BMC Medicine.* 2018; 16(1): 175.
[737] Douglass CH, Pedrana A, Lazarus JV et al. Pathways to ensure universal and affordable access to hepatitis C treatment. *BMC Medicine.* 2018; 16(1): 175.
[738] Hurley R. Slashed cost of hepatitis C drugs spurs drive to eliminate the disease. BMJ. 2018; 361: k1679.
[739] Williams J, Miners A, Harris R et al. The Cost-Effectiveness of One-Time Birth Cohort Screening for Hepatitis C as Part of the National Health Service Health Check Programme in England. *Value in Health*. 2019:

midpoint between $10,000 and $17,000) and modified this in the sensitivity analysis from $10,000 to $17,000 (Table 12, row *v*).

- In their analysis of the cost-effectiveness of one-time birth cohort screening for HCV in England, Williams and collaegues asumed a 50% increase in the cost of DAA for a second course of treatment if SVR is not achieved after the first course of treatment. We have done likewise (Table 12, row *ac*).
- **Follow-up** - Patients on DAA treatment would require an average of 9 follow-up visits to their physician, at weeks 2, 4, 8, 12, 16, 24, 32, 40 and 48 (Table 12, row *x*).[740] Each visit would include the following three lab tests: complete blood count (CBC), thyroid stimulating hormone (TSH) and a renal panel. The costs of the lab tests are estimated at $10.96,[741] $9.90[742] and $31.52,[743] respectively, for a total cost of $52.38[744] (Table 12, row *y*). We have assumed that the entire visit would be utilized to discuss progress and lab results and that a lab visit would be associated with each physician follow-up visit.
- **Costs Avoided** – As noted above, successful treatment with DAA means that a variety of diseases states (and their direct health care costs) are avoided.
- The incremental annual health care cost associated with an HCV infection (non-cirrhosis stages f0 to f3) is $400. This average cost is adjusted for the proportion of patients who are not under care, estimated to range from 39% for stage f0 down to 24% for stage f3.[745] These costs are based on El Saadany et al.'s research and include inpatient care, outpatient visits, diagnostic procedures, surgical procedures, and medication. Costs for each resource used were obtained from the Province of Alberta.[746]
- The incremental annual health care cost associated with compensated cirrhosis (stage f4) is $843. These costs are also based on El Saadany et al.'s research and include inpatient care, outpatient visits, diagnostic procedures, surgical procedures, and medication.[747,748]
- The incremental annual health care cost associated with decompensated cirrhosis is $15,284. These costs are also based on El Saadany et al.'s research and include

[740] McGarry LJ, Pawar VS, Panchmatia HR et al. Economic model of a birth cohort screening program for hepatitis C virus. *Hepatology*. 2012; 55(5): 1344-55.
[741] Fee item 90205 – hematology profile
[742] Fee item 92325 - thyroid stimulating hormone (TSH) – any method
[743] Includes fee items 91000 (primary base fee, $15.62), 91040 (albumin – serum/plasma, $1.55), 91235 (bicarbonate - serum/plasma, $2.37), 91326 (calcium – total, serum/plasma, $1.55), 91366 (chloride - serum/plasma, $1.49), 91421 (creatinine - serum/plasma, $1.52), 91707 (glucose quantitative – serum/plasma, $1.46), 92071 (phosphates – serum/plasma, $1.62), 92100 (potassium – serum/plasma, $1.39), 92231 (sodium – serum/plasma, $1.38) and 92368 (urea – serum/plasma, $1.57).
[744] BC Ministry of Health. Schedule of Fees for the Laboratory Services Outpatient. January 1, 2019. Available on-line at https://www2.gov.bc.ca/assets/gov/health/practitioner-pro/laboratory-services/laboratory_services_schedule_of_fees.pdf. Accessed November 2019.
[745] Myers RP, Krajden M, Bilodeau M et al. Burden of disease and cost of chronic hepatitis C virus infection in Canada. *Canadian Journal of Gastroenterology and Hepatology*. 2014; 28(5): 243-50.
[746] El Saadany S, Coyle D, Giulivi A et al. Economic burden of hepatitis C in Canada and the potential for prevention. *European Journal of Health Economics*. 2005; 6: 159-165.
[747] El Saadany S, Coyle D, Giulivi A et al. Economic burden of hepatitis C in Canada and the potential for prevention. *European Journal of Health Economics*. 2005; 6: 159-165.
[748] Myers RP, Krajden M, Bilodeau M et al. Burden of disease and cost of chronic hepatitis C virus infection in Canada. *Canadian Journal of Gastroenterology and Hepatology*. 2014; 28(5): 243-50.

inpatient care, outpatient visits, diagnostic procedures, surgical procedures, and medication.[749]

- Based on data from Ontario, the cost estimates for the *acute phase of a fatal liver cancer* are $27,560 (95% CI of $25,747 to $29,373) (in 2009 CAD).[750] We converted this to $30,922 in 2017 CDN.
- Based on data from Ontario, the estimated *first year costs* associated with a liver cancer survivor are $32,717 (95% CI of $30,591 to $34,844) (in 2009 CAD).[751] We converted this to $36,708 in 2017 CAD.
- Based on data from the US, the *ongoing annual costs* associated with a liver cancer survivor after the first year are estimated at $6,611 (in 2010 USD) or $6,287 in 2017 CAD.[752] Survival following liver cancer averages 4.7 years (see Reference Document).
- The cost for a liver transplant, including pre-transplant work-up, the transplant and the first year post-transplant care cost $162,901. Annual costs following the first year post-transplant average $9,654.[753]
- Treatment based cures of HCV infection have a positive effect on extrahepatic disease states such as type 2 diabetes, chronic kidney disease and mood and anxiety disorders.[754] We have assumed that the costs associated with being in a state of non-cirrhosis in HCV positive individuals noted above takes into account the potential costs associated with extrahepatic manifestations
- Other costs and assumptions used in assessing cost-effectiveness are detailed in the Reference Document.

Based on these assumptions, the estimated cost per QALY would be $3,170 (Table 12, row *aw*). This represents the potential CE of one-time screening for 83% of the previously unscreened BC birth cohort born between 1945 and 1964 and treating 88% of individuals detected with RNA+ HCV with direct acting antiviral (DAA) treatment.

[749] El Saadany S, Coyle D, Giulivi A et al. Economic burden of hepatitis C in Canada and the potential for prevention. *European Journal of Health Economics*. 2005; 6: 159-165.
[750] de Oliveira C, Bremner K, Pataky R et al. Understanding the costs of cancer care before and after diagnosis for the 21 most common cancers in Ontario: a population-based descriptive study. *Canadian Medical Association Journal Open*. 2013; 1(1): E1-E8.
[751] de Oliveira C, Bremner K, Pataky R et al. Understanding the costs of cancer care before and after diagnosis for the 21 most common cancers in Ontario: a population-based descriptive study. *Canadian Medical Association Journal Open*. 2013; 1(1): E1-E8.
[752] Mariotto A, Robin Y, Shao Y et al. Projections of the cost of cancer care in the United States: 2010–2020. *Journal of the National Cancer Institute*. 2011; 103(2): 117-28. This study included the costs of care for 14 major cancers which did not include liver cancer. We used the 'other' cancer category to estimate ongoing annual costs for liver cancer.
[753] Taylor M, Grieg P, Detsky A, et al. Factors associated with the high cost of liver transplantation in adults. *Canadian Journal of Surgery*. 2002; 45(6): 425-434.
[754] Rossi C, Jeong D, Wong S, et al. Sustained virological response from interferon-based hepatitis C regimens is associated with reduced risk of extrahepatic manifestations. *Journal of Hepatology*. 2019; 71: 1116-1125.

Table 12: CE of Screening to Detect and Treat Hepatitis C Infection in a Birth Cohort of 40,000 (B.C.)			
Row Label	**Variable**	**Base Case**	**Data Source**
a	Median age of Birth Cohort (2019)	65	Table 11, row a
b	Birth Cohort population of 65 year olds	35,996	Table 11, row b
c	Estimated # of individuals in Birth Cohort **unscreened**	24,683	Table 11, row e
d	Adherence with screening	83.3%	Table 11, row l
e	Population screened	20,561	= c * d
f	Estimated # of individuals in Birth Cohort living with **undiagnosed** HVC	183	Table 11, row i
g	Anti-HCV positive tests	152	= d * f
h	Anti-HCV negative tests	20,409	= e - g
i	Cases of undiagnosed RNA+ HCV infection detected through screening	113.3	Table 11, row m
j	Eligible and accepting treatment	87.5%	Table 11, row n
k	Treated cases	99.2	= i + j
	Costs of screening		
l	# of office visits required - 1 to initiate screening, 1 to discuss lab results	2	Assumed
m	Cost of 10-minute office visit	$34.85	Ref Doc
n	Portion of office visit needed	50%	Ref Doc
o	Cost of office visits	$721,838	(e * l * m * n) + (g * l)
p	Lab costs initial screening test	$24.28	√
q	Lab costs per positive screening tests (including 2nd confirmatory test at 6 months)	$469.24	√
r	Costs of lab tests	$570,565	(e * p) + (g * q)
s	Cost of patient time and travel for office visit and per lab test	$59.38	Ref Doc
t	Patient time costs - screening	$2,450,812	(e * l * n * s) + (e * s) + (g * s)
u	Total costs of screening	$3,743,215	= o + r + t
	Cost of treatment - First Round		
v	Drug costs per treatment - antiviral therapy	$13,500	√
w	Costs of antiviral therapy	$1,338,528	= k * v
x	Follow-up visits during treatment	9	√
y	Cost of lab tests / follow-up	$52.38	√
z	Follow-up costs (office visits & lab costs)	$77,840	= k * (x * (m + y))
aa	Patient time (office & lab visits)	$105,976	= k * (x * 2) * s
ab	Total cost of treatment - first round	$1,522,343	
	Cost of treatment - Second Round		
ac	Drug costs per treatment - antiviral therapy	$20,250	= v * 1.5
ad	Effectiveness of antiviral therapy in producing SVR (i.e. a cure)	97.0%	Table 11, row p
ae	Number of patients requiring a second round of treatment	3.0	= k - (k * ad)
af	Costs of antiviral therapy	$60,234	= ac * ae
ag	Follow-up visits during treatment	9	√
ah	Follow-up costs (office visits & lab costs)	$2,335	= (ae * ag) * (m + y)
ai	Patient time (office & lab visits)	$3,179	= (ae * ag) * 2 * s
aj	Total cost of treatment - second round	$65,748	= af + ah + ai
ak	Total cost of screening and treatment	$5,331,307	= u + ab + aj
	Costs Avoided		
al	Costs avoided, living with HCV stages f0 - f3	$399,667	Calculated
am	Costs avoided, living with cirrhosis	$572,608	Calculated
an	Costs avoided, living with decompensated cirrhosis	$1,707,820	Calculated
ao	Costs avoided, living with HCC	$373,370	Calculated
ap	Costs avoided, dying of HCC	$629,710	Calculated
aq	Costs avoided, living with liver transplant	$970,603	Calculated
ar	Total cost avoided (undiscounted)	$4,653,779	= al + am + an + ao + ap + aq + ar
	CE calculation		
as	Net Costs (undiscounted)	$677,528	= ak - ar
at	QALYs saved (undiscounted)	555	Table 11, row aj
au	Costs (1.5% discount rate)	$1,479,696	Calculated
av	QALYs saved (1.5% discount rate)	467	Calculated
aw	**CE ($/QALY saved)**	**$3,170**	= au / av

√ = Estimates from the literature

We also modified several major assumptions and recalculated the cost per QALY as follows:

- Assume the annual progression probabilities are **reduced** as follows:
    - From cirrhosis to hepatic decomposition is reduced from 4.5% to 3.0%
    - From hepatic decomposition to death is reduced from 17.6% to 13.5%
    - From hepatocellular carcinoma to death is reduced from 70.7% to 43.0% in Year 1 and from 16.2% to 11.0% in subsequent years.
    - CE = $3,263
- Assume the annual progression probabilities are **increased** as follows:
    - From cirrhosis to hepatic decomposition is reduced from 4.5% to 6.0%
    - From hepatic decomposition to death is reduced from 17.6% to 21.6%
    - From hepatocellular carcinoma to death is reduced from 70.7% to 77.0% in Year 1 and from 16.2% to 23.0% in subsequent years.
    - CE = $2,905
- Assume that the proportion of the unscreened population within the 1945-64 birth cohort that would accept screening is **reduce**d from 83.3% to 76.6% (Table 11, row l). CE = $3,170 (no change)
- Assume that the proportion of the unscreened population within the 1945-64 birth cohort that would accept screening is **increased** from 83.3% to 90.0% (Table 11, row l). CE = $3,170 (no change)
- Assume that the uptake of treatment is **reduced** from 87.5% to 80.0% (Table 11, row n). CE = $3,922
- Assume that the uptake of treatment is **increase**d from 87.5% to 95.0% (Table 11, row n). CE = $2,537
- Assume there is **mor**e of an annual QoL decrement associated with various disease states follows:
    - Non-cirrhosis from -8.8% to -13.8%
    - Compensated cirrhosis from -13.8% to -18.8%
    - HCC from -10.0% to -15.0%
    - Treatment from -11.3% to -6.3%
    - CE = $2,812
- Assume there is **less** of an annual QoL decrement associated with various disease states follows:
    - Non-cirrhosis from -8.8% to -3.8%
    - Compensated cirrhosis from -13.8% to -8.8%
    - Decompensated cirrhosis from -18.8% to -8.8%
    - HCC from -10.0% to -6.3%
    - Treatment from -11.3% to -16.3%
    - CE = $3,696

- Assume the proportion of an office visit required is **reduced** from 50% to 33% (Table 12, row n). CE = $1,759
- Assume the proportion of an office visit required is **increased** from 50% to 67% (Table 12, row n). CE = $4,582
- Assume the costs of DAA per treatment are **reduced** from $13,500 to $10,000 (Table 12, row v). CE = $2,393
- Assume the costs of DAA per treatment are **increased** from $13,500 to $17,000 (Table 12, row v). CE = $3,947
- Assume the annual treatment costs per disease state are **reduced** by 25%. CE = $5,233
- Assume the annual treatment costs per disease state are **increased** by 25%. CE = $1,107
- Assume the rate of sustained virologic response (SVR) **increases** from 97% to 99% (Table 11, row *p*). CE = $3,067
- Assume the rate of sustained virologic response (SVR) **decreases** from 97% to 95% (Table 11, row *p*). CE = $3,283

Summary

Applying a 1.5% discount rate, the clinically preventable burden (CPB) associated with one-time screening for Hepatitis C infection for 83% of the previously unscreened BC birth cohort born between 1945 and 1964 and treating 88% of individuals detected with RNA+ HCV with direct acting antiviral (DAA) treatment is estimated to be 467 quality-adjusted life years (QALYs) while the cost-effectiveness (CE) is estimated to be $3,170 per QALY (see Table 13).

Table 13: Screening to Detect and Treat Hepatitis C Infection in a Birth Cohort of 40,000 (B.C.)

Summary

	Base Case	Range	
CPB (Potential QALYs Gained)			
1.5% Discount Rate	**467**	388	526
3% Discount Rate	396	329	449
0% Discount Rate	555	463	623
CE ($/QALY) **including** patient time costs			
1.5% Discount Rate	**$3,170**	$1,107	$5,233
3% Discount Rate	$5,330	$3,300	$7,359
0% Discount Rate	$1,222	-$876	$3,320
CE ($/QALY) **excluding** patient time costs			
1.5% Discount Rate	-$2,314	-$251	-$4,378
3% Discount Rate	-$1,128	$902	-$3,157
0% Discount Rate	-$3,395	-$1,297	-$5,493

Our calculated cost per QALY of $3,170 (ranging from $1,107 to $5,233) is substantially lower than the Canadian estimate modelled by Wong et al in 2015 ranging from $34,359 to $44,034.[755] There are a number of important differences between our model and the Wong model.

First, the Wong model is based on screening and treating individual's ages 25-64 years or 45-64 years while our model is based on screening the 1945-64 birth cohort with an average age of 65 years.

Second, the Wong model assumed a price per treatment of approximately $55,000 compared with our current estimate of $13,500. Changing our base case cost per treatment to $55,000 would increase our cost per QALY from $3,170 to $12,283.

Third, the Wong model does not appear to include healthcare costs avoided associated with treatment success. If our model excluded these costs, our cost per QALY would increase from $3,170 to $11,422.

If these last two variables were modified simultaneously in our base case, then our cost per QALY would increase from $3,170 to $20,635.

[755] Wong WW, Tu H-A, Feld JJ et al. Cost-effectiveness of screening for hepatitis C in Canada. *Canadian Medical Association Journal.* 2015; 187(3): E110-E21.

Behavioural Counselling Interventions

Definition

In 2002, the USPSTF published an article outlining its vision for a broader appreciation of the importance of behavioural counselling interventions in clinical care.[756] The paper includes important definitional and context information for this area and we have thus quoted liberally from the paper below.

> *Behavioral counselling interventions address complex behaviors that are integral to daily living; they vary in intensity and scope from patient to patient; they require repeated action by both patient and clinician, modified over time, to achieve health improvement; and they are strongly influenced by multiple contexts (family, peers, worksite, school, and community). Further, "counselling" is a broadly used but imprecise term that covers a wide array of preventive and therapeutic activities, from mental health or marital therapy to the provision of health education and behavior change support. Thus, we have chosen to use the term "behavioral counselling interventions" to describe the range of personal counselling and related behavior-change interventions that are effectively employed in primary care to help patients change health-related behaviors. (p.270)*

> *Behavioral counselling interventions in clinical care are those activities delivered by primary care clinicians and related healthcare staff to assist patients in adopting, changing, or maintaining behaviors proven to affect health outcomes and health status. Common health promoting behaviors include smoking cessation, healthy diet, regular physical activity, appropriate alcohol use, and responsible use of contraceptives. (p. 269-70)*

> *The strongest evidence for the efficacy of primary care behavior-change interventions comes from tobacco-cessation research and, to a lesser extent, problem drinking. Accumulating evidence also shows the effectiveness of similar interventions for other behaviors. These interventions often provide more than brief clinician advice. Effective interventions typically involve behavioral counselling techniques and use of other resources to assist patients in undertaking advised behavior changes. For example, intervention adjuncts to brief clinician advice may involve a broader set of healthcare team members (e.g., nurses, other office staff, health educators, and pharmacists), a number of complementary communication channels (e.g., telephone counselling, video or computer assisted interventions, self-help guides, and tailored mailings), and multiple contacts with the patient. (p. 268)*

In 2014, the USPSTF published an article discussing challenges it encounters in aggregating the behavioural counselling intervention literature, including clear descriptions of the study population, intervention protocols, assessment of outcomes, and linking behaviour changes to health outcomes.[757] Researchers are encouraged to pay closer attention to these issues in designing and writing up their behavioural intervention research.

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[756] Whitlock EP, Orleans CT, Pender N et al. Evaluating primary care behavioral counselling interventions: an evidence-based approach. *American Journal of Preventive Medicine*. 2002; 22(4): 267-84.

[757] Curry S, Grossman D, Whitlock E et al. Behavioral counselling research and evidence-based practice recommendations: U.S. Preventive Services Task Force Perspectives. *Annals of Internal Medicine*. 2014; 160: 407-13.

Canadian Task Force on Preventive Health Care (2001)

A 2001 report from the CTFPHC titled "Counselling for Risky Health Habits: A Conceptual Framework for Primary Care Practitioners" noted that,

> *Risky lifestyle choices contribute to many contemporary health conditions. Primary care practitioners have frequent opportunities to help patients clarify issues and alter adverse behaviour patterns….The six risky behaviours addressed in this paper are appropriate targets for counselling. Some situations respond to brief on-the-spot advice, others require a few repeated counselling sessions utilizing concepts from behavioural theory, and certain ones need referral to a structured counselling program that employs a longer time-frame and allows for the opportunity to use a range of methods.*[758]

The "six risky behaviours" include dietary patterns, unintentional injury, problem drinking, physical inactivity patterns, **risky sexual patterns** and cigarette smoking.

United States Preventive Services Task Force Recommendations (2014)

> *The USPSTF recommends intensive behavioral counselling for all sexually active adolescents and for adults who are at increased risk for STIs. (B recommendation)*
>
> *All sexually active adolescents are at increased risk for STIs. Other risk groups include adults with current STIs or other infections within the past year, adults who have multiple sex partners, and adults who do not consistently use condoms.*
>
> *Clinicians should be aware of populations with a particularly high prevalence of STIs. African Americans have the highest STI prevalence of any racial/ethnic group, and prevalence is higher in American Indians, Alaska Natives, and Latinos than in white persons. Increased STI prevalence rates are also found in men who have sex with men (MSM), persons with low incomes living in urban settings, current or former inmates, military recruits, persons who exchange sex for money or drugs, persons with mental illness or a disability, current or former intravenous drug users, persons with a history of sexual abuse, and patients at public STI clinics.*
>
> *Behavioral counselling interventions can reduce a person's likelihood of acquiring an STI. Interventions ranging in intensity from 30 min to ≥2 h of contact time are beneficial; evidence of benefit increases with intervention intensity. Interventions can be delivered by primary care clinicians or through referral to trained behavioral counselors. Most successful approaches provide basic information about STIs and STI transmission; assess risk for transmission; and provide training in pertinent skills, such as condom use, communication about safe sex, problem solving, and goal setting.*[759]

[758] Canadian Task Force on Preventive Health Care. *Counselling for Risky Health Habits: A Conceptual Framework for Primary Care Practitioners* 2001. Available at http://canadiantaskforce.ca/files/guidelines/2001-risky-health-habits-en.pdf. Accessed February 2015.

[759] LeFevre ML. Behavioral counselling interventions to prevent sexually transmitted infections: US Preventive Services Task Force recommendation statement. *Annals of Internal Medicine*. 2014; 161(12): 894-901.

Modelling the Clinically Preventable Burden

In this section, we will calculate the CPB associated with behavioural counselling interventions for the prevention of sexually transmitted diseases in a British Columbia birth cohort of 40,000.

In estimating CPB, we made the following assumptions:

- The age and sex specific incidence rates per 100,000 for acute hepatitis B are taken from the BCCDC Annual Summary of Reportable Diseases 2016.[760] The age and sex specific incidence rates per 100,000 for human immunodeficiency virus (HIV) are taken from the BCCDC HIV Annual Annual Report 2015.[761] The age and sex specific incidence rates per 100,000 for chlamydia, gonorrhea and syphilis infections are taken from the BCCDC Annual Report 2015.[762] The incidence of human papillomavirus (HPV) infection in females is taken from an Ontario study.[763] We have assumed that the age specific incidence rate for males is the same as for females.[764] We calculated the incidence of herpes simplex virus type 2 (HSV-2) infection based on the number of patients within each age group who had their first herpes-related physician billings in 2006, as reported by the BC Centre for Disease Control.[765] We reduced the rates of first herpes-related visits proportional to the percentage of age-specific laboratory-diagnosed HSV infections in BC that were from genital specimens and were confirmed HSV-2. In 2005, approximately 31% of HSV-2 cases were identified in males and 69% percent in females; therefore, new cases were distributed between sexes according to these proportions (see Table 1).

Table 1: Sexually Transmitted Infections in British Columbia
Rate per 100,000 by Sex and Age Group

	HIV		Chlamydia		Gonorrhea		Hepatitis B - Acute		Syphilis		HPV		HSV-2	
	Female	Male	Female	Male	Female	Male	Female	Male	Female	Male	Female	Male	Female	Male
10-14	-	-	40	2	4	-	-	-	-	-	NA	NA	2.8	1.3
15-19	2	1	1,433	322	121	64	-	-	1	6	25,000	25,000	140.1	63.3
20-24	1	11	1,993	961	195	219	-	-	5	35	8,800	8,800	209.6	94.7
25-29	1	23	1,111	895	162	281	-	-	3	64	8,300	8,300	222.9	100.7
30-39	4	14	427	395	76	202	-	0.3	2	61	13,000	13,000	248.0	112.2
40-59	2	13	86	103	17	69	0.2	0.3	1	49	7,600	7,600	164.9	74.5
60+	1	3	6	17	2	15	-	0.2	0	10	NA	NA	113.0	51.6

NA = not available

[760] BC Centre for Disease Control. *British Columbia Annual Summary of Reportable Diseases 2016*. 2017. Available at http://www.bccdc.ca/resource-gallery/Documents/Statistics%20and%20Research/Statistics%20and%20Reports/Epid/Annual%20Reports/2016CDAnnualReportFinal.pdf. Accessed February 2018.

[761] BC Centre for Disease Control. HIV Annual Report 2015. Available at http://www.bccdc.ca/resource-gallery/Documents/Statistics%20and%20Research/Statistics%20and%20Reports/STI/HIV_Annual_Report_2015-FINAL.pdf. Accessed February 2018.

[762] BC Centre for Disease Control. STI Annual Report 2015. Available at http://www.bccdc.ca/resource-gallery/Documents/Statistics%20and%20Research/Statistics%20and%20Reports/STI/STI_Annual_Report_2015-FINAL.pdf. Accessed February 2018.

[763] Sellors JW, Karwalajtys TL, Kaczorowski J et al. Incidence, clearance and predictors of human papillomavirus infection in women. *Canadian Medical Association Journal*. 2003; 168(4): 421-5.

[764] Giuliano AR, Lu B, Nielson CM et al. Age-specific prevalence, incidence, and duration of human papillomavirus infections in a cohort of 290 US men. *Journal of Infectious Diseases*. 2008; 198(6): 827-35.

[765] Li X, Kim PH-J and Gilbert M. *Trends in Herpes Simplex Virus Cases in British Columbia, 1992-2006*. 2008. Available at http://www.bccdc.ca/NR/rdonlyres/11F4B322-54F7-48AC-A116-6D1081449B98/0/STI_Report_TrendsInHSV19922006_20090520.pdf. Accessed March 2015.

- The age- and sex- specific incidence rates were combined with years of life in a given age group by sex in the BC birth cohort to calculate the expected number of STIs by age and sex (see Tables 2 and 3).

Table 2: Estimated Number of Sexually Transmitted Infections in a *Male* Birth Cohort of 20,000

Age Group	Mean Survival Rate	Individuals in Birth Cohort	Years of Life in Birth Cohort	Chlamydia	HIV	Gonorrhea	Hepatitis B - Acute	Syphilis	HPV	HSV-2
15-19	0.994	19,875	99,374	320	1	63	0	6	24,844	63
20-24	0.991	19,813	99,065	952	11	217	0	34	8,718	94
25-29	0.987	19,734	98,672	883	22	277	0	63	8,190	99
30-34	0.983	19,658	98,289	388	14	198	0	59	12,778	110
35-39	0.978	19,560	97,798	386	13	197	0	59	12,714	110
40-44	0.971	19,427	97,134	100	13	67	0	47	7,382	72
45-49	0.962	19,241	96,203	99	12	66	0	47	7,311	72
50-54	0.949	18,971	94,855	98	12	65	0	46	7,209	71
55-59	0.929	18,570	92,852	96	12	64	0	45	7,057	69
Total Ages 15 - 59			**874,242**	**3,323**	**111**	**1,215**	**2**	**408**	**96,202**	**760**

Table 3: Estimated Number of Sexually Transmitted Infections in a *Female* Birth Cohort of 20,000

Age Group	Mean Survival Rate	Individuals in Birth Cohort	Years of Life in Birth Cohort	Chlamydia	HIV	Gonorrhea	Hepatitis B - Acute	Syphilis	HPV	HSV-2
15-19	0.995	19,897	99,484	1,425	2	120	0	1	24,871	139
20-24	0.993	19,865	99,323	1,979	1	193	0	4	8,740	208
25-29	0.992	19,833	99,163	1,102	1	161	0	3	8,231	221
30-34	0.990	19,795	98,975	423	4	76	0	2	12,867	245
35-39	0.987	19,741	98,706	422	4	75	0	2	12,832	245
40-44	0.983	19,662	98,311	85	2	17	0	1	7,472	162
45-49	0.977	19,546	97,730	84	2	16	0	1	7,427	161
50-54	0.969	19,375	96,873	83	2	16	0	1	7,362	160
55-59	0.956	19,118	95,591	82	2	16	0	1	7,265	158
Total Ages 15 - 59			**884,156**	**5,685**	**21**	**691**	**1**	**17**	**97,067**	**1,699**

- The data in Tables 2 and 3 was used to populate rows *a* - *n* in Table 4.
- High intensity (> 2 hours) behavioural counselling interventions are associated with a 62% (OR = 0.38, 95% CI of 0.24–0.60) reduction in STI incidence in adolescents and a 30% (OR = 0.70, 95% CI of 0.56–0.87) reduction in STI incidence in adults (Table 4, rows *o* & *p*).[766]
- Reductions in quality of life attributable to an infection with chlamydia, gonorrhea, HPV and HSV-2 are based on data provided in the relevant appendixes of the document *Vaccines for the 21st Century: A Tool for Decision Making* (Table 4, rows *y*, *aa*, *dd* & *ee*).[767] These appendixes include an estimated rate for all sequelae following the infection, together with the time in a given state and the relevant change in quality of life over that time period.

[766] O'Connor EA, Lin JS, Burda BU et al. Behavioral sexual risk-reduction counselling in primary care to prevent sexually transmitted infections: an updated systematic evidence review for the US Preventive Services Task Force. *Annals of Internal Medicine*. 2014; 161(12): 874.

[767] Institute of Medicine. *Vaccines for the 21st Century: A Tool for Decision Making.* Washington, DC: National Academy Press; 2000.

- *Vaccines for the 21st Century: A Tool for Decision Making* suggest that chronic pelvic pain is associated with a 0.40 reduction in quality of life for a period of 22.73 years. The GBD study, however, found that moderate pelvic pain is associated a disability weight of 0.114 (95% CI of 0.078 to 0.159).[768] Given the average QoL of women ages less than 30 of 0.914 (see Reference Document), the 0.114 disability weight results in a reduced QoL of 12.5% (95% CI of 8.5% to 17.4%). We therefore modified the assumption in *Vaccines for the 21st Century: A Tool for Decision Making* from 0.40 reduction in quality of life associated with chronic pelvic pain to 0.125.
- *Vaccines for the 21st Century: A Tool for Decision Making* suggest that infertility is associated with a 0.18 reduction in quality of life for 22.73 years. The GBD study, however, found that primary infertility ("wants to have a child and has a fertile partner but the couple cannot conceive") is associated with a disability weight of just 0.008 (95% CI of 0.003 to 0.015).[769] Given the average QoL of women ages less than 50 of approximately 0.886 (see Reference Document), the 0.008 disability weight results in a reduced QoL of 0.9% (95% CI of 0.3% to 1.7%). We therefore modified the assumption in *Vaccines for the 21st Century: A Tool for Decision Making* from 0.18 reduction in quality of life associated with infertility to 0.009.
- We assumed that the average HIV infection would occur at age 40[770] with 44 years of life remaining at a 17% reduced quality of life (Table 4, row *z*).[771] We assumed a reduction of 0.05 QALYs per infection with syphilis (Table 4, row *cc*), roughly equivalent to the calculated reductions for chlamydia (0.049, Table 4, row *y*) and gonorrhea (0.055, Table 4, row *aa*). We assumed an 18.5% reduction in quality of life attributable to a hepatitis B – acute infection (Table 4, row *bb*).[772]
- Other assumptions used in assessing the clinically preventable burden are detailed in the Reference Document.

Based on these assumptions, the CPB associated with behavioural counselling interventions for the prevention of sexually transmitted diseases is 3,285 QALYs (Table 4, row *ff*).

[768] Institute for Health Metrics and Evaluation. *GBD 2016 sequelae, health states, health state lay descriptions, and disability weights*. Available online at http://ghdx.healthdata.org/record/global-burden-disease-study-2016-gbd-2016-disability-weights. Accessed January 2018.
[769] Ibid.
[770] Siegfried N, Uthman OA and Rutherford GW. Optimal time for initiation of antiretroviral therapy in asymptomatic, HIV-infected, treatment-naive adults. *The Cochrane Library*. 2010: 2.
[771] Long EF, Mandalia R, Mandalia S et al. Expanded HIV testing in low-prevalence, high-income countries: a cost-effectiveness analysis for the United Kingdom. *PLoS One*. 2014; 9(4): e95735.
[772] Colombo GL, Gaeta GB, Viganò M et al. A cost-effectiveness analysis of different therapies in patients with chronic hepatitis B in Italy. *ClinicoEconomics and Outcomes Research*. 2011; 3: 37.

Table 4 CPB of Behavioural Counselling Interventions for the Prevention of Sexually Transmitted Infections in a Birth Cohort of 40,000			
Row Label	**Variable**	**Base Case**	**Data Source**
a	Estimated number of STIs in birth cohort as adolescents - Chlamydia	1,745	Tables 2 and 3
b	Estimated number of STIs in birth cohort as adults - Chlamydia	7,263	Tables 2 and 3
c	Estimated number of STIs in birth cohort as adolescents - HIV	4	Tables 2 and 3
d	Estimated number of STIs in birth cohort as adults - HIV	128	Tables 2 and 3
e	Estimated number of STIs in birth cohort as adolescents - Gonorrhea	183	Tables 2 and 3
f	Estimated number of STIs in birth cohort as adults - Gonorrhea	1,722	Tables 2 and 3
g	Estimated number of STIs in birth cohort as adolescents - Hep B-Acute	0	Tables 2 and 3
h	Estimated number of STIs in birth cohort as adults - Hep B-Acute	2	Tables 2 and 3
i	Estimated number of STIs in birth cohort as adolescents - Syphilis	7	Tables 2 and 3
j	Estimated number of STIs in birth cohort as adults - Syphilis	418	Tables 2 and 3
k	Estimated number of STIs in birth cohort as adolescents - HPV	49,715	Tables 2 and 3
l	Estimated number of STIs in birth cohort as adults - HPV	143,554	Tables 2 and 3
m	Estimated number of STIs in birth cohort as adolescents - HSV-2	202	Tables 2 and 3
n	Estimated number of STIs in birth cohort as adults - HSV-2	2,257	Tables 2 and 3
	Benefits Associated with Behavioural Counselling		
o	Effectiveness of high intensity behavioural counselling in reducing STI incidence in adolescents	62%	√
p	Effectiveness of high intensity behavioural counselling in reducing STI incidence in adults	30%	√
q	Adherence with behavioural counselling	29%	Ref Doc
r	Estimated # of chlamydia infections avoided	946	= ((a * o) + (b * p)) * q
s	Estimated # of HIV infections avoided	12	= ((c * o) + (d * p)) * q
t	Estimated # of gonorrhea infections avoided	183	= ((e * o) + (f * p)) * q
u	Estimated # of Hep B-Acute infections avoided	0.2	= ((g * o) + (h * p)) * q
v	Estimated # of syphilis infections avoided	38	= ((i * o) + (j * p)) * q
w	Estimated # of HPV infections avoided	21,428	= ((k * o) + (l * p)) * q
x	Estimated # of HSV-2 infections avoided	233	= ((m * o) + (n * p)) * q
y	Reduction in QALYs per infection - Chlamydia	0.049	√
z	Reduction in QALYs per infection - HIV	7.48	√
aa	Reduction in QALYs per infection - Gonorrhea	0.055	√
bb	Reduction in QALYs per infection - Hep B - Acute	0.185	
cc	Reduction in QALYs per infection - Syphilis	0.050	Assumed
dd	Reduction in QALYs per infection - HPV	0.146	√
ee	Reduction in QALYs per infection - HSV-2	0.0028	√
ff	**Potential QALYs gained, Behavioural Counseling increasing from 0% to 29%**	**3,285**	= r * y + s * z + t * aa + u * bb + v * cc + w * dd * x * ee

√ = Estimates from the literature

We also modified a number of major assumptions and recalculated the CPB as follows:

- Assume the effectiveness of high intensity behavioural counselling interventions in reducing the incidence of STIs is reduced from 62% to 40% in adolescents and from 30% to 13% in adults (Table 4, rows *o & p*): CPB = 1,706 QALYs.
- Assume the effectiveness of high intensity behavioural counselling interventions in reducing the incidence of STIs is increased from 62% to 74% in adolescents and from 30% to 44% in adults (Table 4, rows *o & p*): CPB = 4,498 QALYs.

Modelling Cost-Effectiveness

In this section, we will calculate the CE associated with behavioural counselling interventions for the prevention of sexually transmitted diseases in a British Columbia birth cohort of 40,000.

In estimating CE, we made the following assumptions:

- We have assumed that all individuals between the ages of 15 and 59 who had sexual intercourse within the past 12 months would be eligible for this intervention. Rates of sexually transmitted diseases are relatively rare before age 15 and after age 60 (see Table 1 above). The rates by sex and age group for those who have 'ever had sexual intercourse' and 'had sexual intercourse in the past 12 months' are taken from the 2010 Canadian Community Health Survey Public Use Microdata File.[773] Based on this data, approximately 81% of individuals between the ages of 15 and 59 have been sexually active within the past 12 months (see Table 5).

Table 5: Sexual Behaviours in British Columbia
By Age and Sex, 2010

Age Group	Ever had sexual intercourse		Had sexual intercourse in past 12 months		BC Population in 2010		BC Population at Risk	
	Males	Females	Males	Females	Males	Females	Males	Females
15-17	31.9%	19.3%	28.4%	17.7%	87,147	78,702	24,774	13,932
18-19	70.0%	63.3%	61.8%	59.9%	59,622	54,725	36,876	32,794
20-24	84.4%	87.5%	74.6%	77.7%	154,199	150,826	114,961	117,200
25-29	91.9%	91.2%	87.0%	84.1%	158,599	158,757	138,019	133,532
30-34	99.3%	96.6%	93.6%	93.2%	146,617	146,738	137,211	136,730
35-39	95.7%	96.7%	89.1%	91.1%	148,222	151,380	132,139	137,833
40-44	99.5%	97.9%	91.4%	85.6%	158,902	162,455	145,166	139,097
45-49	99.5%	95.9%	86.1%	82.7%	178,859	182,002	154,079	150,497
50-59	99.5%	95.9%	86.1%	82.7%	328,360	331,907	282,868	274,454
Total			**82.1%**	**80.1%**	**1,420,527**	**1,417,492**	**1,166,093**	**1,136,069**

- **Frequency of screening** - We assumed that a general practitioner would enquire about a patient's sexual behaviours once every four years (Table 7, row *c*).
- **Patient time costs for behavioural counselling intervention** - We assumed three hours of patient time would be required (including travel to and from the session) (Table 7, row *o*).
- **Costs of a behavioural counselling intervention** - We assumed that a clinical nurse specialist with a wage rate of $53.42 per hour ($100,000 per year) would lead the session.[774] Their direct time involvement would be 3.5 hours (2.5 for the session and 1 hour for preparation). To these costs we added 24% for benefits (e.g., dental, long-term disability, etc.), 40% for non-productive paid hours (e.g., statutory holidays, vacations, sick time, educational leave, etc.) and 50% for overhead costs (e.g., use of the facility and support staff). Based on these assumptions, the estimated costs per behavioural counselling intervention would be $487 (Table 7, row *n*). We have

[773] Statistics Canada. *Canadian Community Health Survey Public Use Microdata File 2009-2010 and 2010.* All computations, use and interpretation of these data are entirely that of H. Krueger & Associates Inc.
[774] *Nurse Practitioner (NP) Salary*. Available online at https://www.payscale.com/research/CA/Job=Nurse_Practitioner_(NP)/Salary. Accessed February 2018.

assumed that each session would be attended by an average of 5 individuals (Table 7, row *l*).

- **Costs per infection avoided** - The direct medical costs per infection avoided are taken from a US study (Table 7, rows *x – dd*).[775] These costs, provided in 2010 US dollars, were adjusted to 2017 CAD. When costs were provided separately for males and females, we estimated the combined average costs based on the proportion of infections by sex expected in BC (Table 2 and 3) (see Table 6).

Table 6: Estimated Direct Medical Cost of Selected Sexually Transmitted Infections

		2010 US$			2016 Can$			2017 Can$					
STI	**Sex**	Est	Range		Est	Range		Est	Range		% M/F	Est	Range
Chlamydia													
	Male	$30	$15	$45	$40	$20	$59	$29	$14	$43	37%	$229	$114 $343
	Female	$364	$182	$546	$481	$241	$722	$346	$173	$519	63%		
Gonorrhea													
	Male	$79	$40	$119	$104	$53	$157	$75	$38	$113	64%	$169	$85 $254
	Female	$354	$177	$531	$468	$234	$702	$337	$168	$505	36%		
HBV		$2,667	$2,172	$2,924	$3,525	$2,871	$3,865	$2,536	$2,065	$2,780			
HIV		$304,500	$229,300	$379,700	$402,494	$303,093	$501,895	$289,543	$218,037	$361,049			
HPV													
	Male	$45	$23	$78	$59	$30	$103	$43	$22	$74	50%	$112	$57 $194
	Female	$191	$96	$329	$252	$127	$435	$182	$91	$313	50%		
HSV-2													
	Male	$761	$381	$1,142	$1,006	$504	$1,510	$724	$362	$1,086	31%	$632	$316 $948
	Female	$621	$311	$932	$821	$411	$1,232	$590	$296	$886	69%		
Syphilis		$709	$355	$1,064	$937	$469	$1,406	$674	$338	$1,012			

- Other costs and assumptions used in assessing cost-effectiveness are detailed in the Reference Document.
- Discount rate of 1.5%, varied from 0% to 3% in the sensitivity analysis.

Based on these assumptions, the CE associated with behavioural counselling interventions for the prevention of sexually transmitted diseases is $10,267 per QALY (Table 7, row *kk*).

[775] Owusu-Edusei Jr K, Chesson HW, Gift TL et al. The estimated direct medical cost of selected sexually transmitted infections in the United States, 2008. *Sexually Transmitted Diseases*. 2013; 40(3): 197-201.

Table 7: CE of Behavioural Counselling Interventions for the Prevention of Sexually Transmitted Infections in a Birth Cohort of 40,000			
Row Label	**Variable**	**Base Case**	**Data Source**
a	Years of life between the ages of 15 and 59 in birth cohort	1,758,398	Tables 2 and 3
b	Proportion of years sexually active	81%	Table 5
	Costs of intervention		
c	Frequency of screening to determine sexual activity (every x years)	4	Assumed
d	Total number of screens	439,600	= a / c
e	Cost of 10-minute office visit	$34.85	Ref Doc
f	Value of patient time and travel for office visit	$59.38	Ref Doc
g	Portion of 10-minute office visit for screen	50%	Ref Doc
h	Cost of screening	$20,711,730	= d * (e + f) * g
i	Screen positive for sexual activity	356,076	= d * b
j	Adherence with behavioural counselling	29%	Table 4, row q
k	Attendance at a behavioural counselling intervention	103,262	= i * j
l	Individuals per behavioural counselling intervention	5	Assumed
m	Total number of behavioural counselling interventions	20,652	= k / m
n	Cost per behavioural counselling intervention	$487	√
o	Value of patient time and travel for behavioural counselling intervention	$89.07	√
p	Cost of behavioural counselling interventions	$19,255,251	= (m * n) + (k * o)
	Cost avoided		
q	Estimated # of chlamydia infections avoided	946	Table 4, row r
r	Estimated # of HIV infections avoided	12	Table 4, row s
s	Estimated # of gonorrhea infections avoided	183	Table 4, row t
t	Estimated # of Hep B-Acute infections avoided	0.2	Table 4, row u
u	Estimated # of syphilis infections avoided	38	Table 4, row v
v	Estimated # of HPV infections avoided	21,428	Table 4, row w
w	Estimated # of HSV-2 infections avoided	233	Table 4, row x
x	Cost of chlamydia infection avoided	$229	√
y	Cost of HIV infection avoided	$289,543	√
z	Cost of gonorrhea infection avoided	$169	√
aa	Cost of Hep B-Acute infection avoided	$2,536	√
bb	Cost of syphilis infection avoided	$674	√
cc	Cost of HPV infection avoided	$112	√
dd	Cost of HSV-2 infection avoided	$632	√
	CE calculation		
ee	Cost of intervention over lifetime of birth cohort	$39,966,981	= h + p
ff	Costs avoided	$6,239,820	= q * x + r * y + s * z + t * aa + u * bb + v * cc + w * dd
gg	QALYs saved	3,285	Table 4, row ff
hh	Cost of intervention over lifetime of birth cohort (1.5% discount)	$29,128,113	Calculated
ii	Costs avoided (1.5% discount)	$4,547,608	Calculated
jj	QALYs saved (1.5% discount)	2,394	Calculated
kk	**CE ($/QALY saved)**	**$10,267**	= (hh - ii) / jj

√ = Estimates from the literature

We also modified several major assumptions and recalculated the cost per QALY as follows:

- Assume the effectiveness of high intensity behavioural counselling interventions in reducing the incidence of STIs is reduced from 62% to 40% in adolescents and from 30% to 13% in adults (Table 4, rows *o & p*): CE = $21,687/QALY.
- Assume the effectiveness of high intensity behavioural counselling interventions in reducing the incidence of STIs is increased from 62% to 74% in adolescents and from 30% to 44% in adults (Table 4, rows *o & p*): CE = $6,921/QALY.
- Assume screening to determine sexual activity is less frequent, carried out once every 5 years rather than once every 4 years (Table 7, rows *c*): CE = $7,833/QALY.
- Assume screening to determine sexual activity is more frequent, carried out once every 3 years rather than once every 4 years (Table 7, rows *c*): CE = $14,322/QALY.

- Assume the average number of individuals attending each behavioural counselling intervention is increased from 5 to 10 (Table 7, rows *l*): CE = $8,736/QALY.
- Assume the average number of individuals attending each behavioural counselling intervention is reduced from 5 to 1 (Table 7, rows *l*): CE = $22,513/QALY.
- Assume the average direct cost per HIV infection is reduced from $289,543 to $218,037 (Table 7, rows *y*): CE = $10,524/QALY.
- Assume the average direct cost per HIV infection is increased from $289,543 to $361,049 (Table 7, rows *y*): CE = $10,010/QALY.
- Assume the average direct cost per HPV infection is reduced from $112 to $57 (Table 7, rows *cc*): CE = $10,625/QALY.
- Assume the average direct cost per HPV infection is increased from $112 to $194 (Table 7, rows *cc*): CE = $9,732/QALY.

Summary

Applying a 1.5% discount rate, the clinically preventable burden (CPB) associated with behavioural counselling interventions for the prevention of sexually transmitted diseases is estimated to be 2,394 quality-adjusted life years (QALYs) while the cost-effectiveness (CE) is estimated to be $10,267 per QALY (see Table 8).

Table 8: Behavioural Counselling Interventions for the Prevention of Sexually Transmitted Infections in a Birth Cohort of 40,000

Summary

	Base Case	Range	
CPB (Potential QALYs Gained)			
Gap between 0% and Best in the World (29%)			
1.5% Discount Rate	**2,394**	1,243	3,278
3% Discount Rate	1,790	929	2,451
0% Discount Rate	3,285	1,706	4,498
CE ($/QALY) **including** patient time costs			
1.5% Discount Rate	**$10,267**	$6,921	$22,513
3% Discount Rate	$10,267	$6,921	$22,513
0% Discount Rate	$10,267	$6,921	$22,513
CE ($/QALY) **excluding** patient time costs			
1.5% Discount Rate	$3,494	$1,974	$15,740
3% Discount Rate	$3,494	$1,974	$15,740
0% Discount Rate	$3,494	$1,974	$15,740

United States Preventive Services Task Force Recommendations (2009)

> *Tobacco use, cigarette smoking in particular, is the leading preventable cause of death in the United States. Tobacco use results in more than 400 000 deaths annually from cardiovascular disease, respiratory disease, and cancer. Smoking during pregnancy results in the deaths of about 1000 infants annually and is associated with an increased risk for premature birth and intrauterine growth retardation. Environmental tobacco smoke contributes to death in an estimated 38 000 people annually.*
>
> *The USPSTF strongly recommends that clinicians screen all adults for tobacco use and provide tobacco cessation interventions for those who use tobacco products. (A Recommendation).*
>
> *The USPSTF strongly recommends that clinicians screen all pregnant women for tobacco use and provide augmented pregnancy-tailored counselling to those who smoke. (A Recommendation)*[776]

Canadian Task Force on Preventive Health Care Recommendations (1994)

> *A large body of evidence has accumulated regarding the health effects of smoking. Tobacco use has been consistently linked with a variety of serious pulmonary, cardiovascular and neoplastic diseases. Evaluation of this evidence is beyond the scope of this chapter but detailed reviews and estimates of relative risk for the many tobacco associated diseases have been published elsewhere. Likewise, reviews of the evidence regarding the health consequences of ETS are published elsewhere. In 1992 the U.S. Environmental Protection Agency (EPA) named ETS a Group A carcinogen (shown to cause cancer in humans) at typical environmental levels.*
>
> *There is good evidence to support counselling for smoking cessation in the periodic health examination of individuals who smoke (A Recommendation). Nicotine replacement therapy can be effective as an adjunct (A Recommendation).*
>
> *There is fair evidence to support physicians also referring patients to other programs after offering cessation advice (B Recommendation).*
>
> *There is insufficient evidence to evaluate counselling to reduce ETS exposure (C Recommendation) but it may be useful to combine such counselling with cessation advice, again based on the burden of suffering, the potential benefits of the intervention and the effectiveness of cessation advice.*[777]

Modelling the Clinically Preventable Burden

In this section, we will calculate the CPB associated with behavioural counselling and interventions for the prevention of tobacco use in a British Columbia birth cohort of 40,000.

In estimating CPB, we made the following assumptions:

- The proportion of the BC population that are light smokers (less than 10 cigarettes per day), moderate smokers (10-19 cigarettes per day) and heavy smokers (20 or

[776] U.S. Preventive Services Task Force. Counselling and interventions to prevent tobacco use and tobacco-caused disease in adults and pregnant women: U.S. Preventive Services Task Force reaffirmation recommendation statement. *Annals of Internal Medicine*. 2009; 150(8): 551-5.

[777] Taylor MC and Dingle JL. *Canadian Guide to Clinical Preventive Health Care: Chapter 43: Prevention of Tobacco-Caused Disease*. 1994. Health Canada. Available at http://www.phac-aspc.gc.ca/publicat/clinic-clinique/pdf/s6c43e.pdf. Accessed July 2008.

more cigarettes per day) by age group is based on 2014 CCHS data.[778] No data is available for ages 80+ so we assumed a 50% decline in smoking rate between the ages of 79 and 84 and further 50% decline between the ages of 85 and 89. Between the ages of 18 and 89, the proportion of life years lived with light smoking is 8.0% (200,747 of 2,524,990 life years), moderate smoking is 3.9% (98,886 of 2,524,990 life years) and heavy smoking is 2.4% (59,461 of 2,524,990 life years) (see Table 1).

Table 1: Years of Life Lived and Current Smoking Between the Ages of 18 and 89
in a British Columbia Birth Cohort of 40,000

Age Group	*Mean Survival Rate*	*Individuals in Birth Cohort*	*% of BC Population Current Smokers*			*BC Population Current Smokers*				*Life Years Lived*	*Years Lived as Current Smokers*		
			Light	Mod	Heavy	Light	Mod	Heavy	Total		Light	Mod	Heavy
18-19	0.994	39,744	10.3%	0.4%	0.4%	4,092	143	143	4,378	79,488	8,183	286	287
20-24	0.992	39,682	20.5%	1.9%	0.4%	8,131	767	176	9,074	198,408	40,654	3,835	879
25-29	0.989	39,570	14.9%	5.2%	2.3%	5,905	2,074	907	8,885	197,850	29,523	10,368	4,533
30-34	0.986	39,458	16.6%	5.2%	1.3%	6,552	2,048	518	9,118	197,290	32,759	10,242	2,589
35-39	0.983	39,310	8.9%	6.7%	1.2%	3,513	2,645	489	6,647	196,550	17,566	13,224	2,444
40-44	0.978	39,105	6.8%	5.0%	3.5%	2,672	1,939	1,385	5,996	195,526	13,360	9,693	6,927
45-49	0.970	38,814	4.4%	2.9%	3.2%	1,726	1,119	1,247	4,092	194,070	8,632	5,593	6,235
50-54	0.960	38,390	7.6%	4.1%	4.6%	2,918	1,560	1,766	6,244	191,948	14,590	7,799	8,832
55-59	0.944	37,757	3.9%	7.9%	4.3%	1,468	2,987	1,635	6,089	188,786	7,341	14,933	8,173
60-64	0.920	36,800	3.9%	4.7%	3.5%	1,427	1,746	1,289	4,462	183,998	7,137	8,728	6,446
65-69	0.883	35,332	4.7%	3.5%	3.0%	1,654	1,235	1,061	3,950	176,658	8,269	6,176	5,304
70-74	0.827	33,072	3.7%	3.6%	2.1%	1,208	1,207	701	3,116	165,362	6,038	6,033	3,507
75-79	0.741	29,628	2.9%	0.9%	1.4%	857	253	423	1,532	148,142	4,283	1,264	2,115
80-84	0.614	24,551	1.4%	0.4%	0.7%	355	105	175	635	122,756	1,775	524	876
85-89	0.441	17,632	0.7%	0.2%	0.4%	127	38	63	228	88,158	637	188	315
Total			**8.0%**	**3.9%**	**2.4%**					**2,524,990**	**200,747**	**98,886**	**59,461**

- A significant proportion of smokers quit on their own.[779] According to the *Treating Tobacco Use and Dependence: 2008 Update* document, individuals who quit on their own have a success (abstinence rate) of 10.9%. This increases to 28.0% (95% CI of 23.0% - 33.6%) with 2-3 brief counselling interventions with a primary care provider and the use of medications.[780] We used the rate of 10.9% to populate row *w* in Table 2 and the 28.0% to populate row *x*.
- Other assumptions used in assessing the clinically preventable burden are detailed in the Reference Document.

Based on these assumptions, the CPB associated with behavioural counselling and interventions for the prevention of tobacco use is 5,944 QALYs (Table 2, row *ac*). The CPB of 5,944 represents the gap between no coverage and the 'best in the world' coverage estimated at 51%.

[778] This analysis is based on the Statistics Canada's Canadian Community Health 2014 Public Use Microdata File. All computations, use and interpretation of these data are entirely that of H. Krueger & Associates Inc.
[779] Smith A and Chapman S. Quitting smoking unassisted: the 50-year research neglect of a major public health phenomenon. *Journal of the American Medical Association*. 2014; 311(2): 137-8.
[780] Fiore M, Jaen C, Baker T et al. *Clinical Practice Guideline. Treating Tobacco Use and Dependence: 2008 Update*. 2008. U.S. Department of Health and Human Services. Available at http://www.ahrq.gov/professionals/clinicians-providers/guidelines-recommendations/tobacco/clinicians/treating_tobacco_use08.pdf. Accessed January 2014.

Table 2: CPB of Behavioural Counselling and Interventions to Prevent Tobacco Use in a BC Birth Cohort of 40,000			
Label	**Variable**	**Base Case**	**Data Source**
	Estimated current status		
a	# of life years lived between the ages of 18-89 in birth cohort	2,524,990	Table 1
b	% of life years at light smoking (<10 cigarettes / day)	8.0%	Table 1
c	# of life years at light smoking	200,747	= (a * b)
d	% of life years at moderate smoking (10-19 cigarettes / day)	3.9%	Table 1
e	# of life years at moderate smoking	98,886	= (a * d)
f	% of life years at heavy smoking (≥20 cigarettes / day)	2.4%	Table 1
g	# of life years at heavy smoking	59,461	= (a * f)
	Life years lost due to Smoking		
h	% of life years lost due to light smoking	10.2%	Ref Doc
i	# of life years lost due to light smoking	20,478	= (c * h)
j	% of life years lost due to moderate smoking	18.4%	Ref Doc
k	# of life years lost due to moderate smoking	18,188	= (e * j)
l	% of life years lost due to heavy smoking	28.0%	Ref Doc
m	# of life years lost due to heavy smoking	16,634	= (g * l)
n	Life years lost due to smoking	**55,300**	= i + k + m
	QALYs lost due to Smoking		
o	% of QoL lost due to light smoking	3.7%	Ref Doc
p	# of QALYs lost due to light smoking	6,590	= (c - i) * o
q	% of QoL lost due to moderate smoking	3.9%	Ref Doc
r	# of QALYs lost due to moderate smoking	3,140	= (e - k) * q
s	% of QoL lost due to heavy smoking	7.3%	Ref Doc
t	# of QALYs lost due to heavy smoking	3,131	= (g - m) * s
u	QALYs lost due to smoking	**12,862**	= p + r + t
v	**Total QALYs lost due to smoking**	**68,162**	= n + u
	Benefits **if 51% of smokers received counselling and an intervention**		
w	Quit rate without intervention	10.9%	V
x	Quit rate with intervention	28.0%	V
y	QALYs gained without intervention	7,430	= v * w
z	QALYs gained with intervention with 100% adherence	19,085	= v * x
aa	Net QALYs gained with 100% adherence	11,656	= z - y
ab	Estimated adherence with screening and intervention	51%	Ref Doc
ac	**Potential QALYs gained, Screening & Intervention from 0% to 51%**	**5,944**	= aa * ab

V = Estimates from the literature

We also modified a number of major assumptions and recalculated the CPB as follows:

- Assume the disutility of light smoking is reduced from 3.7% to 2.1% (Table 2, row *o*), the disutility of moderate smoking is reduced from 3.9% to 2.2% (Table 2, row *q*) and the disutility of heavy smoking is reduced from 7.3% to 5.0% (Table 2, row *s*): CPB = 5,499 QALYs.
- Assume the disutility of light smoking is increased from 3.7% to 5.3% (Table 2, row *o*), the disutility of moderate smoking is increased from 3.9% to 5.5% (Table 2, row *q*) and the disutility of heavy smoking is increased from 7.3% to 9.7% (Table 2, row *s*): CPB = 6,408 QALYs.
- Assume that the quit rate with intervention (2-3 sessions + medication) is reduced from 28.0% to 23.0% (Table 2, row *x*): CPB = 4,206 QALYs.
- Assume that the quit rate with intervention (2-3 sessions + medication) is increased from 28.0% to 33.6% (Table 2, row *x*): CPB = 7,891 QALYs.

Modelling Cost-Effectiveness

In this section, we will calculate the CE associated with behavioural counselling and interventions for the prevention of tobacco use in a British Columbia birth cohort of 40,000.

In estimating CE, we made the following assumptions:

- For modelling purposes, we assumed that of the smokers who would successfully quit as a result of the intervention, 50% would quit at age 30, 25% at age 40 and 25% at age 50.
- **Average cost of smoking cessation aids per quit attempt** – in 2011, BC PharmaCare estimated the costs for pharmacological aids to smoking cessation based on a 12 week supply including mark-up and dispensing fees.[781] Varenicline (Champix®) was estimated to cost $336, buproprion (Zyban®) $209, nicotine patch $273 and nicotine gum $122-$289. In deriving the average cost we assumed that 57% of all smokers would use either varenicline or buproprion and 43% of all smokers would use either the nicotine patch or nicotine gum. The mid-point for the cost estimate of nicotine gum was used. Based on these assumptions, the average cost of smoking cessation aids per quit attempt in BC was $257.87 (in 2011 CAD) or $272.41 (in 2017 CAD).
- **Portion of counselled who use a smoking cessation aid** – Because the effectiveness of the intervention is based on 2-3 brief counselling sessions and the use of medication, we have assumed the 100% of those counselled would use a smoking cessation aid.
- In estimating the costs avoided due to the intervention, we assumed annual costs avoided of $785 per light smoker, $1,386 per moderate smoker and $2,050 per heavy smoker (see Reference Document). These costs avoided, however, are not fully realized until 20 years following smoking cessation.[782,783] This gradual increase in costs avoided was incorporated into the model.
- The later in life smoking cessation occurs, the fewer the benefits. Based on data provided by Jha and colleagues,[784] we have assumed that 91.3% of potential benefits would occur if smoking cessation occurred at age 30, 82.6% at age 40 and 56.5% at age 50.
- Other costs and assumptions used in assessing cost-effectiveness are detailed in the Reference Document.
- Discount rate of 1.5%, varied from 0% to 3% in the sensitivity analysis.

Based on these assumptions, the CE associated with behavioural counselling and interventions for the prevention of tobacco use is -$1,863 / QALY (Table 3, row *y*).

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[781] BC Ministry of Health. *Effective Pharmacological Aids to Smoking Cessation*. 2011. Available at http://www.health.gov.bc.ca/pharmacare/pdf/sc-prod-info.pdf. Accessed January 2014.

[782] Kenfield S, Stampfer M, Rosner B, Colditz GA. Smoking and smoking cessation in relation to mortality in women. Journal of the American Medical Association. 2008; 299(17): 2037-47.

[783] Krueger H, Turner D, Krueger J, Ready E. The economic benefits of risk factor reduction in Canada: Tobacco smoking, excess weight and physical inactivity. *Canadian Journal of Public Health*. 2014; 105(1): e69-e78.

[784] Jha P, Ramasundarahettige C, Landsman V et al. 21st-century hazards of smoking and benefits of cessation in the United States. *New England Journal of Medicine*. 2013; 368(4): 341-50.

Table 3: CE of Behavioural Counselling and Interventions to Prevent Tobacco Use in a BC Birth Cohort of 40,000			
Row Label	**Variable**	**Base Case**	**Data Source**
a	# of life years lived between the ages of 18-89 in birth cohort	2,524,990	Table 1
b	# of life years lived as smokers between the ages of 18-89 in birth cohort	359,095	Table 2, row c + Table 2, row e + Table 2, row g
	Estimated cost of screening		
c	Number of annual screens to assess willingness to quit	359,095	= b
d	Proportion of office visit required	50%	See Ref Doc
e	Cost of 10-minute office visit	$34.85	See Ref Doc
f	Patient time costs / office visit	$59.38	See Ref Doc
g	Estimated cost of screening	$16,918,757	= (e + f) * d * c
	Estimated cost of intervention		
h	Average # of smokers in birth cohort ages 20-29	8,979	Table 1
i	Estimated adherence with screening and intervention	51%	Table 2, row ab
j	# of brief counselling interventions	3	√
k	Cost of smoking cessation aids	$272.41	√
l	Estimated cost of intervention	$5,037,004	= ((h*i)*j)*(e+f+k)
m	Average # of smokers in birth cohort ages 30-39	7,882	Table 1
n	Estimated cost of intervention	$4,421,696	= ((m*i)*j)*(e+f+k)
o	Average # of smokers in birth cohort ages 40-49	5,044	Table 1
p	Estimated cost of intervention	$2,829,413	= ((o*i)*j)*(e+f+k)
q	**Total cost of interventions**	**$12,288,114**	= l + n + p
r	**Estimated costs avoided due to intervention**	**$49,085,691**	Calculated
	CE Calculation		
s	Cost of intervention over lifetime of birth cohort	$29,206,871	= g + q
t	Costs avoided due to intervention over lifetime of birth cohort	$49,085,691	= r
u	QALYs saved	5,944	Table 2, row ac
v	Cost of intervention over lifetime of birth cohort (1.5% discount)	$21,019,352	Calculated
w	Costs avoided due to intervention over lifetime of birth cohort (1.5% discount)	$27,143,609	Calculated
x	QALYs saved (1.5% discount)	3,287	Calculated
y	**CE ($/QALY saved)**	**-$1,863**	= (v - w) / x

√ = Estimates from the literature

We also modified a number of major assumptions and recalculated the cost per QALY as follows:

- Assume the disutility of light smoking is reduced from 3.7% to 2.1% (Table 2, row *o*), the disutility of moderate smoking is reduced from 3.9% to 2.2% (Table 2, row *q*) and the disutility of heavy smoking is reduced from 7.3% to 5.0% (Table 2, row *s*): CE = -$2,014.
- Assume the disutility of light smoking is increased from 3.7% to 5.3% (Table 2, row *o*), the disutility of moderate smoking is increased from 3.9% to 5.5% (Table 2, row *q*) and the disutility of heavy smoking is increased from 7.3% to 9.7% (Table 2, row *s*): CE = -$1,728.
- Assume that the quit rate with intervention (2-3 sessions + medication) is reduced from 28.0% to 23.0% (Table 2, row *x*): CE = $779
- Assume that the quit rate with intervention (2-3 sessions + medication) is increase from 28.0% to 33.6% (Table 2, row *x*): CE = -$3,441.
- Assume the proportion of an office visit required for screening is reduced from 50% to 33% (Table 3, row *d*): CE = -$3,122.
- Assume the proportion of an office visit required for screening is increased from 50% to 67% (Table 3, row *d*): CE = -$604.

Summary

Applying a 1.5% discount rate, the clinically preventable burden (CPB) associated with behavioural counselling and interventions for the prevention of tobacco use is estimated to be 3,287 quality-adjusted life years (QALYs) while the cost-effectiveness (CE) is estimated to result in cost savings of $1,863 per QALY (see Table 4).

Table 4: Behavioural Counselling and Interventions to Prevent Tobacco Use in a BC Birth Cohort of 40,000

Summary

	Base Case	Range	
CPB (Potential QALYs Gained)			
Gap between No Service and 'Best in the World' (51%)			
1.5% Discount Rate	**3,287**	2,326	4,364
3% Discount Rate	1,833	1,297	2,433
0% Discount Rate	5,944	4,206	7,891
Gap between BC Current (19%) and 'Best in the World' (51%)			
1.5% Discount Rate	1,225	867	1,626
3% Discount Rate	683	483	906
0% Discount Rate	2,214	1,567	2,940
CE ($/QALY) **including** patient time costs			
1.5% Discount Rate	**-$1,863**	-$3,441	$779
3% Discount Rate	-$226	-$1,867	$3,731
0% Discount Rate	-$3,344	-$4,556	-$1,314
CE ($/QALY) **excluding** patient time costs			
1.5% Discount Rate	-$4,633	-$5,527	-$3,135
3% Discount Rate	-$3,449	-$4,635	-$1,462
0% Discount Rate	-$5,472	-$6,160	-$4,322

Alcohol Misuse Screening and Brief Intervention

United States Preventive Services Task Force Recommendations (2013)

The USPSTF uses the term "alcohol misuse" to define a spectrum of behaviors, including risky or hazardous alcohol use (for example, harmful alcohol use and alcohol abuse or dependence). Risky or hazardous alcohol use means drinking more than the recommended daily, weekly, or per-occasion amounts resulting in increased risk for health consequences. For example, the National Institute on Alcohol Abuse and Alcoholism (NIAAA) and the U.S. Department of Agriculture define "risky use" as consuming more than 4 drinks on any day or 14 drinks per week for men, or more than 3 drinks on any day or 7 drinks per week for women (as well as any level of consumption under certain circumstances). "Harmful alcohol use" (defined by the International Statistical Classification of Diseases and Related Health Problems, Tenth Revision) is a pattern of drinking that causes damage to physical or mental health.

"Alcohol abuse" (defined by the Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition) is drinking that leads an individual to recurrently fail in major home, work, or school responsibilities; use alcohol in physically hazardous situations (such as while operating heavy machinery); or have alcohol-related legal or social problems. "Alcohol dependence" (or alcoholism) (defined by the Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition) includes physical cravings and withdrawal symptoms, frequent consumption of alcohol in larger amounts than intended over longer periods, and a need for markedly increased amounts of alcohol to achieve intoxication.

An estimated 30% of the U.S. population is affected by alcohol misuse, and most of these persons engage in risky use. More than 85 000 deaths per year are attributable to alcohol misuse; it is the estimated third leading cause of preventable deaths in the United States.

The U.S. Preventive Services Task Force recommends screening and behavioral counselling interventions to reduce alcohol misuse by adults, including pregnant women, in primary care settings (B Recommendation).

The USPSTF concludes that the evidence is insufficient to recommend for or against screening and behavioral counselling interventions to prevent or reduce alcohol misuse by adolescents in primary care settings (I Statement).[785]

Canadian Task Force on Preventive Health Care Recommendations (1994)

In 1989 the Canadian Task Force on the Periodic Health Examination concluded that there was fair evidence that routine case-finding for problem drinking, and that brief counselling intervention in patients identified thereby was effective in reducing alcohol consumption and related consequences. The studies which yielded this evidence have since been confirmed by seven new randomized controlled trials in study populations that included both men and women aged 18-60 years. Standardized interviewing strategies and questionnaires are more sensitive than clinical judgement and can be used routinely with all adults to raise the index of clinical suspicion of problem drinking. When problem drinkers are identified, either simple advice or brief counselling is effective in reducing alcohol consumption and diminishing the negative consequences of drinking. The intervention of simple advice or brief counselling is appropriate for the patient with mild to moderate as opposed to severe alcohol

[785] Moyer VA. Screening and behavioral counselling interventions in primary care to reduce alcohol misuse: U.S. preventive services task force recommendation statement. *Annals of Internal Medicine*. 2013; 159(3): 210-8.

dependency. Problem drinking or mild to moderate, rather than severe dependency is the focus of this report.

Routine active case-finding of problem drinking by physicians is highly recommended on the basis of the high prevalence of this problem in medical practices, its association with adverse consequences before the stage of dependency is reached, and its amenability to a counselling intervention by physicians. Detection by biomarkers is not recommended, although these may be used to confirm clinical suspicions raised by use of the CAGE query, MAST or AUDIT questionnaires, and may be useful for monitoring the patient's progress. Either simple advice or the brief counselling intervention may be used with equal effectiveness in reducing alcohol consumption in problem drinkers. The counselling intervention is probably most effective in the context of an established and effective doctor-patient relationship.[786]

Modelling the Clinically Preventable Burden

In this section, we will calculate the CPB associated with behavioural counselling and interventions for the prevention of alcohol misuse in a British Columbia birth cohort of 40,000.

In estimating CPB, we made the following assumptions:

- The proportion of the BC population with low alcohol use (less than 1.5 drinks a day for females and 3 drinks a day for males), hazardous alcohol use (1.5 to 3 drinks a day for females and 3 to 4.5 drinks per day for males) and harmful alcohol use (more than 3 drinks a day for females and 4.5 drinks a day for males) by age group is based on 2014 CCHS data.[787] Alcohol consumption rates are adjusted for underreporting.[788,789,790] Individuals who consume alcohol are grouped into these three categories based on their weekly consumption patterns.
- A significant proportion of individuals with low alcohol consumption levels consume their alcohol via binge drinking. A female binge drinker is defined as a female who consumes at least *four* drinks (containing 13.6g of ethanol) on one occasion at least once per month during the past 12 months. A male binge drinker is defined as a male who consumes at least *five* drinks on one occasion at least once per month during the past 12 months.
- For modelling purposes, alcohol misuse is defined as any individuals with hazardous or harmful alcohol consumption levels *and* binge drinkers within the low consumption category.
- In a BC birth cohort of 40,000, an estimated 39.1% of life years lived (between the ages of 18 and 79 (905,864 of 2,314,076) are lived with alcohol misuse (see Table 1).

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[786] Haggerty JL. *Canadian Guide to Clinical Preventive Health Care: Chapter 42: Early Detection and Counselling of Problem Drinking*. 1994. Health Canada. Available at http://www.phac-aspc.gc.ca/publicat/clinic-clinique/pdf/s6c42e.pdf. Accessed July 2008.

[787] This analysis is based on the Statistics Canada's Canadian Community Health 2014 Public Use Microdata File. All computations, use and interpretation of these data are entirely that of H. Krueger & Associates Inc.

[788] Boniface S, Kneale J and Shelton N. Actual and perceived units of alcohol in a self-defined "usual glass" of alcoholic drinks in England. *Alcoholism: Clinical and Experimental Research*. 2013; 37(6): 978-83.

[789] Kerr WC and Stockwell T. Understanding standard drinks and drinking guidelines. *Drug and Alcohol Review*. 2012; 31(2): 200-5.

[790] White AM, Kraus CL, Flom JD et al. College students lack knowledge of standard drink volumes: implications for definitions of risky drinking based on survey data. *Alcoholism: Clinical and Experimental Research*. 2005; 29(4): 631-8.

Table 1: Years of Life Lived and Current Alcohol Use Between the Ages of 18 and 79
in a British Columbia Birth Cohort of 40,000

Age Group	Mean Survival Rate	Individuals in Birth Cohort	% of BC Population Current Drinkers			BC Population Current Drinkers					Years Lived as Current Drinkers				
			Low	Hazardous	Harmful	Low	Low-Non-Binge	Low-Binge	Hazardous	Harmful	Life Years Lived	Low-Non-Binge	Low-Binge	Hazardous	Harmful
18-19	0.994	39,744	49.2%	5.5%	5.4%	19,555	9,247	10,308	2,192	2,127	79,488	18,494	20,615	4,385	4,254
20-24	0.992	39,682	49.2%	5.5%	5.3%	19,523	9,232	10,291	2,188	2,123	198,408	46,160	51,455	10,940	10,613
25-29	0.989	39,570	49.1%	5.4%	5.2%	19,442	9,194	10,248	2,153	2,069	197,850	45,968	51,240	10,765	10,347
30-34	0.986	39,458	57.5%	6.0%	5.0%	22,693	10,731	11,962	2,383	1,966	197,290	53,655	59,809	11,916	9,831
35-39	0.983	39,310	57.5%	6.0%	5.0%	22,616	10,695	11,921	2,377	1,964	196,550	53,473	59,607	11,886	9,820
40-44	0.978	39,105	57.5%	6.0%	5.0%	22,491	10,635	11,855	2,362	1,949	195,526	53,177	59,276	11,810	9,745
45-49	0.970	38,814	57.1%	6.8%	4.6%	22,147	10,473	11,674	2,652	1,777	194,070	52,365	58,372	13,262	8,885
50-54	0.960	38,390	57.1%	6.8%	4.6%	21,904	10,358	11,546	2,623	1,757	191,948	51,791	57,731	13,116	8,785
55-59	0.944	37,757	57.1%	6.8%	4.6%	21,545	10,188	11,357	2,580	1,729	188,786	50,941	56,784	12,901	8,644
60-64	0.920	36,800	54.0%	7.4%	3.5%	19,886	9,404	10,483	2,706	1,293	183,998	47,019	52,413	13,529	6,465
65-69	0.883	35,332	54.0%	7.4%	3.5%	19,092	9,028	10,064	2,598	1,239	176,658	45,142	50,320	12,992	6,197
70-74	0.827	33,072	43.1%	8.3%	3.1%	14,262	6,744	7,518	2,751	1,040	165,362	33,722	37,590	13,757	5,199
75-79	0.741	29,628	43.0%	8.4%	3.1%	12,742	6,025	6,717	2,481	924	148,142	30,127	33,583	12,403	4,622
Total			**53.2%**	**6.6%**	**4.5%**						**2,314,076**	**582,035**	**648,794**	**153,663**	**103,407**
													28.0%	**6.6%**	**4.5%**

- Alcohol misuse results in life years lost due to both chronic and acute (binge drinking) conditions. Solberg and colleagues estimated that life years lost due to acute conditions are 2.14 times that of chronic conditions.[791] That is, for every death due to chronic alcohol conditions, there would be 2.14 deaths due to acute alcohol conditions (Table 2, row *j*).
- The meta-analysis for the USPSTF found an improvement of 10.9% (95% CI of 8.3% to 13.4%) in the proportion of adults achieving recommended drinking limits associated with brief counselling interventions (Table 2, row *s*).[792]
- Other costs and assumptions used in assessing CPB are detailed in the Reference Document.

Based on these assumptions, the CPB associated with behavioural counselling for the prevention of alcohol misuse is 2,175 QALYs (Table 2, row *v*). The CPB of 2,175 represents the gap between no coverage and the 'best in the world' coverage estimated at 30%.

[791] Solberg M, Maciosek M, Edwards N. Primary care interventions to reduce alcohol misuse: Ranking its health impact and cost-effectiveness. *American Journal of Preventive Medicine*. 2008; 34(2): 143-152.
[792] Jonas DE, Garbutt JC, Amick HR et al. Behavioral counselling after screening for alcohol misuse in primary care: a systematic review and meta-analysis for the U.S. Preventive Services Task Force. *Annals of Internal Medicine*. 2012; 157(9): 645-54.

Table 2: CPB of Behavioural Counselling to Prevent Alcohol Misuse in a BC Birth Cohort of 40,000			
Label	**Variable**	**Base Case**	**Data Source**
	Estimated current status		
a	# of life years lived between the ages of 18 -79 in birth cohort	2,314,076	Table 1
b	% of life years at low alcohol use - binge	28.0%	Table 1
c	# of life years at low alcohol use - binge	648,794	= (a * b)
d	% of life years at hazardous alcohol use	6.6%	Table 1
e	# of life years at hazardous alcohol use	153,663	= (a * d)
f	% of life years at harmful alcohol use	4.5%	Table 1
g	# of life years at harmful alcohol use	103,407	= (a * f)
	Life years lost due to Alcohol Misuse		
h	% of life years lost due to harmful alcohol use	4.8%	Ref Doc
i	# of life years lost due to chronic harmful alcohol use	4,955	= (g * h)
j	Ratio of life years lost to acute vs. chronic alcohol misuse	2.14	√
k	# of life years lost due to acute alcohol misuse	10,605	= i * j
l	Life years lost due to alcohol misuse	**15,559**	= i + k
	QALYs lost due to Alcohol Misuse		
m	% of QoL lost due to hazardous alcohol use	14.5%	Ref Doc
n	# of QALYs lost due to hazardous alcohol use	22,288	= e * m
o	% of QoL lost due to harmful alcohol use	27.7%	Ref Doc
p	# of QALYs lost due to harmful alcohol use	28,656	= g * o
q	QALYs lost due to alcohol misuse	**50,945**	= n + p
r	**Total QALYs lost due to alcohol misuse**	**66,504**	= l + q
	***Benefits* if 30% of individuals who misuse alcohol received counselling**		
s	% of adults achieving recommended drinking levels with intervention	10.9%	√
t	QALYs gained with intervention with 100% adherence	7,249	= r * s
u	Estimated adherence with screening and intervention	30%	Ref Doc
v	**Potential QALYs gained, Screening & Intervention from 0% to 51%**	**2,175**	= t * u

√ = Estimates from the literature

We also modified several major assumptions and recalculated the CPB as follows:

- Assume that the QoL reduction associated with hazardous alcohol consumption is reduced from 14.5% to 9.7% and the QoL reduction associated with harmful alcohol consumption is reduced from 27.7% to 18.9% (Table 2, rows *m & o*): CPB = 1,633.
- Assume that the QoL reduction associated with hazardous alcohol consumption is increased from 14.5% to 20.9% and the QoL reduction associated with harmful alcohol consumption is reduced from 27.7% to 38.6% (Table 2, rows *m & o*): CPB = 2,861.
- Assume that the effectiveness of counselling at changing behaviour is reduced from 10.9% to 8.3% (Table 2, row *s*): CPB = 1,656.
- Assume that the effectiveness of counselling at changing behaviour is increased from 10.9% to 13.4% (Table 2, row *s*): CPB = 2,673.

Modelling Cost-Effectiveness

In this section, we will calculate the CE associated with behavioural counselling for the prevention of alcohol misuse in a British Columbia birth cohort of 40,000.

In estimating CE, we made the following assumptions:

- For modelling purposes, we assumed that 50% of the prevention of alcohol misuse due to the intervention would occur at age 30, 25% at age 40 and 25% at age 50.

- BC guidelines for alcohol screening and brief interventions recommend screening annually[793] while economic evaluations have assumed that screening would occur at least once a year to at least once every 10 years.[794,795,796] For modelling purposes we assumed screening would occur annually in the base case and modified this to once every 5 years in the sensitivity analysis.
- The 2013 USPSTF review found no evidence to determine the optimal interval for screening but did note that brief multi-contact (each contact is 6 to 15 minutes) interventions are most effective, requiring up to 120 minutes of total counselling contact.[797] For modelling purposes we assumed 9 contacts of 10-minutes in the base case analysis (Table 3, row *j*) and modified this from 6 to 12 contacts of 10-minutes in the sensitivity analysis.
- Other costs and assumptions used in assessing cost-effectiveness are detailed in the Reference Document.
- Discount rate of 1.5%, varied from 0% to 3% in the sensitivity analysis.

Based on these assumptions, the CE associated with behavioural counselling for the prevention of alcohol misuse is $23,607 / QALY (Table 3, row *x*).

[793] BC Ministry of Health and British Columbia Medical Association. *BC Guidelines: Problem Drinking* 2013. Available at http://www2.gov.bc.ca/gov/content/health/practitioner-professional-resources/bc-guidelines/problem-drinking. Accessed August 2017.
[794] Purshouse R, Brennan A, Rafia R et al. Modelling the cost-effectiveness of alcohol screening and brief interventions in primary care in England. *Alcohol and Alcoholism*. 2012; 48(2): 180-8.
[795] Angus C, Scafato E, Ghirini S et al. Cost-effectiveness of a programme of screening and brief interventions for alcohol in primary care in Italy. *BioMed Central Family Practice*. 2014; 15(1): 1-26.
[796] Zur R and Zaric G. A microsimulation cost–utility analysis of alcohol screening and brief intervention to reduce heavy alcohol consumption in Canada. *Addiction*. 2016; 111(5): 817-31.
[797] Moyer VA. Screening and behavioral counselling interventions in primary care to reduce alcohol misuse: U.S. preventive services task force recommendation statement. *Annals of Internal Medicine*. 2013; 159(3): 210-8.

Table 3: CE of Behavioural Counselling to Prevent Alcohol Misuse in a BC Birth Cohort of 40,000			
Row Label	**Variable**	**Base Case**	**Data Source**
a	# of life years lived between the ages of 18-79 in birth cohort	2,314,076	Table 1
b	Screening rate	35%	Ref Doc
	Estimated cost of screening		
c	Number of annual screens to assess alcohol consumption habits	809,927	= a * b
d	Proportion of office visit required	50%	See Ref Doc
e	Cost of 10-minute office visit	$34.85	See Ref Doc
f	Patient time costs / office visit	$59.38	See Ref Doc
g	Estimated cost of screening	$38,159,692	= (e + f) * d * c
	Estimated cost of intervention		
h	# of drinkers who misuse alcohol at age 30	16,311	Table 1
i	Estimated adherence with intervention	30%	Table 2, row u
j	# of brief counselling interventions	9	v
k	Estimated cost of intervention	$4,149,934	= (h*i*j)*(e+f)
l	# of drinkers who misuse alcohol at age 40	16,166	Table 1
m	Estimated cost of intervention	$4,113,041	= (l*i*j)*(e+f)
n	# of drinkers who misuse alcohol at age 50	15,926	Table 1
o	Estimated cost of intervention	$4,052,034	= (o*i*j)*(e+f)
p	**Total cost of interventions**	**$12,315,009**	= l + n + p
q	**Estimated costs avoided due to intervention**	**$14,351,678**	Calculated
	CE Calculation		
r	Cost of intervention over lifetime of birth cohort	$50,474,700	= g + p
s	Costs avoided due to intervention over lifetime of birth cohort	$14,351,678	= q
t	QALYs saved	2,175	Table 2, row v
u	Cost of intervention over lifetime of birth cohort (1.5% discount)	$36,325,203	Calculated
v	Costs avoided due to intervention over lifetime of birth cohort (1.5% discount)	$7,936,250	Calculated
w	QALYs saved (1.5% discount)	1,203	Calculated
x	**CE ($/QALY saved)**	**$23,607**	= (u - v) / w

v = Estimates from the literature

We also modified several major assumptions and recalculated the CE as follows:

- Assume that the QoL reduction associated with hazardous alcohol consumption is decreased from 14.5% to 9.7% and the QoL reduction associated with harmful alcohol consumption is decreased from 27.7% to 18.9% (Table 2, rows *m & o*): CE = $31,444.
- Assume that the QoL reduction associated with hazardous alcohol consumption is increased from 14.5% to 20.9% and the QoL reduction associated with harmful alcohol consumption is increased from 27.7% to 38.6% (Table 2, rows *m & o*): CE = $17,941.
- Assume that the effectiveness of counselling at changing behaviour is reduced from 10.9% to 8.3% (Table 2, row *s*): CE = $33,069.
- Assume that the effectiveness of counselling at changing behaviour is increased from 10.9% to 13.4% (Table 2, row *s*): CE = $19,972.
- Assume that screening is carried out less frequently, once every five years rather than annually (Table 3, row *c*): CE = $5,338.
- Assume that the portion of an office visit used for screening is reduced from 50% to 33% (Table 3, row *d*): CE = $15,843.
- Assume that the portion of an office visit used for screening is increased from 50% to 67% (Table 3, row *d*): CE = $31,372.
- Assume that the number of brief counselling interventions is reduced from 9 to 6 (Table 3, row *j*): CE = $21,150.

- Assume that the number of brief counselling interventions is increased from 9 to 12 (Table 3, row *j*): CE = $26,064.

Summary

Applying a 1.5% discount rate, the clinically preventable burden (CPB) associated with behavioural counselling for the prevention of alcohol misuse is estimated to be 1,203 quality-adjusted life years (QALYs) while the cost-effectiveness (CE) is estimated to result in cost savings of $23,607 per QALY (see Table 4).

Table 4: Behavioural Counselling to Prevent Alcohol Misuse in a BC Birth Cohort of 40,000

Summary

	Base Case	Range	
CPB (Potential QALYs Gained)			
Gap between No Service and 'Best in the World' (30%)			
1.5% Discount Rate	**1,203**	903	1,582
3% Discount Rate	671	503	882
0% Discount Rate	2,175	1,633	2,861
CE ($/QALY) **including** patient time costs			
1.5% Discount Rate	**$23,607**	$5,338	$33,069
3% Discount Rate	$33,475	$9,237	$46,029
0% Discount Rate	$16,611	$2,573	$23,881
CE ($/QALY) **excluding** patient time costs			
1.5% Discount Rate	$4,572	-$2,185	$8,072
3% Discount Rate	$8,222	-$742	$12,864
0% Discount Rate	$1,985	-$3,207	$4,674

Screening for and Management of Obesity

Canadian Task Force on Preventive Health Care (2015)

We recommend measuring height and weight and calculating BMI at appropriate primary care visits. (Strong recommendation; very low-quality evidence)

We recommend that practitioners not offer formal, structured interventions aimed at preventing weight gain in normal-weight adults. (Weak recommendation; very low-quality evidence)

For adults who are obese (BMI 30–39.9) and are at high risk of diabetes, we recommend that practitioners offer or refer to structured behavioural interventions aimed at weight loss. (Strong recommendation; moderate-quality evidence)

For adults who are overweight or obese, we recommend that practitioners offer or refer to structured behavioural interventions aimed at weight loss. (Weak recommendation; moderate-quality evidence)

For adults who are overweight or obese, we recommend that practitioners not routinely offer pharmacologic interventions (orlistat or metformin) aimed at weight loss. (Weak recommendation; moderate-quality evidence)[798]

United States Preventive Services Task Force Recommendations (2012)

The USPSTF recommends screening all adults for obesity. Clinicians should offer or refer patients with a body mass index (BMI) of 30 kg/m^2 or higher to intensive, multicomponent behavioral interventions. This is a B recommendation.

Intensive, multicomponent behavioral interventions for obese adults include the following components:

- *Behavioral management activities, such as setting weight-loss goals*
- *Improving diet or nutrition and increasing physical activity*
- *Addressing barriers to change*
- *Self-monitoring*
- *Strategizing how to maintain lifestyle changes*

The USPSTF found that the most effective interventions were comprehensive and of high intensity (12 to 26 sessions in a year).

Behavioral intervention participants lost an average of 6% of their baseline weight (4 to 7 kg [8.8 to 15.4 lb]) in the first year with 12 to 26 treatment sessions compared with little or no weight loss in the control group participants. A weight loss of 5% is considered clinically important by the U.S. Food and Drug Administration (FDA).[799]

[798] Canadian Task Force on Preventive Health Care. Recommendations for prevention of weight gain and use of behavioural and pharmacologic interventions to manage overweight and obesity in adults in primary care. *Canadian Medical Association Journal*. 2015; 187(3): 184-95.

[799] Moyer VA. Screening for and management of obesity in adults: US Preventive Services Task Force recommendation statement. *Annals of Internal Medicine*. 2012; 157(5): 373-8.

Modelling the Clinically Preventable Burden

In this section, we will calculate the CPB associated with screening for and management of obesity in adults aged 18 or older in a British Columbia birth cohort of 40,000.

In modelling CPB, we made the following assumptions:

- Based on 2014 prevalence rates of obesity (based on self-reported height and weight) by age group and sex in BC,[800] a total of 344,743 life years lived between the ages of 18 and 79 in a birth cohort of 40,000 individuals are in the obese class I or II category (Tables 1 & 2, Table 3, row *a*).

Table 1: Prevalence of Excess Weight in a *Male* Birth Cohort of 20,000

Age Group	Mean Survival Rate	Individuals in Birth Cohort	Years of Life in Birth Cohort	Prevalence of Excess Weight				# of Years with Excess Weight			
				Overweight	Class I	Class II	Class III	Overweight	Class I	Class II	Class III
18-19	0.993	19,867	39,733	19.3%	4.8%	0.3%	0.2%	7,653	1,903	118	61
20-24	0.991	19,813	99,065	31.2%	7.7%	0.7%	0.2%	30,913	7,629	660	211
25-29	0.987	19,734	98,672	36.6%	9.3%	2.4%	0.8%	36,082	9,191	2,372	746
30-34	0.983	19,658	98,289	42.7%	14.4%	4.6%	0.0%	41,927	14,137	4,493	0
35-39	0.978	19,560	97,798	27.8%	21.0%	3.6%	0.1%	27,234	20,573	3,500	118
40-44	0.971	19,427	97,134	37.4%	20.2%	3.5%	0.1%	36,284	19,656	3,396	56
45-49	0.962	19,241	96,203	45.4%	10.4%	5.5%	0.2%	43,678	9,991	5,304	195
50-54	0.949	18,971	94,855	37.1%	25.8%	1.3%	0.3%	35,186	24,473	1,232	290
55-59	0.929	18,570	92,852	47.3%	11.4%	2.0%	1.6%	43,958	10,565	1,855	1,476
60-64	0.898	17,967	89,835	41.2%	15.8%	3.1%	1.7%	36,989	14,225	2,822	1,567
65-69	0.853	17,052	85,261	44.9%	16.2%	4.2%	0.2%	38,256	13,818	3,565	158
70-74	0.783	15,668	78,342	47.7%	17.4%	3.6%	0.4%	37,342	13,633	2,802	308
75-79	0.681	13,616	68,078	34.3%	8.0%	3.0%	0.7%	23,374	5,439	2,072	478
Total Ages 18-79			**1,136,117**	**38.6%**	**14.5%**	**3.0%**	**0.5%**	**438,876**	**165,233**	**34,191**	**5,665**

Table 2: Prevalence of Excess Weight in a *Female* Birth Cohort of 20,000

Age Group	Mean Survival Rate	Individuals in Birth Cohort	Years of Life in Birth Cohort	Prevalence of Excess Weight				# of Years with Excess Weight			
				Overweight	Class I	Class II	Class III	Overweight	Class I	Class II	Class III
18-19	0.995	19,891	39,781	10.2%	3.5%	0.0%	0.0%	4,050	1,403	0	0
20-24	0.993	19,865	99,323	17.7%	3.5%	1.0%	0.0%	17,582	3,488	957	0
25-29	0.992	19,833	99,163	15.2%	4.0%	4.2%	0.2%	15,082	3,928	4,117	150
30-34	0.990	19,795	98,975	20.2%	5.7%	3.7%	1.9%	19,963	5,645	3,675	1,918
35-39	0.987	19,741	98,706	21.7%	11.0%	5.5%	2.0%	21,463	10,849	5,436	2,021
40-44	0.983	19,662	98,311	23.9%	10.7%	1.2%	4.0%	23,531	10,500	1,215	3,947
45-49	0.977	19,546	97,730	29.4%	6.2%	0.5%	0.9%	28,771	6,083	516	919
50-54	0.969	19,375	96,873	30.3%	15.4%	2.2%	1.3%	29,385	14,871	2,166	1,264
55-59	0.956	19,118	95,591	28.1%	8.2%	3.1%	2.1%	26,884	7,853	2,944	2,008
60-64	0.936	18,726	93,630	27.3%	14.4%	6.0%	3.0%	25,572	13,491	5,630	2,777
65-69	0.906	18,113	90,567	34.5%	11.6%	5.0%	1.2%	31,222	10,482	4,517	1,059
70-74	0.857	17,144	85,720	24.6%	9.4%	5.9%	1.9%	21,068	8,054	5,070	1,625
75-79	0.780	15,608	78,041	28.0%	14.3%	1.6%	0.9%	21,847	11,153	1,265	702
Total Ages 18-79			**1,172,411**	**24.4%**	**9.2%**	**3.2%**	**1.6%**	**286,419**	**107,802**	**37,508**	**18,390**

- Research for the USPSTF found that behavioral intervention participants lost an average of 6% or 3 kg (6.6 lb) of their baseline weight (95% CI of 4 to 7 kg [8.8 to 15.4 lb]) in the first year with 12 to 26 treatment sessions, compared with little or no

[800] Statistics Canada. *Canadian Community Health Survey Public Use Microdata File 2014*. All computations, use and interpretation of these data are entirely that of H. Krueger & Associates Inc.

weight loss in the control group participants.[801] Research for the CTFPHC found similar results with an average weight loss of 3.02 kg (95% CI of 2.52 to 3.52).[802] In addition, waist circumference was reduced by an average of 2.78 cm (95% CI of 2.22 to 3.34) and BMI was reduced by 1.11kg/m^2 (95% CI of 0.84 to 1.39). On average, one out of every five participants (95% CI of 4 to 7) lost at least 5% of their body weight (Table 3, row *c*) and one out of nine (95% CI of 7 to 12) lost more than 10% of their body weight. A weight loss of 5% is considered clinically important.

- Other assumptions used in assessing the clinically preventable burden are detailed in the Reference Document.

Based on these assumptions, the CPB associated with screening for and management of obesity is 2,287 QALYs (Table 3, row *i*).

Table 3: CPB of Screening for and Management of Obesity in Adults in a Birth Cohort of 40,000

Row Label	Variable	Base Case	Data Source
a	Years of life lived with Class I or II obesity	344,733	Tables 1 and 2
b	Adherence with an intensive, multicomponent behavioral intervention	33%	Ref Doc
c	Number needed to treat to achieve a clinically important reduction in weight (≥5% of body weight)	5	√
d	Reduced years of life lived with Class I or II obesity due to intervention	22,752	= (a * b) / c
	Benefits Associated with Screening and Management		
e	Reduction in quality of life - Class I / II obesity vs. overweight	6.96%	Ref Doc
f	QALYs gained	1,584	= d * e
g	Reduction in years of life lived - Class I / II obesity vs. overweight	3.09%	Ref Doc
h	QALYs gained	703	= d * g
i	**Potential QALYs gained, management increasing from 0% to 33%**	**2,287**	= f + h

√ = Estimates from the literature

We also modified a major assumption and recalculated the CPB as follows:

- Assume that one out of every four participants lost at least 5% of their body weight after completing an intensive, multicomponent behavioral intervention, rather than one out of every five participants (Table 3, row *c*): CPB = 2,858 QALYs.
- Assume that one out of every seven participants lost at least 5% of their body weight after completing an intensive, multicomponent behavioral intervention, rather than one out of every five participants (Table 3, row *c*): CPB = 1,633 QALYs.

Modelling Cost-Effectiveness

In this section, we will calculate the CE associated with screening for and management of obesity in adults aged 18 or older in a British Columbia birth cohort of 40,000.

In modelling CE, we made the following assumptions:

- **Frequency of screening** - We assumed that a general practitioner would measure a patient's height and weight in order to calculate BMI and discuss physical activity and healthy eating once every two years (Table 4, row *g*).

[801] LeBlanc ES, O'Connor E, Whitlock EP et al. Effectiveness of primary care–relevant treatments for obesity in adults: a systematic evidence review for the US Preventive Services Task Force. *Annals of Internal Medicine*. 2011; 155(7): 434-47.

[802] Peirson L, Douketis J, Ciliska D et al. Treatment for overweight and obesity in adult populations: a systematic review and meta-analysis. *Canadian Medical Association Open Access Journal*. 2014; 2(4): e306-e17.

- **Cost of an intensive, multicomponent behavioral intervention** - The per person costs of such interventions in the literature vary substantially, ranging from $269 to $3,267 (converted to 2017 CAD).[803,804,805,806] The difference in costs is largely attributable to the ratio of facilitators to clients. The intervention costing $3,267 per person involved case managers teaching a 16-week curriculum on a one-to-one basis.[807] The intervention costing $269 per person was set up for 16 group sessions of up to 18 persons.[808] We used the mean cost of three of the four interventions (excluding the $3,267 per person intervention) for an estimated cost of $607 per person per intervention (Table 4, row *m*).
- **Patient time costs for intensive, multicomponent behavioral intervention** - We assumed three hours of patient time would be required (including travel to and from the session) for an average of 18 sessions, the mid-point between 12 and 24 sessions (Table 4, rows *q*).
- Other costs and assumptions used in assessing cost-effectiveness are detailed in the Reference Document.
- Discount rate of 1.5%, varied from 0% to 3% in the sensitivity analysis.

Based on these assumptions, the CE associated with screening for and management of obesity is $12,160 per QALY (Table 4, row *ff*).

[803] Gustafson A, Khavjou O, Stearns SC et al. Cost-effectiveness of a behavioral weight loss intervention for low-income women: the Weight-Wise Program. *Preventive Medicine*. 2009; 49(5): 390-5.
[804] Krukowski RA, Tilford JM, Harvey-Berino J et al. Comparing behavioral weight loss modalities: incremental cost-effectiveness of an internet-based versus an in-person condition. *Obesity*. 2011; 19(8): 1629-35.
[805] Neumann A, Schwarz P and Lindholm L. Estimating the cost-effectiveness of lifestyle intervention programmes to prevent diabetes based on an example from Germany: Markov modelling. *Cost-effectiveness and Resource Allocation*. 2011; 9(1): 17.
[806] Group DPPR. Costs associated with the primary prevention of type 2 diabetes mellitus in the diabetes prevention program. *Diabetes Care*. 2003; 26(1): 36-47.
[807] Ibid.
[808] Gustafson A, Khavjou O, Stearns SC et al. Cost-effectiveness of a behavioral weight loss intervention for low-income women: the Weight-Wise Program. *Preventive Medicine*. 2009; 49(5): 390-5.

Table 4: CE of Screening for and Management of Obesity in Adults in a Birth Cohort of 40,000			
Row Label	**Variable**	**Base Case**	**Data Source**
a	Individuals in birth cohort at age 40	39,089	Tables 1 & 2
b	Total life years between age 18 and 70	1,998,347	Tables 1 & 2
c	Proportion of years with Class I / II obesity without intervention	14.9%	Tables 1 & 2
d	Years with Class I / II obesity without intervention	344,733	Tables 1 & 2
e	Adherence with screening in primary care	73%	Ref Doc
f	Adherence with an intensive, multicomponent behavioral intervention	33%	Ref Doc
	Costs of intervention		
g	Frequency of measuring height and weight and asking about physical activity and diet between age 18 and 70 (every x years)	2	Assumed
h	Total number of screens	729,397	= (b * e) / g
i	Cost of 10-minute office visit	$34.85	Ref Doc
j	Value of patient time and travel for office visit	$59.38	Ref Doc
k	Portion of 10-minute office visit for screen	50%	Ref Doc
l	Cost of screening	$34,365,530	= h * (I + j) * k
m	Costs per person of an intensive, multicomponent behavioral intervention	$607	√
n	Individuals eligible for an intensive, multicomponent behavioral intervention	5,837	= a * c
o	Individuals enrolled in an intensive, multicomponent behavioral intervention	1,926	= n * f
p	Costs of an intensive, multicomponent behavioral intervention	$1,169,244	= o * m
q	# of treatments per intensive, multicomponent behavioral intervention	18	√
r	Value of patient time and travel for per intervention treatment	$89.07	√
s	Value of patient time and travel for intervention	$3,088,306	= o * q * r
	Cost avoided		
t	Number needed to treat to achieve a clinically important reduction in weight (≥5% of body weight)	5	√
u	Individuals achieving a clinically important reduction in weight (≥5% of body weight)	385	= o / t
v	Years with Class I / II obesity avoided with intervention	22,752	= (u / n) * d
w	Excess direct costs per year attributable to obesity	$805	Ref Doc
x	Excess direct costs per year attributable to overweight	$227	Ref Doc
w	Costs avoided	$13,150,883	=(w - x) *v
	CE calculation		
z	Cost of intervention over lifetime of birth cohort	$38,623,081	= l + p + s
aa	Costs avoided	$13,150,883	= w
bb	QALYs saved	2,287	Table 3, row i
cc	Cost of intervention over lifetime of birth cohort (1.5% discount)	$26,777,542	Calculated
dd	Costs avoided (1.5% discount)	$9,117,562	Calculated
ee	QALYs saved (1.5% discount)	1,452	Calculated
ff	**CE ($/QALY saved)**	**$12,160**	= (cc-dd)/ee

√ = Estimates from the literature

We also modified several major assumptions and recalculated the cost per QALY as follows:

- Assume that one out of every four participants lost at least 5% of their body weight after completing an intensive, multicomponent behavioral intervention rather than one out of every five participants (Table 3, row *c*): CE = $8,472 per QALY.

- Assume that one out of every seven participants lost at least 5% of their body weight after completing an intensive, multicomponent behavioral intervention rather than one out of every five participants (Table 3, row *c*): CE = $19,535 per QALY.
- Assume that the frequency of measuring height and weight and asking about physical activity and diet would occur every year rather than once every two years (Table 4, row *g*): CE = $28,565 per QALY.
- Assume that the frequency of measuring height and weight and asking about physical activity and diet would occur every three years rather than once every two years (Table 4, row *g*): CE = $6,691 per QALY.
- Assume the proportion of an office visit required for screening/referral is reduced from 50% to 33% (Table 4, row *k)*: CE = $6,582 per QALY.
- Assume the proportion of an office visit required for screening/referral is increased from 50% to 67% (Table 4, row *k)*: CE = $17,738 per QALY.
- Assume that the costs per person of an intensive, multicomponent behavioral intervention are reduced from $607 to $269 (Table 4, row *m*): CE = $11,849 per QALY.
- Assume that the costs per person of an intensive, multicomponent behavioral intervention are increased from $607 to $3,267 (Table 4, row *m*): CE = $14,606 per QALY.

Summary

Applying a 1.5% discount rate, the clinically preventable burden (CPB) associated with screening for and management of obesity is estimated to be 1,452 quality-adjusted life years (QALYs) while the cost-effectiveness (CE) is estimated to result in cost savings of $12,160 per QALY (see Table 5).

Table 5: Screening for and Management of Obesity in Adults in a Birth Cohort of 40,000
Summary

	Base Case	Range	
CPB (Potential QALYs Gained)			
Gap between 0% and Best in the World (33%)			
1.5% Discount Rate	**1,452**	1,037	1,815
3% Discount Rate	959	685	1,199
0% Discount Rate	2,287	1,633	2,858
CE ($/QALY) **including** patient time costs			
1.5% Discount Rate	**$12,160**	$6,582	$28,565
3% Discount Rate	$13,219	$7,155	$31,053
0% Discount Rate	$11,140	$6,030	$26,169
CE ($/QALY) **excluding** patient time costs			
1.5% Discount Rate	$348	-$1,715	$6,415
3% Discount Rate	$378	-$1,865	$6,974
0% Discount Rate	$318	-$1,571	$5,877

United States Preventive Service Task Force Recommendations (2012)

> *Falls are the leading cause of injury in adults aged 65 years or older. Between 30% and 40% of community dwelling adults aged 65 years or older fall at least once per year.*
>
> *The USPSTF recommends exercise or physical therapy and vitamin D supplementation to prevent falls in community-dwelling adults aged 65 years or older who are at increased risk for falls. (Grade B recommendation)*
>
> *The USPSTF does not recommend automatically performing an in-depth multifactorial risk assessment in conjunction with comprehensive management of identified risks to prevent falls in community-dwelling adults aged 65 years or older because the likelihood of benefit is small. In determining whether this service is appropriate in individual cases, patients and clinicians should consider the balance of benefits and harms on the basis of the circumstances of prior falls, comorbid medical conditions, and patient values. (Grade C recommendation)*[809]

More specifically, the USPSTF suggests annual screening for risk using "a pragmatic, expert-supported approach to identifying high risk persons (based on) a history of falls and mobility problems and the results of a timed Get-Up-and-Go test. The test is performed by observing the time it takes a person to rise from an armchair, walk 3 meters (10 feet), turn, walk back, and sit down again." Exercise should consist of at least 150 minutes of moderate intensity activity per week while Vitamin D supplementation of 800 IU per day should occur for at least one year.[810]

Note that the 2003 recommendations from the CTFPHC apply only to individuals living in long-term care facilities, rather than the general population of community-dwelling elderly.[811]

Modelling the Clinically Preventable Burden

In this section, we will calculate the CPB associated with preventing falls in the community-dwelling elderly.

In estimating CPB, we made the following assumptions:

- We first estimated the number of life years lived in a BC cohort of 40,000 from age 65 to death as well as the average life expectancy for this cohort (see Table 1). The 765,288 life years lived was used to populate row *a* of Table 2 while the average life expectancy of 12.5 years was used to populate row *c* of Table 2.

[809] Moyer VA. Prevention of falls in community-dwelling older adults: U.S. Preventive Services Task Force recommendation statement. *Annals of Internal Medicine*. 2012; 157(3): 197-204.
[810] Ibid.
[811] Canadian Task Force on Preventive Health Care. *Prevention of Falls in Long-Term Care Facilities: Systematic Review and Recommendations* 2003. Available at http://canadiantaskforce.ca/wp-content/uploads/2012/09/CTF_FallsPrevn_TR_Jun03.pdf?0136ff. Accessed November 2013.

Table 1: Deaths and Years of Life Lived Between the Ages of 65 and Death
in a British Columbia Birth Cohort of 40,000

Age Group	*Mean Survival Rate*	*Individuals in Birth Cohort*	*Life Years Lived*	Life Expectancy
60-64	0.920	36,800		
65-69	0.883	35,332	176,658	19.2
70-74	0.827	33,072	165,362	15.3
75-79	0.741	29,628	148,142	11.8
80-84	0.614	24,551	122,756	8.7
85-89	0.441	17,632	88,158	6.1
90+	0.321	12,842	64,212	4.8
Total			**765,288**	**12.5**

- An estimated 94.3% of life years in this cohort are lived in the community (Table 1, row *b*).[812]
- Fall-related hospitalizations occur at a rate of 14.19 per 1,000 elderly in BC (Table 1, row *d*).[813]
- An estimated 30% of individuals die within one year after a fall-related hospitalization (Table 1, row *f*).[814]
- Individuals who survive a fall-related hospitalization have a 20% reduced life expectancy (Table 1, row *h*).[815]
- Individuals who survive a fall-related hospitalization have a .20 reduction in quality of life in year 1 following the hospitalization (Table 1, row *k*) and 0.06 reduction per year thereafter (Table 1, row *m*).[816]
- Interventions involving exercise or physical therapy in reducing falls in community-dwelling elderly have an effectiveness rate of 13% (RR of 0.87: 95% CI of 0.81 to 0.94) (Table 1, row *p*).[817]
- Current delivery of screening and counselling regarding exercise interventions is assumed to be 18% (Table 1, row *r*) (see Reference Document).
- Adherence with exercise intervention is assumed to be 30% (Table 1, row *s*).
- Other assumptions used in assessing the clinically preventable burden are detailed in the Reference Document.

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[812] BC Stats. *2006 Census Fast Facts: Living Arrangements of Seniors in British Columbia*. 2008. Available at http://www.bcstats.gov.bc.ca/Files/ac5baf3d-1490-437c-bc2c-7a6dfc7699f7/LivingArrangementofSeniorsinBritishColumbia.pdf. Accessed February 2018.

[813] Scott V, Wagar L and Elliot S. *Falls & Related Injuries Among Older Canadians: Fall Related Hospitalizations & Prevention Initiatives*. 2010. Available at http://www.hiphealth.ca/media/research_cemfia_phac_epi_and_inventor_20100610.pdf. Accessed February 2018.

[814] Ibid.

[815] Frick KD, Kung JY, Parrish JM et al. Evaluating the cost-effectiveness of fall prevention programs that reduce fall-related hip fractures in older adults. *Journal of the American Geriatrics Society*. 2010; 58(1): 136-41.

[816] Ibid.

[817] Michael YL, Whitlock EP, Lin JS et al. Primary care-relevant interventions to prevent falling in older adults: a systematic evidence review for the U.S. Preventive Services Task Force. *Annals of Internal Medicine*. 2010; 153(12): 815-25.

The role of vitamin D in fracture prevention is contentious.[818,819,820] The 2012 USPSTF review noted above, for example, has suggested that vitamin D supplementation reduced the risk of falling by 17% (RR of 0.83 [95% CI of 0.77 to 0.89]).[821] The Cochrane review, on the other hand, found no reduction in the risk of falling associated with vitamin D supplementation ((RR of 0.96 [95% CI of 0.89 to 1.03]) although the reviewers did acknowledge that vitamin D supplementation may lower this risk in "people with lower vitamin D levels before treatment."[822] Both groups agree, however, that group and home based exercise as well as home safety interventions reduce the rate of falls and the risk of falls.

Since the 2012 USPSTF review and recommendations regarding the prevention of falls in the community-dwelling elderly, the USPSTF has released (in May 2013) an updated assessment of the use of vitamin D and calcium supplementation to prevent fractures in adults. [823,824] The updated recommendations include the following:

> *The USPSTF concludes that the current evidence is insufficient to assess the balance of the benefits and harms of combined vitamin D and calcium supplementation for the primary prevention of fractures in premenopausal women or in men. (Grade I recommendation)*
>
> *The USPSTF concludes that the current evidence is insufficient to assess the balance of the benefits and harms of daily supplementation with greater than 400 IU of vitamin D_3 and greater than 1,000 mg of calcium for the primary prevention of fractures in noninstitutionalized postmenopausal women. (Grade I recommendation)*
>
> *The USPSTF recommends against daily supplementation with 400 IU or less of vitamin D_3 and 1,000 mg or less of calcium for the primary prevention of fractures in noninstitutionalized postmenopausal women. (Grade D recommendation).*

We have therefore focused on the role of exercise in the prevention of falls in the community-dwelling elderly.

Based on these assumptions, the CPB associated with screening and interventions to reduce falls in community-dwelling elderly is 429 (see Table 2, row *t*). The CPB of 429 represents the gap between no coverage and the 'best in the world' coverage estimated at 18% for screening for risk and 30% for adherence with recommended exercise regimen.

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[818] Rosen CJ. Vitamin D supplementation: bones of contention. *The Lancet*. 2014; 383(9912): 108-10.
[819] Reid IR, Bolland MJ and Grey A. Effects of vitamin D supplements on bone mineral density: a systematic review and meta-analysis. *The Lancet*. 2014; 383(9912): 146-55.
[820] Bischoff-Ferrari HA, Willett WC, Orav EJ et al. A pooled analysis of vitamin D dose requirements for fracture prevention. *New England Journal of Medicine*. 2012; 367: 40-9.
[821] Michael YL, Whitlock EP, Lin JS et al. Primary care-relevant interventions to prevent falling in older adults: a systematic evidence review for the U.S. Preventive Services Task Force. *Annals of Internal Medicine*. 2010; 153(12): 815-25.
[822] Gillespie LD, Robertson MC, Gillespie WJ et al. Interventions for preventing falls in older people living in the community. Cochrane Database of Systematic Reviews. 2012
[823] U.S. Preventive Services Task Force. *Vitamin D and Calcium Supplementation to Prevent Fractures, Topic Page*. 2013. Available at http://www.uspreventiveservicestaskforce.org/uspstf/uspsvitd.htm. Accessed February 2018.
[824] Moyer VA. Vitamin D and calcium supplementation to prevent fractures in adults: U.S. Preventive Services Task Force Recommendation Statement. *Annals of Internal Medicine*. 2013; 158: 691-6.

Table 2: CPB of Screening and Intervention to Reduce Falls in a Birth Cohort of 40,000 (B.C.)			
Row Label	**Variable**	**Base Case**	**Data Source**
a	Years lived ages 65+	765,288	Table 1
b	Adjusted for community-dwelling elderly	0.943	√
c	Average life expectancy	12.5	Table 1
d	Fall-related hospitalizations /1,000	14.19	√
e	Fall-related hospitalizations	10,240	=(a*b)/1000*d
f	Deaths in year following hospital admission	0.30	√
g	Fall-related hospitalization LYs lost due to deaths	38,473	=e*f*c
h	Reduced life expectancy for survivors of fall-related hospitalization	0.20	√
i	Fall-related hospitalization LYs lost in survivors	17,954	=e*(1-f)*c*h
j	Fall-related hospitalization LYs lived in survivors	71,817	=e*(1-f)*c-i
k	Reduction in QoL associated with surviving a fall-related hospitalization - Year 1	0.20	√
l	QALYs lost associated with surviving a fall-related hospitalization - Year 1	1,434	=e*(1-f)*k
m	Reduction in QoL associated with surviving a fall-related hospitalization - subsequent years	0.06	√
n	QALYs lost associated with surviving a fall-related hospitalization - subsequent years	3,232	=(j-(1-f)-i)*m
o	Total QALYs lost	61,093	=g+i+k+n
p	Effectiveness of exercise at reducing falls	13.0%	√
q	QALYs gained based on 100% adherence	7,942	= o * p
r	Delivery of screening and counseling	18.0%	Ref Doc
s	Adherence with exercise	30.0%	Assumed
t	**QALYs gained, CPB**	**429**	= q * r * s

√ = Estimates from the literature

We also modified a number of major assumptions and recalculated the CPB as follows:

- Assume that the proportion of the elderly who die within one year following their falls-related hospitalization is decreased from 30% to 25% (Table 2, row f): CPB = 395.
- Assume that the proportion of the elderly who die within one year following their falls-related hospitalization is increased from 30% to 35% (Table 2, row f): CPB = 463.
- Assume the effectiveness of exercise interventions is decreased from 13% to 6% (Table 2, row *p*): CPB = 198.
- Assume the effectiveness of exercise interventions is increased from 13% to 19% (Table 2, row *p*): CPB = 627.

Modelling Cost-Effectiveness

In this section, we will calculate the CPB associated with preventing falls in the community-dwelling elderly.

In estimating CE, we made the following assumptions:

- **Cost per hour of exercise** – This is easily the most significant cost and thus drives the estimate of CE (Table 3, row *m*). We have estimated the cost of $5.00 per hour (e.g., the approximate cost of admission to a community exercise facility), but have also included a sensitivity analysis from $0 (e.g., walking) to $15 (e.g., the cost per hour for a commercially-based group exercise program).[825]
- **Falls-related hospitalization** – The cost of a falls-related hospitalization is taken from the Canadian Institute of Health Information Patient Cost Estimator.[826] We used the average cost in British Columbia associated with a hospitalization for a primary procedure of case-mix group 727 *Fixation/repair hip/femur* of $11,897 (Table 3, row *o*).
- Other costs and assumptions used in assessing cost-effectiveness are detailed in the Reference Document.
- Discount rate of 1.5%, varied from 0% to 3% in the sensitivity analysis.

Based on these assumptions, the CE associated with screening and interventions to reduce falls in community-dwelling elderly are estimated at $35,213/QALY (see Table 3, row z).

[825] Mr. Jeordie Kerr. Owner, Cross-fit South Delta. Personal communication. February 2018.

[826] Canadian Institute for Health Information. *Patient Cost Estimator*. 2014. Available at http://www.cihi.ca/cihi-ext-portal/internet/en/applicationnew/spending+and+health+workforce/spending/cihi020209. Accessed February 2018.

Table 3: CE of Screening and Intervention to Reduce Falls in a Birth Cohort of 40,000 (B.C.)			
Row Label	**Variable**	**Base Case**	**Data Source**
a	Years lived ages 65+ as community dwelling elderly	721,667	Table 2, row a * Table 2, row b
	Costs of screening		
b	Cost of 10-minute office visit	$34.85	Ref Doc
c	Value of patient time and travel for office visit	$59.38	Ref Doc
d	Portion of 10-minute office visit for screen	50%	Ref Doc
e	Delivery of screening and counseling	18%	Table 2, row r
f	Cost of screening over lifetime of birth cohort	$6,120,238	= (a * e) * (b + c) * d
	Costs of interventions		
g	Proportion of elderly with falls in previous year	0.30	√
h	Portion of 10-minute office visit for referral to exercise program	50%	Ref Doc
i	Cost of referrals	$1,836,071	= (a * f) * e * ((b + c) * d)
j	Adherence with exercise recommendation	30%	Table 2, row s
k	Life years lived with exercise in at risk individuals	11,691	= a * e * g * j
l	Hours of exercise (3 times per week for 1 hour)	1,823,796	= k * 52 * 3
m	Cost per hour of exercise	$5.00	√
n	Cost of intervention (exercise)	$9,118,979	= l * m
	Costs avoided		
o	Reduction in fall-related hospitalizations	166	= (k / a) * Table 2, row e
p	Cost of a fall-related hospitalization	$11,897	√
q	Cost avoided	$1,973,656	= o * p
	CE calculation		
r	Cost of initial screen	$6,120,238	= f
s	Costs of referral and intervention	$10,955,050	= i + n
t	Costs avoided	$1,973,656	= q
u	QALYs saved	429	Table 2, row t
v	Cost of initial screen (1.5% discount rate)	$5,226,698	Calculated
w	Costs of referral and intervention (1.5% discount rate)	$9,355,639	Calculated
x	Costs avoided (1.5% discount rate)	$1,685,507	Calculated
y	QALYs saved (1.5% discount rate)	366	Calculated
z	**CE ($/QALY saved)**	**$35,213**	= (v + w - x) / y

√ = Estimates from the literature

We also modified a number of major assumptions and recalculated the CE as follows:

- Assume that the proportion of the elderly who die within one year following their falls-related hospitalization is decreased from 30% to 25% (Table 2, row *f*): CE = $38,213 / QALY.
- Assume that the proportion of the elderly who die within one year following their falls-related hospitalization is increased from 30% to 35% (Table 2, row *f*): CE = $32,649 / QALY.
- Assume the effectiveness of exercise interventions is decreased from 13% to 6% (Table 2, row *p*): CE = $76,294 / QALY.
- Assume the effectiveness of exercise interventions is increased from 13% to 19% (Table 2, row *p*): CE = $24,093 / QALY.
- Assume the cost of an hour of exercise is decreased from $5 to $0 (Table 3, row *m*): CE = $13,950 / QALY.
- Assume the cost of an hour of exercise is increased from $5 to $15 (Table 3, row *m*): CE = $77,738 / QALY.

Summary

Applying a 1.5% discount rate, the clinically preventable burden (CPB) associated with screening and interventions to reduce falls in community-dwelling elderly is estimated to be 366 quality-adjusted life years (QALYs) while the cost-effectiveness (CE) is estimated to result in cost savings of $35,213 per QALY (see Table 4).

Table 4: Screening and Intervention to Reduce Falls in the Community-Dwelling Elderly

Summary

	Base Case	Range	
CPB (Potential QALYs Gained)			
Gap between 0% and 'Best in the World' (18% screening / 30% exercise adherence)			
1.5% Discount Rate	**366**	169	535
3% Discount Rate	315	145	460
0% Discount Rate	429	198	627
CE ($/QALY) **including** patient time costs			
1.5% Discount Rate	**$35,213**	$13,950	$77,738
3% Discount Rate	$35,213	$13,950	$77,738
0% Discount Rate	$35,213	$13,950	$77,738
CE ($/QALY) **excluding** patient time costs			
1.5% Discount Rate	$23,522	$2,259	$66,048
3% Discount Rate	$23,522	$2,259	$66,048
0% Discount Rate	$23,522	$2,259	$66,048

Preventive Medication / Devices

Routine Aspirin Use for the Prevention of Cardiovascular Disease and Colorectal Cancer

Background

In 2007, the USPSTF recommended "against the routine use of aspirin… to prevent colorectal cancer in individuals at average risk for colorectal cancer" with a D recommendation.[827] In 2009, the USPSTF recommended "the use of aspirin for men age 45 to 79 years when the potential benefit due to a reduction in myocardial infarctions outweighs the potential harm due to an increase in gastrointestinal hemorrhage". The USPSTF also recommended "the use of aspirin for women age 55 to 79 years when the potential benefit of a reduction in ischemic strokes outweighs the potential harm of an increase in gastrointestinal hemorrhage". Both of these 2009 recommendations were A recommendations.[828]

In a 2014 update of the BC LPS, members of the Lifetime Prevention Schedule Expert Committee (LPSEC) reviewed key research that had been published since the 2009 USPSTF recommendations[829,830,831] calling into question the clinical effectiveness of low-dose aspirin in primary prevention.[832,833,834] A major concern of this new research was that the evidence used for the 2009 USPSTF recommendations appeared to overestimate the benefits of the use of aspirin in primary prevention (e.g. a reduction in cardiovascular disease) and to underestimate the harms (e.g. gastrointestinal bleeding and hemorrhagic stroke). Based on this updated evidence on clinical effectiveness, the LPSEC found that the routine use of low-dose aspirin in primary prevention no longer passed the initial test for inclusion on the BC LPS, namely that the maneuver is not clinically effective (i.e. benefits do not significantly outweigh harms).[835]

In the process of updating both their 2007 and 2009 recommendation on the routine use of aspirin to prevent colorectal cancer and cardiovascular diseases, the USPSTF commissioned

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[827] U.S. Preventive Services Task Force. Routine aspirin or nonsteroidal anti-inflammatory drugs for the primary prevention of colorectal cancer. *Annals of Internal Medicine*. 2007; 146(5): 361-4.

[828] U.S. Preventive Services Task Force. Aspirin for the prevention of cardiovascular disease: U.S. Preventive Services Task Force recommendation statement. *Annals of Internal Medicine*. 2009; 150(6): 396-404.

[829] Baigent C, Blackwell L, Collins R et al. Aspirin in the primary and secondary prevention of vascular disease: collaborative meta-analysis of individual participant data from randomised trials. *The Lancet*. 2009; 373(9678): 1849-60.

[830] Seshasai SR, Wijesuriya S, Sivakumaran R et al. Effect of aspirin on vascular and nonvascular outcomes: meta-analysis of randomized controlled trials. *Archives of Internal Medicine*. 2012; 172(3): 209-16.

[831] Sutcliffe P, Connock M, Gurung T et al. Aspirin for prophylactic use in the primary prevention of cardiovascular disease and cancer: a systematic review and overview of reviews. *Health Technology Assessment*. 2013; 17(43): 1-253.

[832] Selak V, Elley CR, Wells S et al. Aspirin for primary prevention: yes or no? *Journal of Primary Health Care*. 2010; 2(2): 92-9.

[833] Raju NC and Eikelboom JW. The aspirin controversy in primary prevention. *Current Opinion in Cardiology*. 2012; 27(5): 499-507.

[834] Patrono C. Low-dose aspirin in primary prevention: cardioprotection, chemoprevention, both, or neither? *European Heart Journal*. 2013; 34(44): 3403-11.

[835] H. Krueger & Associates Inc. *Establishing Priorities among Effective Clinical Prevention Services in British Columbia: Summary and Technical Report.* July 16, 2014.

three systematic evidence reviews[836,837,838] and one decision analysis using simulation modelling.[839]

The systematic review by Guirguis-Blake and colleagues noted that very-low dose aspirin use (≤100mg daily) for primary prevention reduced the risk of nonfatal myocardial infarction by 17% (RR of 0.83, 95% CI of 0.74 – 0.94) and nonfatal stroke by 14% (RR of 0.86, 95% CI of 0.76 – 0.98) but they found no reduction in all-cause or cardiovascular mortality.[840]

The systematic review by Chubak and co-authors noted that using aspirin (in dosages ranging from 50 to 500mg daily) for primary prevention reduced the incidence of colorectal cancer by 40% (RR of 0.60, 95% CI of 0.47 – 0.76) but only in secondary studies which followed individuals for at least 10 years. In addition, the use of aspirin for approximately 5 years reduced the risk of death from CRC about 20 years later by 33% (RR of 0.67, 95% CI of 0.52 – 0.86). Aspirin's effect on ***total cancer*** mortality and incidence was not clearly established.[841]

The systematic review by Whitlock et al. found that very-low dose aspirin use (≤100mg daily or every other day) increased the risk of major gastrointestinal bleeding by 58% (RR of 1.58, 95% CI of 1.29 – 1.95) and the risk of haemorrhagic stroke by 27% (RR of 1.27, 95% CI of 0.96 – 1.68).[842]

To help disentangle the "uncertain relationship between the benefits and harms of long-term aspirin use", the USPSTF commissioned the decision analysis by Dehmer and colleagues.[843] The decision analysis found that the results of net gains (as measured by QALYs) were quite sensitive to all assumptions about the relative risks of both benefits and harms, including baseline risks for GI bleeding. In addition, the results are highly sensitive to assumptions made about the potential disutility associated with regular aspirin use. Their base-case scenario assumed no disutility associated with regular aspirin use.

The collation of this evidence resulted in the following recommendation by the USPSTF.

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[836] Guirguis-Blake J, Evans C, Senger C et al. Aspirin for the primary prevention of cardiovascular events: a systematic evidence review for the U.S. Preventive Services Task Force. *Annals of Internal Medicine*. 2016; 164(12): 804-13.

[837] Chubak J, Whitlock E, Williams S et al. Aspirin for the prevention of cancer incidence and mortality: systematic evidence reviews for the U.S. Preventive Services Task Force. *Annals of Internal Medicine*. 2016; 164(12): 814-25.

[838] Whitlock E, Burda B, Williams S et al. Bleeding risks with aspirin use for primary prevention in adults: a systematic review for the U.S. Preventive Services Task Force. *Annals of Internal Medicine*. 2016; 164(12): 826-35.

[839] Dehmer S, Maciosek M, Flottemesch T et al. Aspirin for the primary prevention of cardiovascular disease and colorectal cancer: a decision analysis for the US Preventive Services Task Force. *Annals of Internal Medicine*. 2016; 164(12): 777-86.

[840] Guirguis-Blake J, Evans C, Senger C et al. Aspirin for the primary prevention of cardiovascular events: a systematic evidence review for the U.S. Preventive Services Task Force. *Annals of Internal Medicine*. 2016; 164(12): 804-13.

[841] Chubak J, Whitlock E, Williams S et al. Aspirin for the prevention of cancer incidence and mortality: systematic evidence reviews for the U.S. Preventive Services Task Force. *Annals of Internal Medicine*. 2016; 164(12): 814-25.

[842] Whitlock E, Burda B, Williams S et al. Bleeding risks with aspirin use for primary prevention in adults: a systematic review for the U.S. Preventive Services Task Force. *Annals of Internal Medicine*. 2016; 164(12): 826-35.

[843] Dehmer S, Maciosek M, Flottemesch T et al. Aspirin for the primary prevention of cardiovascular disease and colorectal cancer: a decision analysis for the US Preventive Services Task Force. *Annals of Internal Medicine*. 2016; 164(12): 777-86.

United States Preventive Services Task Force Recommendations (2016)[844]

The USPSTF recommends initiating low dose aspirin use for the primary prevention of CVD and CRC in adults aged 50 to 59 years who have a 10% or greater 10-year CVD risk, are not at increased risk for bleeding, have a life expectancy of at least 10 years, and are willing to take low-dose aspirin daily for at least 10 years. (B recommendation)

The decision to initiate low-dose aspirin use for the primary prevention of CVD and CRC in adults aged 60 to 69 years who have a 10% or greater 10-year CVD risk should be an individual one. Persons who are not at increased risk for bleeding, have a life expectancy of at least 10 years, and are willing to take low-dose aspirin daily for at least 10 years are more likely to benefit. Persons who place a higher value on the potential benefits than the potential harms may choose to initiate low-dose aspirin. (C recommendation)

Risk factors for gastrointestinal (GI) bleeding with aspirin use include higher dose and longer duration of use, history of GI ulcers or upper GI pain, bleeding disorders, renal failure, severe liver disease, and thrombocytopenia. Other factors that increase risk for GI or intracranial bleeding with low-dose aspirin use include concurrent anticoagulation or nonsteroidal anti-inflammatory drug (NSAID) use, uncontrolled hypertension, male sex, and older age.

Modelling the Clinically Preventable Burden

In this section, we will calculate the CPB associated with initiating low dose aspirin use for the primary prevention of CVD and CRC in adults between the ages of 50 and 59 years who have a 10% or greater 10-year CVD risk, are not at increased risk for bleeding, have a life expectancy of at least 10 years, and are willing to take low-dose aspirin daily for at least 10 years.

In estimating CPB, we made the following assumptions:

- Based on BC life tables for 2010 to 2012, there are a total of 380,576 life years lived between the ages of 50 and 59 in a BC birth cohort of 40,000 (see Table 1).
- Based on BC life tables for 2010 to 2012, a total of 1,072 deaths would be expected between the ages of 50-59, a further 2,460 deaths between the ages of 60-69 and 5,808 deaths between the ages of 70-79 in a BC birth cohort of 40,000 (see Table 1).
- Based on BC vital statistics data, 601 of 5,076 (11.8%) deaths in 45-64 year olds in 2011 were due to cardiovascular disease (ICD-10 codes I00-I51) and 191 of 5,076 (3.8%) deaths were due to cerebrovascular disease (ICD-10 codes I60-I69).[845] This data was used to estimate that approximately 190 of the 1,611 (11.8%) deaths between the ages of 55-64 in the birth cohort would be due to cardiovascular disease and 61 (3.8%) due to cerebrovascular disease (see Table 1).

[844] Bibbins-Domingo K. Aspirin use for the primary prevention of cardiovascular disease and colorectal cancer: US Preventive Services Task Force recommendation statement. *Annals of Internal Medicine*. 2016; 164(12): 836-45.

[845] British Columbia Vital Statistics Agency. *Selected Vital Statistics and Health Status Indicators: One Hundred and Fortieth Annual Report*. 2011. British Columbia Ministry of Health. Available at http://www2.gov.bc.ca/assets/gov/birth-adoption-death-marriage-and-divorce/statistics-reports/annual-reports/2011/pdf/ann2011.pdf. Accessed January 2017.

- Based on BC Cancer Agency data, there were 3,021[846] new cases of colorectal cancers (CRC) in BC in 2012 and 1,099[847] deaths due to CRC that same year. An estimated 19.9%[848] of deaths (or 219 in BC in 2012) from CRC are in individuals between the ages of 60-69. Since the effectiveness of aspirin on reducing the incidence of CRC only appears after approximately ten years, the age range of 65-74 is being used in the modelling when considering CRC ***incidence***. Similarly, the age range of 75-84 is being used in the modelling when considering CRC ***mortality*** due to the 20-year lag time observed for this outcome in the research.[849] An estimated 26.9%[850] of deaths (or 296 in BC in 2012) from CRC are in individuals between the ages of 70-79.
- Based on BC vital statistics data, there were 31,776 deaths in BC in 2011.[851] An estimated 12.5% of these deaths (or 3,972) are in individuals between the ages of 60-69 and 22.2% (or 7,065) in individuals between the ages of 70-79.[852] The 219 deaths from CRC between the ages of 60-69 therefore represents approximately 5.3% of all deaths in this age cohort. In the birth cohort of 40,000, 5.3% of deaths between the ages of 60-69 represents 130 deaths due to CRC (see Table 1). The 296 deaths from CRC represents approximately 4.2% of all deaths in this age cohort. In the birth cohort of 40,000, 4.2% of deaths between the ages of 70-79 represents 244 deaths due to CRC (see Table 1).

Table 1: Deaths and Selected Causes of Death Between the Ages of 50 and 84
in a British Columbia Birth Cohort of 40,000

Age Group	*Mean Survival Rate*		*Individuals in Birth Cohort*			*Life Years Lived*	*Deaths in Birth Cohort*		*Deaths due to* Cardiovascular Disease		*Deaths due to* Cerebrovascular Disease		Colorectal Cancer	
	Males	Females	Males	Females	Total		%	#	%	#	%	#	%	#
45-49	0.963	0.977	19,263	19,546	38,809									
50-54	0.950	0.969	19,003	19,375	38,378	191,890	1.1%	431						
55-59	0.931	0.956	18,619	19,118	37,737	188,686	1.7%	641	11.8%	76	3.8%	24		
60-64	0.902	0.936	18,041	18,726	36,767	183,834	2.6%	970	11.8%	115	3.8%	37	5.3%	51
65-69	0.858	0.906	17,164	18,113	35,277	176,387	4.2%	1,489					5.3%	79
70-74	0.792	0.857	15,837	17,144	32,981	164,903	7.0%	2,297					4.2%	96
75-79	0.693	0.780	13,861	15,608	29,469	147,346	11.9%	3,511					4.2%	147
80-84	0.553	0.661	11,053	13,228	24,281	121,405	21.4%	5,188					4.2%	218

[846] BC Cancer Agency. *New Cancer Diagnoses for 2012 by Cancer Type, Age at Diagnosis and Gender*. 2012. Provincial Health Services Authority,. Available at http://www.bccancer.bc.ca/statistics-and-reports-site/Documents/Cancer_Incidence_Counts_2012.pdf. Accessed February 2017.
[847] BC Cancer Agency. *Cancer Deaths in British Columbia, 2012 by Cancer Type, Age at Death and Gender*. 2012. Provincial Health Services Authority,. Available at http://www.bccancer.bc.ca/statistics-and-reports-site/Documents/Cancer_Mortality_Counts_2013.pdf. Accessed February 2017.
[848] Canadian Cancer Society's Advisory Committee on Cancer Statistics. *Canadian Cancer Statistics 2016, Special Topic: HPV-Associated Cancers*. 2016. Canadian Cancer Society. Available at http://www.colorectal-cancer.ca/IMG/pdf/Canadian-Cancer-Statistics-2016-EN.pdf. Accessed February 2017.
[849] Chubak J, Whitlock E, Williams S et al. Aspirin for the prevention of cancer incidence and mortality: systematic evidence reviews for the U.S. Preventive Services Task Force. *Annals of Internal Medicine*. 2016; 164(12): 814-25.
[850] Canadian Cancer Society's Advisory Committee on Cancer Statistics. *Canadian Cancer Statistics 2016, Special Topic: HPV-Associated Cancers*. 2016. Canadian Cancer Society. Available at http://www.colorectal-cancer.ca/IMG/pdf/Canadian-Cancer-Statistics-2016-EN.pdf. Accessed February 2017.
[851] British Columbia Vital Statistics Agency. *Selected Vital Statistics and Health Status Indicators: One Hundred and Fortieth Annual Report*. 2011. British Columbia Ministry of Health. Available at http://www2.gov.bc.ca/assets/gov/birth-adoption-death-marriage-and-divorce/statistics-reports/annual-reports/2011/pdf/ann2011.pdf. Accessed January 2017.
[852] Jayaraman J and Joseph K. Determinants of place of death: a population-based retrospective cohort study. *BioMed Central Palliative Care*. 2013; 12(19): 1-9.

- We are not aware of any information which indicates the proportion of adults aged 50 to 59 years in BC who have had a cardiovascular or bleeding risk assessment. Nor are we aware of BC-specific data on the proportion of adults at intermediate or higher risk of CVD and low bleeding risk who are taking aspirin over the longer term for primary prevention purposes. Research suggests that 73.3% of Canadians between the ages of 40 and 59 are at low risk (defined as a mean 10-year risk of a CVD event of less than 10%), 10.3% are at intermediate risk (mean 10-year risk of a CVD event of 10%-19%) and 16.4% are at high risk (mean 10-year risk of a CVD event of ≥20%)[853] (see Table 2).

Table 2: Estimated Number of Canadian Adults Ages 20-79 By CVD Risk Status, 2007 to 2011

Age Group	Population	Estimated # by CVD Risk Status			Estimated % by CVD Risk Status		
		Low	Int.	High	Low	Int.	High
20-39	8,983,467	8,893,999	4,335	85,133	99.0%	0.05%	0.95%
40-59	9,863,690	7,231,730	1,014,437	1,617,523	73.3%	10.3%	16.4%
60-79	5,186,843	1,011,071	1,148,828	3,026,944	19.5%	22.1%	58.4%
Total	**24,034,000**	**17,136,800**	**2,167,600**	**4,729,600**	**71.3%**	**9.0%**	**19.7%**

- We assumed that the average age at which a cardiovascular or cerebrovascular event was prevented due to the use of aspirin would be 60 (Table 3, rows *q* & *x*). For the prevention of a CRC event, this would be 70.4 (Table 3, row *ae*). For the prevention of a death due to CRC, this would be 80 (Table 3, row *aj*). Based on BC life tables for 2010 to 2012, the average life expectancy of a 60 year old is 25.1 years (Table 3, rows *y* & *z*), that of a 70.4 year old is 16.5 years (Table 3, rows *af* & *ag*) and that of an 80 year old is 9.9 years (Table 3, row *ak*).[854]
- Very-low dose aspirin use (≤100mg daily) for primary prevention reduces the risk of nonfatal myocardial infarction by 17% (RR of 0.83, 95% CI of 0.74 – 0.94) (Table 3, row *ao*) and nonfatal stroke by 14% (RR of 0.86, 95% CI of 0.76 – 0.98) (Table 3, row *aq*), but does not reduce all-cause or cardiovascular mortality.[855]
- Use of aspirin (in dosages ranging from 50 to 500mg daily) for primary prevention reduces the incidence of colorectal cancer by 40% (RR of 0.60, 95% CI of 0.47 – 0.76) (Table 3, row *as*) but only in secondary studies which followed individuals for at least 10 years.[856]
- The use of aspirin for approximately 5 years reduces the risk of death from CRC about 20 years later by 33% (RR of 0.67, 95% CI of 0.52 – 0.86) (Table 3, row *au*).[857]
- The rate of a major bleeding event in a 50-69 year old not taking aspirin is 1.99 per 1,000 person-years (95% CI 1.82 to 2.18) (Table 3, row *az*). The rate of a major bleeding event in a 50-69 year old who is taking aspirin increases to 3.21 per 1,000 person-years (95% CI 2.93 to 3.53) (Table 3, row *ba*). Sixty-five percent of bleeding

[853] Hennessy D, Tanuseputro P, Tuna M et al. Population health impact of statin treatment in Canada. *Health Reports*. 2016; 27(1): 20-8.
[854] See http://www.statcan.gc.ca/pub/84-537-x/2013005/tbl-eng.htm. Accessed January 2017.
[855] Guirguis-Blake J, Evans C, Senger C et al. Aspirin for the primary prevention of cardiovascular events: a systematic evidence review for the U.S. Preventive Services Task Force. *Annals of Internal Medicine*. 2016; 164(12): 804-13.
[856] Chubak J, Whitlock E, Williams S et al. Aspirin for the prevention of cancer incidence and mortality: systematic evidence reviews for the U.S. Preventive Services Task Force. *Annals of Internal Medicine*. 2016; 164(12): 814-25.
[857] Ibid.

events are episodes of gastrointestinal bleeding (Table 3, row *bc*) while 35% are episodes of intracranial hemorrhage (Table 3, row *bd*).[858]

- In a study of 936 patients with acute upper gastrointestinal bleeding (AUGIB) in the UK, 42 (4.5%) had died by day 28 following the bleeding episode (Table 3, row *bg*). The mean QoL score at 28 days for surviving patients was 0.735 compared to 0.86 for the general UK population, a disutility of 14.5% (Table 3, row *bo*). We have assumed that this disutility lasts for a one-year period.[859]
- An estimated 40% of patients die within 28 days after a haemorrhagic stroke (Table 3, row *bh*).[860]
- Other assumptions used in assessing the clinically preventable burden are detailed in the Reference Document.

Based on these assumptions, the CPB associated with screening for and initiating use of low-dose aspirin for the primary prevention of CVD and CRC in adults aged 50 to 59 years who have a 10% or greater 10-year CVD risk, are not at increased risk for bleeding, have a life expectancy of at least 10 years, and are willing to take low-dose aspirin daily for at least 10 years is 1,098 QALYs (Table 3, row *bs*). This is based on the assumption of moving from no aspirin use in this intermediate to high risk cohort to 24% of this cohort initiating and sustaining aspirin use.

[858] De Berardis G, Lucisano G, D'ettorre A et al. Association of aspirin use with major bleeding in patients with and without diabetes. *Journal of American Medical Association*. 2012; 307(21): 2286-94.
[859] Campbell H, Stokes E, Bargo D et al. Costs and quality of life associated with acute upper gastrointestinal bleeding in the UK: cohort analysis of patients in a cluster randomised trial. *British Medical Journal Open*. 2015; 5(4): e007230.
[860] Krueger H, Lindsay P, Cote R et al. Cost avoidance associated with optimal stroke care in Canada. *Stroke*. 2012; 43(8): 2198-206.

Table 3: CPB of Screening for and Initiating Use of Aspirin in Adults Between the Ages of 50 and 59 Years with an Intermediate or Higher Risk of CVD in a Birth Cohort of 40,000			
Label	**Variable**	**Base Case**	**Data Source**
	Estimated current status		
a	# of life years lived between the ages of 55-64 in birth cohort	372,520	Table 1
b	% of life years at low risk of CVD	73.3%	Table 2
c	% of life years at intermediate risk of CVD	10.3%	Table 2
d	% of life years at high risk of CVD	16.4%	Table 2
e	# of life years at low risk	273,119	= (a * b)
f	# of life years at intermediate risk	38,312	= (a * c)
g	# of life years at high risk	61,089	= (a * d)
h	Total deaths in birth cohort between the ages of 55-64	1,611	Table 1
i	Cardiovascular deaths in birth cohort between the ages of 55-64	190	Table 1
j	Cerebrovascular deaths in birth cohort between the ages of 55-64	61	Table 1
k	Total deaths in birth cohort between the ages of 65-74	3,786	Table 1
l	Colorectal cancer deaths in birth cohort between the ages of 65-74	175	Table 1
m	Total deaths in birth cohort between the ages of 75-84	8,700	Table 1
n	Colorectal cancer deaths in birth cohort between the ages of 75-84	365	Table 1
o	# of nonfatal ***cardiovascular*** events per fatal event	5.09	See Ref Doc
p	# of nonfatal cardiovascular events	968	= (i * o)
q	Average age of individual with a cardiovascular event	60	√
r	Life years lived with a nonfatal cardiovascular event	18.8	√
s	Life years lost due to a nonfatal cardiovascular event	6.3	See Ref Doc
t	QoL reduction living with a nonfatal cardiovascular event (for 1 month)	0.125	See Ref Doc
u	**QALYs lost due to nonfatal cardiovascular events**	**6,286**	= (p * s) + (p * r * t)/12
v	Ratio of nonfatal ***cerebrovascular*** events per fatal event	4.58	See Ref Doc
w	# of nonfatal cerebrovascular events	280	= (j * u)
x	Average age of individual with a cerebrovascular event	60	√
y	Life years lived with a nonfatal cerebrovascular event	19.7	√
z	Life years lost due to a nonfatal cerebrovascular event	5.5	See Ref Doc
aa	QoL reduction living with a nonfatal cerebrovascular event	0.264	See Ref Doc
ab	**QALYs lost due to nonfatal cerebrovascular events**	**3,001**	= (w * z) + (w * y * aa)
ac	Ratio of nonfatal ***colorectal cancer*** events per fatal event	4.32	See Ref Doc
ad	# of nonfatal colorectal cancer events, ages 65-74	758	= (l * aa)
ae	Average age of individual with colorectal cancer	70.4	See Ref Doc
af	Life years lived with colorectal cancer	6.6	See Ref Doc
ag	Life years lost due to nonfatal colorectal cancer	9.9	See Ref Doc
ah	QoL reduction living with a nonfatal colorectal cancer event	0.065	See Ref Doc
ai	**QALYs lost due to nonfatal colorectal cancer events**	**7,825**	= (ad * ag) + (ad * af * ah)
aj	Average age of individual dying from colorectal cancer	80	√
ak	Life expectancy of a 80 year old in BC	9.9	√
al	**QALYs lost due to deaths from colorectal cancer**	**3,617**	= (n * ak)

Table 3 (continued): CPB of Screening for and Initiating Use of Aspirin in Adults Between the Ages of 50 and 59 Years with an Intermediate or Higher Risk of CVD in a Birth Cohort of 40,000			
Label	**Variable**	**Base Case**	**Data Source**
	Benefits if 24% of intermediate & high risk individuals were on aspirin		
am	% of life years at intermediate or high risk on aspirin	24%	See Ref Doc
an	# of life years at intermediate or high risk on aspirin	23,856	= (f + g) * am
ao	% reduction in risk of cardiovascular disease associated with aspirin use	17%	√
ap	**QALYs gained due to cardiovascular disease events avoided with 24% aspirin usage**	**256**	= (u * am * ao)
aq	% reduction in cerebrovascular events associated with aspirin use	14%	√
ar	**QALYs gained due to cerebrovascular disease events avoided with 24% aspirin usage**	**101**	= (ab * am * aq)
as	% reduction in colorectal cancer events associated with aspirin use, ages 60-69	40%	√
at	**QALYs gained due to a reduction in nonfatal colorectal cancer events associated with 24% aspirin use**	**751**	= (ai * am * as)
au	% reduction in colorectal cancer deaths associated with aspirin use, ages 70-79	33%	√
av	**QALYs gained due to a reduction in colorectal cancer deaths associated with 24% aspirin use**	**286**	= (al * am * au)
aw	***Total QALYs gained*** if 24% of intermediate & high risk individuals were on aspirin	**1,395**	= (an + aq + at + av)
	Harms if 24% of intermediate & high risk individuals were on aspirin		
ax	Disutility per year associated with taking pills for cardiovascular prevention	-0.0032	See Ref Doc
ay	Disutility associated with taking pills for cardiovascular prevention	-76	= (an * ax)
az	Risk of major bleeding event in age group 50-69 per 1,000 person-years, no aspirin	1.99	√
ba	Risk of major bleeding event in age group 50-69 per 1,000 person-years, with aspirin	3.21	√
bb	Major bleeding events in cohort due to aspirin	29	=((ak/1000)*ba)-((ak/1000)*az)
bc	Proportion of major bleeding events - gastrointestinal bleeding	0.65	√
bd	Proportion of major bleeding events - haemorrhagic stroke	0.35	√
be	Gastrointestinal bleeding events attributable to aspirin use	19	= (bb * bc)
bf	Haemorrhagic strokes attributable to aspirin use	10	= (bb * bd)
bg	Death rate following a gastrointestinal bleeding event	0.045	√
bh	Death rate following a haemorrhagic stroke	0.40	√
bi	Deaths due to a gastrointestinal bleeding event	0.9	= (be * bg)
bj	Deaths due to a haemorrhagic stroke	4.1	= (bf * bh)
bk	Average age of individual with a major bleeding event	60	√
bl	Life years lived following a non-fatal gastrointestinal bleeding event	29.6	√
bm	Life years lived following a non-fatal haemorrhagic stroke	24.1	= (bl - bn)
bn	Life years lost following a non-fatal haemorrhagic stroke	5.5	See Ref Doc
bo	QoL reduction living with a gastrointestinal bleed (1 year only)	-0.145	√
bp	QALYs lost due to gastrointestinal bleeding	-28	=(-bi*bl)+((be-bi)*bo)
bq	QALYs lost due to haemorrhagic stroke	-193	=(-bj*bl)-((bf-bj)*bn)-((bf-bj)*bm*aa)
br	***Total QALYs lost*** if 100% of intermediate & high risk individuals were on aspirin	**-297**	= ay + bp + bq
bs	**Net QALYs gained, Screening & Intervention from 0% to 24%**	**1,098**	= (aw + br)

√ = Estimates from the literature

For our sensitivity analysis, we modified a number of major assumptions and recalculated the CPB as follows:

- Assume that decreased risk of cardiovascular disease events associated with aspirin use is reduced from 17% to 6% (Table 3, row *ao*), the decreased risk of cerebrovascular disease events is reduced from 14% to 2% (Table 3, row *aq*), the decreased risk of incident CRC is reduced from 40% to 24% (Table 3, row *as*) and the decreased risk of mortality due to CRC is reduced from 33% to 14% (Table 3, row *au*): CPB = 380.
- Assume that decreased risk of cardiovascular disease events associated with aspirin use is increased 17% to 26% (Table 3, row *ao*), the decreased risk of cerebrovascular disease events is increased from 14% to 24% (Table 3, row *aq*), the decreased risk of incident CRC is increased from 40% to 53% (Table 3, row *as*) and the decreased risk

of mortality due to CRC is increased from 33% to 48% (Table 3, row *au*): CPB = 1,680.

- Assume that the disutility per year associated with taking pills for cardiovascular prevention is reduced from -0.0033 to 0.000 (Table 3, row *ax*): CPB = 1,174.
- Assume that the disutility per year associated with taking pills for cardiovascular prevention is increased from -0.0033 to -0.0044 (Table 3, row *ax*): CPB = 1,069.
- Assume that the rate of a major bleeding event in a 50-69 year old not taking aspirin is reduced from 1.99 to 1.82 per 1,000 person-years (Table 3, row *az*) while the rate of a major bleeding event in a 50-69 year old who is taking aspirin is reduced from 3.21 to 2.93 per 1,000 person-years (Table 3, row *ba*): CPB = 1,118.
- Assume that the rate of a major bleeding event in a 50-69 year old not taking aspirin is increased from 1.99 to 2.18 per 1,000 person-years (Table 3, row *az*) while the rate of a major bleeding event in a 50-69 year old who is taking aspirin is increased from 3.21 to 3.53 per 1,000 person-years (Table 3, row *ba*): CPB = 1,074.

Modelling Cost-Effectiveness

In this section, we will calculate the CE associated with initiating low dose aspirin use for the primary prevention of CVD and CRC in adults between the ages of 50 and 59 years who have a 10% or greater 10-year CVD risk, are not at increased risk for bleeding, have a life expectancy of at least 10 years, and are willing to take low-dose aspirin daily for at least 10 years.

In estimating CE, we made the following assumptions:

- **Screening for CVD risk** - The USPSTF notes that it used the ACC/AHA Pooled Cohort Equations to calculate the 10-year risk of CVD events in their analysis and identified key risk factors for GI bleeding: higher doses and longer duration of aspirin use, GI ulcers or upper GI pain, bleeding disorders, renal failure, severe liver disease, thrombocytopenia, concurrent anticoagulation or nonsteroidal anti-inflammatory drug use, uncontrolled hypertension, male sex and older age. [861]
- The need to concurrently screen for CVD risk, bleeding risk and willingness to take low-dose aspirin daily for at least 10 years has recently led to the development of a clinical decision support tool called the Aspirin Guide.[862,863]
- We have assumed that the CVD screening and bleeding risk assessment would take place three times between the ages of 50 and 59 (beginning, mid-point and end of this age range). This would involve screening individuals to determine their risk status and whether or not aspirin would be recommended as well as for follow-up purposes for individuals taking aspirin for primary prevention purposes (Table 3, row *e*).
- Completion of a CVD risk assessment includes a physician visit and a full lipid profile (total cholesterol [TC]; high density lipoprotein cholesterol [HDL-C]; low-density lipoprotein cholesterol [LDL-C], non-HDL-C; and triglycerides [TG]). The

[861] Bibbins-Domingo K. Aspirin use for the primary prevention of cardiovascular disease and colorectal cancer: US Preventive Services Task Force recommendation statement. *Annals of Internal Medicine*. 2016; 164(12): 836-45.
[862] Mora S and Manson J. Aspirin for primary prevention of atherosclerotic cardiovascular disease: advances in diagnosis and treatment. *Journal of the American Medical Association Internal Medicine*. 2016; 176(8): 1195-204.
[863] Mora S, Ames J and Manson J. Low-dose aspirin in the primary prevention of cardiovascular disease: shared decision making in clinical practice. *Journal of the American Medical Association*. 2016; 316(7): 709-10.

full lipid profile costs $21.31 (Table 3, row *l*).[864] Note that a CVD risk assessment is required when considering both statins (see previous modelling section) and aspirin for the primary prevention of CVD.

- We assumed that a 10-minute office visit would be required for the initial screening. If the results indicate a low risk of CVD, then the follow-up would consist of a phone call to the patient. If the results indicate an intermediate or high risk of CVD, then a follow-up visit would be required to discuss the results and the possibility of taking aspirin.
- **Cost of aspirin therapy –** The cost of 100 – 81mg aspirin tablets at London Drugs is $14.99.[865] We assumed an annual cost of $54.70 (Table 3, row *t*).
- We assumed an annual follow-up visit with a clinician for patients taking aspirin for preventative purposes (Table 3, row *v*).
- Other costs incurred or avoided and assumptions used in assessing cost-effectiveness are detailed in the Reference Document.
- Discount rate of 1.5%, varied from 0% to 3% in the sensitivity analysis.

Based on these assumptions, the CE associated with screening for and initiating use of low-dose aspirin for the primary prevention of CVD and CRC in adults between the ages of 50 and 59 years who have a 10% or greater 10-year CVD risk, are not at increased risk for bleeding, have a life expectancy of at least 10 years, and are willing to take low-dose aspirin daily for at least 10 years is $2,302 / QALY (Table 3, row *bi*).

[864] Ministry of Health. *Cardiovascular Disease – Primary Prevention* 2014. Available at http://www2.gov.bc.ca/assets/gov/health/practitioner-pro/bc-guidelines/cvd.pdf. Accessed January 2017.
[865] See http://www.londondrugs.com/. Accessed February 2017.

Table 4: CE of Screening for and Initiating Use of Aspirin in Adults Between the Ages of 50 and 59 Years with an Intermediate or Higher Risk of CVD in a Birth Cohort of 40,000			
Row Label	**Variable**	**Base Case**	**Data Source**
a	# of individuals alive at age 59 in birth cohort	37,737	Table 1
b	# of life years lived between the ages of 55-64 in birth cohort	372,520	Table 3
c	% of life years at intermediate or high risk	26.7%	Table 3
d	# of life years at intermediate or high risk	99,401	= (b * c)
e	Lifetime number of screens	3.0	Assumed
f	Adherence with offers to receive screening	33%	See Ref Doc
g	Total # of screens in birth cohort	37,360	= (a * e * f)
	Estimated cost of screening		
h	Number of office visits associated with screening - low risk	1	Expert Opinion
i	Number of office visits associated with screening - medium or high risk	2	Expert Opinion
j	Cost of 10-minute office visit	$34.85	V
k	Cost of a follow-up phone call	$15.00	V
l	Cost to measure cholesterol	$21.31	V
m	Health care costs of screening - low risk	$1,949,142	= (1 - c) * g * h * (j + k + l)
n	Health care costs of screening - medium and high risk	$907,264	= ((c * g) * i) * (j + l * 0.5)
o	Patient time required / office visit (hours)	2	V
p	Value of patient time (per hour)	$29.69	V
q	Value of patient time and travel for screening	$2,810,376	=(((c * g * i) + ((1 - c) * g * h))) * o * p
	Estimated cost of intervention		
r	Adherence with long-term aspirin therapy in intermediate & high risk cohort	24.0%	See Ref Doc
s	Years on aspirin therapy	23,856	= (d * r)
t	Cost of aspirin therapy / year	$54.70	V
u	Cost of aspirin therapy	$1,304,933	= (s * t)
v	Follow-up office visits / year on aspirin therapy	1.0	Expert Opinion
w	Health care costs of intervention	$831,388	= s * v * j
x	Value of patient time and travel for intervention	$1,416,579	= s * v * o * p
	Estimated costs avoided due to intervention		
y	# of nonfatal cardiovascular events avoided	39.5	= Table 3, row p * Table 3, row ao * r
z	# of nonfatal cerebrovascular events avoided	9.4	= Table 3, row w * Table 3, row aq * r
aa	# of nonfatal colorectal cancer events avoided	72.7	= Table 3, row ad * Table 3, row as * r
ab	# of fatal colorectal cancer events avoided	28.9	= Table 3, row n * Table 3, row au * r
ac	First year costs avoided per nonfatal cardiovascular event avoided	$33,934	See Ref Doc
ad	First year costs avoided per nonfatal cerebrovascular event avoided	$21,139	See Ref Doc
ae	First year costs avoided per nonfatal colorectal cancer event avoided	$40,080	See Ref Doc
af	Costs avoided per fatal colorectal cancer event avoided	$49,197	See Ref Doc
ag	First year costs avoided	$5,878,221	=(y*ac)+(z*ad)+(aa*ae)+(ab*af)
ah	Post-first-year annual costs avoided for nonfatal cardiovascular events avoided	$2,278	See Ref Doc
ai	Duration of post-first year annual costs	12.1	See Ref Doc
aj	Post-first-year annual costs avoided for nonfatal cerebrovascular events avoided	$6,246	See Ref Doc
ak	Duration of post-first year annual costs	9.3	See Ref Doc
al	Post-first-year annual costs avoided for nonfatal colorectal cancer events avoided	$3,687	See Ref Doc
am	Duration of post-first year annual costs	6.6	See Ref Doc
an	Post-first-year costs avoided for nonfatal cardiovascular events avoided	$1,088,300	= (y * ah * ai)
ao	Post-first-year costs avoided for nonfatal cerebrovascular events avoided	$547,297	= (z * aj * ak)
ap	Post-first-year costs avoided for nonfatal colorectal cancer events avoided	$1,770,154	= (aa * al * am)
aq	Costs avoided due to intervention	$9,283,971	= ag + an + ao + ap
	Estimated costs incurred due to intervention		
ar	# of gastrointestinal bleeds incurred	18.9	= Table 3, row be
as	# of nonfatal haemorrhagic strokes incurred	6.1	= Table 3, row bf - Table 3, row bj
at	# of fatal haemorrhagic strokes incurred	4.1	= Table 3, row bj
au	Costs per nonfatal gastrointestinal bleed	$6,425	See Ref Doc
av	Cost per fatal haemorrhagic stroke	$9,583	See Ref Doc
aw	First year costs per nonfatal cerebrovascular event	$21,139	See Ref Doc
ax	Post-first-year costs for nonfatal cerebrovascular events	$6,246	See Ref Doc
ay	Duration of post-first year annual costs	9.3	See Ref Doc
az	Costs incurred due to intervention	$515,625	= (ar * au) + (at * av) + (as * ay * ax)
	CE Calculation		
ba	Cost of intervention over lifetime of birth cohort	$9,219,683	= m + n + q + u + w + x
bb	Costs avoided due to intervention over lifetime of birth cohort	$9,283,971	= aq
bc	Costs incurred due to intervention over lifetime of birth cohort	$515,625	= az
bd	Net QALYs saved	1,098	Table 3, row bs
be	Cost of intervention over lifetime of birth cohort (1.5% discount)	$8,045,187	Calculated
bf	Costs avoided due to intervention over lifetime of birth cohort (1.5% discount)	$6,864,254	Calculated
bg	Costs incurred due to intervention over lifetime of birth cohort (1.5% discount)	$449,939	Calculated
bh	Net QALYs saved (1.5% discount)	708	Calculated
bi	**CE ($/QALY saved)**	**$2,302**	= (be + bg - bf) / bh

V = Estimates from the literature

For our sensitivity analysis, we modified a number of major assumptions and recalculated the CE as follows:

- Assume that decreased risk of cardiovascular disease events associated with aspirin use is reduced from 17% to 6% (Table 3, row *ao*), the decreased risk of cerebrovascular disease events is reduced from 14% to 2% (Table 3, row *aq*), the decreased risk of incident CRC is reduced from 40% to 24% (Table 3, row *as*) and the decreased risk of mortality due to CRC is reduced from 33% to 14% (Table 3, row *au*): CE = $24,255.
- Assume that decreased risk of cardiovascular disease events associated with aspirin use is increased 17% to 26% (Table 3, row *ao*), the decreased risk of cerebrovascular disease events is increased from 14% to 24% (Table 3, row *aq*), the decreased risk of incident CRC is increased from 40% to 53% (Table 3, row *as*) and the decreased risk of mortality due to CRC is increased from 33% to 48% (Table 3, row *au*): CE = -$1,189.
- Assume that the disutility per year associated with taking pills for cardiovascular prevention is reduced from -0.0033 to 0.000 (Table 3, row *ax*): CE = $2,105.
- Assume that the disutility per year associated with taking pills for cardiovascular prevention is increased from -0.0033 to -0.0044 (Table 3, row *ax*): CE = $2,387.
- Assume that the rate of a major bleeding event in a 50-69 year old not taking aspirin is reduced from 1.99 to 1.82 per 1,000 person-years (Table 3, row *az*) while the rate of a major bleeding event in a 50-69 year old who is taking aspirin is reduced from 3.21 to 2.93 per 1,000 person-years (Table 3, row *ba*): CE = $2.191.
- Assume that the rate of a major bleeding event in a 50-69 year old not taking aspirin is increased from 1.99 to 2.18 per 1,000 person-years (Table 3, row *az*) while the rate of a major bleeding event in a 50-69 year old who is taking aspirin is increased from 3.21 to 3.53 per 1,000 person-years (Table 3, row *ba*): CE = $2,441.

Summary

Applying a 1.5% discount rate, the clinically preventable burden (CPB) associated with screening for and initiating use of low-dose aspirin for the primary prevention of CVD and CRC in adults between the ages of 50 and 59 years who have a 10% or greater 10-year CVD risk, are not at increased risk for bleeding, have a life expectancy of at least 10 years, and are willing to take low-dose aspirin daily for at least 10 years is estimated to be 708 quality-adjusted life years (QALYs) while the cost-effectiveness (CE) is estimated to result in cost savings of $2,302 per QALY (see Table 5).

Table 5: Screening for and Initiating Use of Aspirin in Adults Aged 50 to 59 Years with an Intermediate or Higher Risk of CVD in a Birth Cohort of 40,000

Summary

	Base Case	Range	
CPB (Potential QALYs Gained)			
Gap between No Service and 'Best in the World' (24%)			
1.5% Discount Rate	708	217	1,108
3% Discount Rate	501	131	802
0% Discount Rate	***1,098***	380	1,680
CE ($/QALY) **including** patient time costs			
1.5% Discount Rate	***$2,302***	-$1,189	$24,255
3% Discount Rate	$4,736	$233	$38,547
0% Discount Rate	$411	-$2,106	$14,098
CE ($/QALY) **excluding** patient time costs			
1.5% Discount Rate	-$2,905	-$4,518	$7,238
3% Discount Rate	-$1,730	-$3,807	$13,873
0% Discount Rate	-$3,439	-$4,622	$2,972

Folic Acid Supplementation in Reproductive-age Women for the Prevention of Neural Tube Defects (NTDs)

United States Preventive Services Task Force Recommendations (2017)[866]

The USPSTF recommends that all women who are planning or capable of pregnancy take a daily supplement containing 0.4 to 0.8 mg (400-800µg) of folic acid (Grade A recommendation).

The critical period of supplementation starts at least 1 month before conception and continues through the first 2 to 3 months.

Modelling the Clinically Preventable Burden

In this section, we will calculate the CPB associated with advising all women of reproductive age to take a daily supplement containing 0.4 to 0.8 mg (400-800µg) of folic acid.

In estimating CPB, we made the following assumptions:

What are Neural Tube Defects?

- "NTDs are major birth defects of the brain and spine that occur early in pregnancy as a result of improper closure of the embryonic neural tube, which can lead to death or varying degrees of disability. The two most common NTDs are anencephaly and spina bifida." [867]
- Anencephaly is a serious birth defect in which a baby is born without parts of the brain and skull.
- "Spina bifida is a congenital malformation in which the spinal column is split (bifid) as a result of failed closure of the embryonic neural tube, during the fourth week post-fertilization."[868]
- NTDs are caused by a variety of genetic and non-genetic factors, although the contributing role of each is not fully known. Between 10% and 60% of NTDs have a genetic component. Lack of folic acid is perhaps the best known risk factor but there are a number of potential behavioural and environmental risk factors, such as alcohol use, smoking, poor nutrition, valproic acid use and indoor air pollution. Consequently, some women who take folic acid supplements in the periconceptional period still experience NTD-affected pregnancies.[869]
- The WHO has wrestled with determining what proportion of NTDs are preventable given optimal (<906 nmol/L) red blood cell folate concentrations in the population. If

[866] Bibbins-Domingo K, Grossman D, Curry S et al. Folic acid supplementation for the prevention of neural tube defects: US Preventive Services Task Force recommendation statement. *Journal of American Medical Association*. 2017; 317(2): 183-9.
[867] Williams J, Mai C, Mulinare J et al. Updated estimates of neural tube defects prevented by mandatory folic acid fortification - United States, 1995–2011. *Morbidity and Mortality Weekly Report*. 2015; 64(1): 1-5.
[868] Copp A, Adzick N, Chitty L et al. Spina bifida. *Nature Reviews Disease Primers*. 2015; 1: 1-45.
[869] Ibid.

these levels are uniformly achieved, the rate of NTDs could fall somewhere within the range of 4 to 9 per 10,000 live births.[870, 871]

Prevalence of Neural Tube Defects

- Between 1993 and 2002, a total of 2,446 NTDs were among live births, still births and terminations of pregnancies in seven Canadian Provinces.[872] Of the 2,446 neural tube defects identified in seven Canadian provinces between 1993 and 2002, 1,466 (60%) were terminations of pregnancy, 112 (5%) were stillbirth and 868 (35%) were live birth. The majority of NTDs were either spina bifida (53%) or anencephaly (34%) (see Table 1).[873]

Table 1: NTDS by Diagnostic Category and Pregnancy Outcome In Seven Canadian Provinces, 1993 to 2002.

	Pregnancy Outcome				
Diagnostic Category	Induced Abortion	Stillbirth	Live Birth	Total	% of Total
Spina bifida	595	35	656	1,286	53%
Anencephaly	668	67	95	830	34%
Encephalocele	160	8	115	283	12%
Unspecified NTD	24	0	0	24	1%
Iniencephaly	19	2	2	23	1%
All NTDs	**1,466**	**112**	**868**	**2,446**	
% of Total	60%	5%	35%		

- Based on data from these seven provinces between January 1, 1993 and September 30, 1997, the prevalence of NTDs among live births, still births and terminations of pregnancies was 15.8 per 10,000 live births.[874] BC's rate, at 9.6 per 10,000, was the lowest of the seven provinces (see Table 2).

Table 2: Prevalance of NTDS / 10,000 Births In Seven Canadian Provinces January 1, 1993 to September 30, 1997

Province	**Rate**
N/L	45.6
NS	27.2
PEI	20.8
PQ	17.7
MB	15.4
AB	11.2
BC	9.6
Combined	**15.8**

[870] World Health Organization. *Guideline: Optimal Serum and Red Blood Cell Folate Concentrations in Women of Reproductive Age for Prevention of Neural Tube Defects*. 2015. World Health Organization. Available at http://www.who.int/iris/handle/10665/161988. Accessed February 2017.

[871] Tinker S, Hamner H, Qi Y et al. US women of childbearing age who are at possible increased risk of a neural tube defect-affected pregnancy due to suboptimal red blood cell folate concentrations, National Health and Nutrition Examination Survey 2007 to 2012. *Birth Defects Research Part A: Clinical and Molecular Teratology*. 2015; 103(6): 517-26.

[872] The seven provinces include Newfoundland & Labrador, Prince Edward Island, Nova Scotia, Quebec, Manitoba, Alberta and British Columbia.

[873] De Wals P, Tairou F, Van Allen M et al. Reduction in neural-tube defects after folic acid fortification in Canada. *New England Journal of Medicine*. 2007; 357(2): 135-42.

[874] Ibid.

Evidence of the Effectiveness of Folic Acid Supplementation in Reducing the Prevalence of NTDs

- In Hungary in the mid-1980s, 7,540 women planning to conceive were randomly assigned to receive a prenatal vitamin supplement (including 0.8 mg of folic acid) or a trace element supplement, starting one month prior to conception and for three months after conception. In the evaluation of 4,704 pregnancies and 4,122 live births, 28 congenital malformations were observed in the experimental group vs. 47 in the control group. Six of the congenital malformations in the control group were neural-tube defects (NTDs) vs. none in the experimental group.[875] Given the results of this trial, RCTs are no longer considered ethically possible because of the clear benefits of folic acid supplementation.[876]

- Other cohort and case control studies completed between 1976 and 1998 consistently found evidence of a protective effect associated with folic acid supplementation.[877]

- Case control studies since 1998 have not consistently demonstrated a protective association with folic acid supplementation, but these studies tend to be weakened by misclassification and recall bias.[878]

Fortification of Grain Products with Synthetic Folic Acids

- The evidence of the effectiveness of folic acid supplementation in reducing the prevalence of NTDs noted above led to a 1992 recommendation by the US Public Health Service that all women of childbearing age consume 400µg (0.4 mg) of folic acid daily, followed by the US Food and Drug Administration authorization to add synthetic folic acid to grain products in March of 1996 with mandatory compliance by January of 1998.[879]

- In Canada, the milling industry began fortification early in 1997 to meet US requirements for imported flour. On November 11, 1998, fortification of all types of white flour, enriched pasta and cornmeal became mandatory in Canada.[880, 881]

- The prevalence of NTDs among live births, still births and terminations of pregnancies declined from 10.7 cases per 10,000 live births before the implementation of food fortification in the US (1995 to 1996) to 7.0 cases per 10,000 live births after fortification.[882]

- In Canada, the prevalence of neural tube defects among live births, still births and terminations of pregnancies decreased from 15.8 to 8.6 per 10,000 live births between January 1, 1993 and December 31, 2002 (see Table 3).[883] The time period was divided into three 'fortification' periods. The pre-fortification period ran from January 1, 1993 to September 30, 1997 to coincide with the beginning of flour

[875] Czeizel A and Dudás I. Prevention of the first occurrence of neural-tube defects by periconceptional vitamin supplementation. *New England Journal of Medicine*. 1992; 327(26): 1832-5.
[876] Viswanathan M, Treiman K, Kish-Doto J et al. Folic acid supplementation for the prevention of neural tube defects: an updated evidence report and systematic review for the US Preventive Services Task Force. *Journal of American Medical Association*. 2017; 317(2): 190-203.
[877] Ibid.
[878] Ibid.
[879] Williams L, Mai C, Edmonds L et al. Prevalence of spina bifida and anencephaly during the transition to mandatory folic acid fortification in the United States. *Teratology*. 2002; 66(1): 33-9.
[880] De Wals P, Tairou F, Van Allen M et al. Reduction in neural-tube defects after folic acid fortification in Canada. *New England Journal of Medicine*. 2007; 357(2): 135-42.
[881] Ray J. Efficacy of Canadian folic acid food fortification. *Food and Nutrition Bulletin*. 2008; 29(2): S225-30.
[882] Williams J, Mai C, Mulinare J et al. Updated estimates of neural tube defects prevented by mandatory folic acid fortification - United States, 1995–2011. *Morbidity and Mortality Weekly Report*. 2015; 64(1): 1-5.
[883] De Wals P, Tairou F, Van Allen M et al. Reduction in neural-tube defects after folic acid fortification in Canada. *New England Journal of Medicine*. 2007; 357(2): 135-42.

fortification in Canada. The partial fortification period ran from October 1, 1997 to March 31, 2000 based on evidence from Ontario that red-cell folate levels in the population started to increase in April 1997 and reached a plateau in February 1999.[884] The full fortification period ran from April 1, 2000 to December 31, 2002. The biggest reduction between the pre-fortification and full fortification periods was observed in Newfoundland and Labrador (from 45.6 to 7.6 per 10,000) while the smallest reduction was observed in BC (from 9.6 to 7.5 per 10,000). BC already had the lowest prevalence of NTDs (at 9.6 per 10,000) in the country before fortification (see Table 3).

Table 3: Prevalance of NTDS / 10,000 Births In Seven Canadian Provinces According to Fortification Period

	Fortification Period		
Province	Prefortification	Partial Fortification	Full Fortification
N/L	45.6	14.2	7.6
NS	27.2	13.2	12.6
PEI	20.8	10.6	0.0
PQ	17.7	12.7	9.7
MB	15.4	8.8	9.3
AB	11.2	7.3	6.7
BC	9.6	10.8	7.5
Combined	**15.8**	**10.9**	**8.6**

- The prevalence of neural tube defects among live births, still births and terminations of pregnancies declined from 11.3 cases per 10,000 live births before the implementation of food fortification in Ontario (1994 to 1997) to 5.8 cases per 10,000 live births after fortification (1998 to 2000).[885] Ontario's data was not included in Tables 1 to 3 because the review by De Wals et al. focussed on seven provinces rather than all of Canada.

Modelling in a BC Birth Cohort of 40,000

- Based on BC life tables for 2010 to 2012, an estimated 19,672 females would survive through to age 44 in a BC birth cohort of 40,000 (see Table 4). Note that the birth cohort includes both males and females. Our analysis focusses on just the females of reproductive age in this cohort. Based on age specific fertility rates,[886] an estimated 28,110 live births would occur between the ages of 15 and 44 in this cohort of females (see Table 4).

- For modelling purposes, we have assumed that the pre-fortification rate of NTDs in BC would be approximately 11 / 10,000 live births, followed by a rate of 7.5 / 10,000 live births post-fortification (see Table 3). We have chosen the higher rate of 10.8 (rounded to 11) seen during the partial fortification period in BC (see Table 3) rather than the 9.6 seen during prefortification as a conservative approach (recognizing that the lower 9.6 seen during prefortification in BC may be an anomaly as the rate was reduced from prefortification to partial fortification in all provinces except BC). Furthermore, we have assumed that this could be further reduced to 5.8 / 10,000 live

[884] Ray J, Vermeulen M, Boss S et al. Declining rate of folate insufficiency among adults following increased folic acid food fortification in Canada. *Canadian Journal of Public Health*. 2002; 93(4): 249-53.
[885] Ray J, Meier C, Vermeulen M et al. Association of neural tube defects and folic acid food fortification in Canada. *The Lancet*. 2002; 360(9350): 2047-8.
[886] See http://www.bcstats.gov.bc.ca/StatisticsBySubject/Demography/VitalStatistics.aspx. Accessed February 2017.

births based on Ontario's full fortification rate noted above.[887] In the sensitivity analysis, we modelled the effect of reducing this rate to 4.0 / 10,000, the lowest range considered achievable by the WHO given optimal red blood cell folate concentrations in the population.[888]

- We have also assumed that 39% (830 of 2,116) of pregnancies with NTD would be anencephaly and 61% (1,286 of 2,116) spina bifida (see Table 1). Furthermore, 11.4% of pregnancies with anencephaly and 51% of pregnancies with spina bifida would result in a live birth (see Table 1). Based on these assumptions, an estimated 9.6 live births with spina bifida would have occurred in the birth cohort pre-fortification. The estimated post-fortification status would be 6.5 live births with spina bifida with the potential to be further reduced to 5.1 live births with spina bifida if Ontario's rate of 5.8 / 10,000 were achieved (see Table 4). Likewise, an estimated 0.9 live births with anencephaly would occur post-fortification with the potential to reduce this to 0.7 live births with anencephaly if Ontario's rate of 5.8 / 10,000 were achieved (see Table 4).

Table 4: Females Ages 15-44, Live Births and Pregnancies with Neural Tube Defects
in a British Columbia Birth Cohort of 40,000

					Estimated Prefortification Status					***Estimated Current Status***					***Estimated Potential Status***				
Age **Group**	*Mean Survival* Females	*Females in Birth Cohort*	*Life Years Lived*	# of Live Births	Est. # of NTDs	Anen-cephaly	Spina Bifida	*Live Birth with* Anen-cephaly	Spina Bifida	Est. # of NTDs	Anen-cephaly	Spina Bifida	*Live Birth with* Anen-cephaly	Spina Bifida	Est. # of NTDs	Anen-cephaly	Spina Bifida	*Live Birth with* Anen-cephaly	Spina Bifida
15-19	0.995	19,900	99,499	759	0.8	0.3	0.5	0.0	0.3	0.6	0.2	0.3	0.0	0.2	0.4	0.2	0.3	0.0	0.1
20-24	0.993	19,868	99,339	3,241	3.6	1.4	2.2	0.2	1.1	2.4	1.0	1.5	0.1	0.8	1.9	0.7	1.1	0.1	0.6
25-29	0.992	19,836	99,179	7,489	8.2	3.2	5.0	0.4	2.6	5.6	2.2	3.4	0.3	1.7	4.3	1.7	2.6	0.2	1.3
30-34	0.990	19,799	98,997	9,894	10.9	4.3	6.6	0.5	3.4	7.4	2.9	4.5	0.3	2.3	5.7	2.3	3.5	0.3	1.8
35-39	0.987	19,748	98,738	5,575	6.1	2.4	3.7	0.3	1.9	4.2	1.6	2.5	0.2	1.3	3.2	1.3	2.0	0.1	1.0
40-44	0.984	19,672	98,358	1,153	1.3	0.5	0.8	0.1	0.4	0.9	0.3	0.5	0.0	0.3	0.7	0.3	0.4	0.0	0.2
Total			**594,110**	**28,110**	**30.9**	**12.1**	**18.8**	**1.4**	**9.6**	**21.1**	**8.3**	**12.8**	**0.9**	**6.5**	**16.3**	**6.4**	**9.9**	**0.7**	**5.1**

- A 2015 Cochrane Review found that there is high quality evidence that daily folic acid supplementation (alone or in combination with other vitamins and minerals) prevents NTDs when compared with no intervention/placebo or vitamins and minerals without folic acid (RR of 0.31, 95% CI of 0.17 to 0.58). The review also found no evidence of an increase in cleft palate, cleft lip, congenital cardiovascular defects, miscarriages or any other birth defects associated with daily folic acid supplementation.[889]
- The 2017 USPSTF review found no significant evidence of potential harms associated with folic acid supplementation.[890]

[887] Ray J, Meier C, Vermeulen M et al. Association of neural tube defects and folic acid food fortification in Canada. *The Lancet*. 2002; 360(9350): 2047-8.
[888] World Health Organization. *Guideline: Optimal Serum and Red Blood Cell Folate Concentrations in Women of Reproductive Age for Prevention of Neural Tube Defects*. 2015. World Health Organization. Available at http://www.who.int/iris/handle/10665/161988. Accessed February 2017.
[889] De-Regil L, Peña-Rosas J, Fernández-Gaxiola A et al. Effects and safety of periconceptional oral folate supplementation for preventing birth defects. *Cochrane Database of Systematic Reviews.* 2015.
[890] Bibbins-Domingo K, Grossman D, Curry S et al. Folic acid supplementation for the prevention of neural tube defects: US Preventive Services Task Force recommendation statement. *Journal of American Medical Association*. 2017; 317(2): 183-9.

- "Spina bifida results from the incomplete closure of the tissue and bone surrounding the spinal cord. Children born with spina bifida can have mild to severe disabilities depending on the location of the lesion along the spinal cord."[891]
- The mortality rate is substantially higher for individuals with moderate to severe spina bifida than for less severe cases. Oakeshott and colleagues have followed a cohort of individuals with spina bifida for 50 years and found that just 12% with moderate to severe spina bifida survived to age 50, while 54% of those with less severe spina bifida survived to age 50.[892, 893]
- We used this survival data to compare life expectancy in the general population vs. a population with a sacral lesion (least severe) or a lumbar lesion (moderate to severe) (see Table 5). If we use 100% to represent the normal life-span of the general population, a person with a sacral lesion will have a life expectancy of 60.6% (or a loss of 39.4% of a normal life expectancy, Table 6, row *m*) and a person with a lumbar lesion will have a life expectancy of 25.1% (or a loss of 74.9% of a normal life expectancy, Table 6, row *n*).

Table 5: Survival and Year of Life in a Birth Cohort of 40,000
The General Population Compared to Individuals with Spina Bifida

						Individuals with Spina Bifida					
	General Population					**Lower Lesion (less severe)**			***Higher Lesion (more severe)***		
Age Group	Mean Survival Rate Male	Female	Total	Individuals in Birth Cohort	Years of Life in Birth	Mean Survival Rate	Individuals in Birth Cohort	Years of Life in Birth	Mean Survival Rate	Individuals in Birth Cohort	Years of Life in Birth
0-4	0.996	0.996	0.996	39,846	199,230	0.818	32,727	163,636	0.649	25,965	129,825
5-9	0.995	0.996	0.996	39,823	199,115	0.764	30,545	152,727	0.526	21,053	105,263
10-14	0.995	0.995	0.995	39,809	199,043	0.745	29,818	149,091	0.491	19,649	98,246
15-19	0.994	0.995	0.994	39,773	198,864	0.691	27,636	138,182	0.456	18,246	91,228
20-24	0.991	0.993	0.992	39,683	198,417	0.673	26,909	134,545	0.368	14,737	73,684
25-29	0.987	0.992	0.989	39,572	197,859	0.655	26,182	130,909	0.333	13,333	66,667
30-34	0.983	0.990	0.986	39,451	197,253	0.618	24,727	123,636	0.298	11,930	59,649
35-39	0.977	0.987	0.982	39,293	196,463	0.600	24,000	120,000	0.211	8,421	42,105
40-44	0.971	0.983	0.977	39,075	195,375	0.545	21,818	109,091	0.175	7,018	35,088
45-49	0.961	0.977	0.969	38,765	193,826	0.545	21,818	109,091	0.123	4,912	24,561
50-54	0.947	0.969	0.958	38,310	191,551	0.534	21,363	106,816	0.111	4,457	22,286
55-59	0.926	0.955	0.941	37,627	188,136	0.517	20,680	103,401	0.094	3,774	18,872
60-64	0.894	0.935	0.915	36,591	182,955	0.491	19,644	98,220	0.068	2,738	13,690
65-69	0.847	0.904	0.875	35,009	175,045	0.452	18,062	90,310	0.029	1,156	5,780
70-74	0.776	0.854	0.815	32,600	162,999	0.391	15,653	78,265		0	0
75-79	0.673	0.777	0.725	28,992	144,961	0.301	12,045	60,226		0	0
80+	0.531	0.659	0.595	23,809	119,047	0.172	6,862	34,312		0	0
Total					**3,140,140**			**1,902,458**			**786,945**
% Compared to General Population								60.6%			25.1%

[891] Tilford J, Grosse S, Robbins J et al. Health state preference scores of children with spina bifida and their caregivers. *Quality of Life Research*. 2005; 14(4): 1087-98.
[892] Oakeshott P, Hunt G, Poulton A et al. Expectation of life and unexpected death in open spina bifida: a 40-year complete, non-selective, longitudinal cohort study. *Developmental Medicine & Child Neurology*. 2009; 52(8): 749-53.
[893] Oakeshott P, Reid F, Poulton A et al. Neurological level at birth predicts survival to the mid-40s and urological deaths in open spina bifida: a complete prospective cohort study. *Developmental Medicine & Child Neurology*. 2015; 57(7): 634-8.

- The research by Oakeshott and colleagues was based on 117 consecutive infants born with spina bifida between 1963 and 1971 in the UK who have been followed until 2013. Of these 117 infants, 40 (34%) died before the age of 5.[894] The 1-year survival of infants born with spina bifida in the US has improved from 87.1% during 1983 to 1987 to 93.6% during 1998 to 2002.[895] To take into account the possibility of better long-term survival of infants currently born with spina bifida, we increased the calculated life expectancy of infants with both a sacral (Table 6, row *m*) and lumbar lesion (Table 6, row *n*) by 25% in the sensitivity analysis.
- Based on a consecutive cohort of 117 children with spina bifida in the UK, the distribution of children were 33.9% (Table 6, row *g*) with a sacral lesion, 28.6% (Table 6, row *h*) with a lower lumbar lesion and 37.5% (Table 6, row *i*) with a higher lumbar lesion.[896]
- Based on a study of 98 children with spina bifida in Arkansas, the average loss in QoL associated with spina bifida was 41%, ranging from 34% (6% to 62%) for the sacral lesion (Table 6, row *j*), 42% (22% to 62%) for the lower lumbar lesion (Table 6, row *k*) and 52% (25% to 78%) for the upper lumbar lesion (Table 6, row *l*). We used plus or minus one standard deviation provided by Tilford et al. in the sensitivity analysis.[897] There was also a modest 5% reduction in the QoL of caregivers. This reduction, however, was only significantly different from control caregivers for the group of parents caring for the most severe children (10% reduction in QoL). A subsequent, more in depth analysis of these caregivers identified less sleep and less frequent engagement in leisure and social activities as key differences compared with a sample of control caregivers.[898]
- Verhoef and colleagues used the SF-36 to compare the QoL in 164 young adults (ages 16 to 25) with spina bifida in Holland. Compared to the average Dutch population ages 16-25, young adults with spina bifida experienced a significant decrement in physical functioning (51%), role limitations due to physical health problems (22%), bodily pain (9%) and general health (17%). No significant differences were observed in vitality, social functioning and role limitations due to emotional health problems or mental health.[899]
- The life expectancy of an infant born in BC of 82.2 years (Table 6, row *o*) is based on life tables for 2010 to 2012 for BC.
- De Wals and colleagues found that there were 656 live births with spina bifida in seven Canadian provinces between 1993 and 2002. At the same time, 1,466 pregnancies with a diagnosed NTD resulted in an induced abortion (see Table 1).[900]

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[894] Oakeshott P, Reid F, Poulton A et al. Neurological level at birth predicts survival to the mid-40s and urological deaths in open spina bifida: a complete prospective cohort study. *Developmental Medicine & Child Neurology*. 2015; 57(7): 634-8.

[895] Shin M, Kucik J, Siffel C et al. Improved survival among children with spina bifida in the United States. *Journal of Pediatrics*. 2012; 161(6): 1132-7.e3.

[896] Oakeshott P, Hunt G, Poulton A et al. Expectation of life and unexpected death in open spina bifida: a 40-year complete, non-selective, longitudinal cohort study. *Developmental Medicine & Child Neurology*. 2009; 52(8): 749-53.

[897] Tilford J, Grosse S, Robbins J et al. Health state preference scores of children with spina bifida and their caregivers. *Quality of Life Research*. 2005; 14(4): 1087-98.

[898] Grosse S, Flores A, Ouyang L et al. Impact of spina bifida on parental caregivers: findings from a survey of Arkansas families. *Journal of Child and Family Studies*. 2009; 18(5): 574-81.

[899] Verhoef M, Post M, Barf H et al. Perceived health in young adults with spina bifida. *Developmental Medicine & Child Neurology*. 2007; 49(3): 192-7.

[900] De Wals P, Tairou F, Van Allen M et al. Reduction in neural-tube defects after folic acid fortification in Canada. *New England Journal of Medicine*. 2007; 357(2): 135-42.

We have assumed that for every live birth with spina bifida avoided, an estimated 2.23 abortions (1,466 / 656) would be avoided.

- Other assumptions used in assessing the clinically preventable burden are detailed in the Reference Document.

Based on these assumptions, the CPB associated with advising all women who are planning or capable of pregnancy to take a daily supplement containing 0.4 to 0.8 mg (400-800µg) of folic acid is 95 QALYs (see Table 6, row *ac*). The 95 QALYs is based on moving from the current NTD rate in BC of 7.5 per 10,000 births to 5.8 per 10,000 births, the post fortification rate observed in Ontario.

Table 6: CPB Associated with Advising Women Ages 15 to 44 to Take a Daily Supplement Containing 0.4 to 0.8 mg of Folic Acid in a Birth Cohort of 40,000

Row Label	Variable	Base Case	Data Source
a	Average # of females ages 15-44 in birth cohort	19,767	Table 4
b	Life years lived between the ages of 15 and 44	594,110	Table 4
c	Live births between the ages of 15 and 44	28,110	Table 4
d	Estimated live births with spina bifida prefortification	9.6	Table 4
e	Estimated live births with spina bifida currently	6.5	Table 4
f	Estimated potential live births with spina bifida post fortification	5.1	Table 4
g	Proportion of children with spina bifida with a sacral lesion (least severe)	33.9%	√
h	Proportion of children with spina bifida with a lower lumbar lesion	28.6%	√
i	Proportion of children with spina bifida with a higher lumbar lesion (most severe)	37.5%	√
j	Loss in QoL with a sacral lesion	34.0%	√
k	Loss in QoL with a lower lumbar lesion	42.0%	√
l	Loss in QoL with a upper lumbar lesion	52.0%	√
m	Reduction in life expectancy with a sacral lesion	39.4%	√
n	Reduction in life expectancy with a lumbar lesion	74.9%	√
o	Average life expectancy in BC at birth (in years)	82.2	√
p	Births with sacral lesion spina bifida avoided (9.6 to 5.1)	1.5	= (d - f) * g
q	Births with lumbar lesion spina bifida avoided (9.6 to 5.1)	3.0	= (d - f) - p
r	Life years gained due to sacral lesion spina bifida avoided	49.8	= m * o * p
s	Life years gained due to lumbar lesion spina bifida avoided	184.4	= n * o * q
t	QALYs gained due to sacral lesion spina bifida avoided	26.0	= p * (1 - m) * o * j
u	QALYs gained due to lumbar lesion spina bifida avoided	29.0	= q * (1 -n) * o * (k + l) / 2
v	**Total QALYs gained due to spina bifida avoided (9.6 to 5.1)**	**289**	= r + s + t + u
w	Births with sacral lesion spina bifida avoided (6.5 to 5.1)	0.5	= (e - f) * g
x	Births with lumbar lesion spina bifida avoided (6.5 to 5.1)	1.0	= (e - f) - w
y	Life years gained due to sacral lesion spina bifida avoided	16.3	= m * o * w
z	Life years gained due to lumbar lesion spina bifida avoided	60.3	= n * o * x
aa	QALYs gained due to sacral lesion spina bifida avoided	8.5	= w * (1 - m) * o * j
ab	QALYs gained due to lumbar lesion spina bifida avoided	9.5	= x * (1 -n) * o * (k + l) / 2
ac	**Total QALYs gained due to spina bifida avoided (6.5 to 5.1)**	**95**	= y + z + aa + ab

√ = Estimates from the literature

For our sensitivity analysis, we modified a number of major assumptions and recalculated the CPB as follows:

- Assume that the loss in QoL associated with a sacral lesion is reduced from 34% to 6% (Table 6, row *j*), the loss in QoL associated with a lower lumbar lesion is reduced from 42% to 22% (Table 6, row *k*) and the loss in QoL associated with an upper lumbar lesion is reduced from 52% to 25% (Table 6, row *l*): CPB = 83.

- Assume that the loss in QoL associated with a sacral lesion is increased from 34% to 62% (Table 6, row *j*), the loss in QoL associated with a lower lumbar lesion is

increased from 42% to 62% (Table 6, row *k*) and the loss in QoL associated with an upper lumbar lesion is increased from 52% to 78% (Table 6, row *l*): CPB = 106.

- Assume that the reduction in life expectancy with either a sacral and lumbar lesion is increased by 25%, giving people with spina bifida a longer lifespan. (Table 6, rows *m* & *n*): CPB = 105.
- Reduce the incidence of NTDs from 5.8 to 4.0 / 10,000 live births: CPB = 194.

Modelling Cost-Effectiveness

In this section, we will calculate the CE associated with advising all women of reproductive age to take a daily supplement containing 0.4 to 0.8 mg (400-800µg) of folic acid.

In estimating CE, we made the following assumptions:

- Approximately half of all pregnancies are unplanned. Therefore clinicians should advise all women who are capable of pregnancy to take daily folic acid supplements.[901]
- In a survey of 499 women, the majority (95%) indicated that they prefer to receive information about preconception health from their primary care physician. Only 39% of these women, however, could recall their physician ever discussing this topic.[902]
- Mazza and colleagues in Australia found that low levels of engagement between primary care providers and women regarding preconception care are due to a number of perceived barriers, including "time constraints, the lack of women presenting at the preconception stage, the numerous competing preventive priorities within the general practice setting, issues relating to the cost of and access to preconception care, and the lack of resources for assisting in the delivery of preconception care guidelines."[903]
- Does a clinician's advice increase the uptake of daily folic acid supplements during the periconceptional period? In a study of 1,173 women with a median age of 32 in the UK, 51% reported receiving advice on issues such as smoking, alcohol use, healthy diet and folic acid intake from a health professional prior to becoming pregnant. Women who received this advice were significantly more likely to take folic acid supplements (76%) than women who did not receive this advice (37%).[904]
- For modelling purposes, we assumed that 70% (ranging from 60% to 80% in the sensitivity analysis) (Table 7, row *b*) of clinicians would advise women ages 15 to 44 to take a daily supplement containing 0.4 to 0.8 mg of folic acid and that 76% (ranging from 66% to 86%) (Table 7, row *e*) of women would follow this advice.
- For modelling purposes, we assumed this advice would need to be given every three years (Table 7, row *c*) and modified this from every one to five years in the sensitivity analysis.

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[901] Bibbins-Domingo K, Grossman D, Curry S et al. Folic acid supplementation for the prevention of neural tube defects: US Preventive Services Task Force recommendation statement. *Journal of American Medical Association*. 2017; 317(2): 183-9.

[902] Frey K and Files J. Preconception healthcare: what women know and believe. *Maternal and Child Health Journal*. 2006; 10(1): 73-7.

[903] Mazza D, Chapman A and Michie S. Barriers to the implementation of preconception care guidelines as perceived by general practitioners: a qualitative study. *BioMed Central Health Services Research*. 2013; 13(36): 1-8.

[904] Stephenson J, Patel D, Barrett G et al. How do women prepare for pregnancy? Preconception experiences of women attending antenatal services and views of health professionals. *Plos One*. 2014; 9(7): e103085.

- **Cost of folic acid supplements** – The cost of folic acid supplements averages $0.043 per tablet at London Drugs.[905] We assumed an annual cost of $15.70 (Table 7, row g).
- **Costs avoided** – Average incremental medical expenditures comparing patients with spina bifida and those without are $41,460 (in 2003 USD) in the first year of life, $14,070 per year from ages 1 -17, $13,339 per year from ages 18-44 and $10,134 per year from ages 45-64.[906]
- Based on a study of the same 98 children and their caregivers, the caregivers worked an average of 7.5 to 11.3 hours less per week (depending on their children's disability severity) than matched control caregivers.[907]
- Grosse and co-authors estimated the lifetime costs associated with spina bifida to be $791,900 (in 2014 USD). This includes $513,500 in medical costs, $63,500 in special education and developmental service costs and $214,900 in parental time costs.[908] We converted the medical costs to equivalent 2017 Canadian costs; $454,745 in medical costs (Table 7, row *r*), $79,203 in special education and developmental service costs (Table 7, row *s*) and $268,043 in parental time costs (Table 7, row *t*).[909]
- Parental time costs are excluded from the base model (Table 7, row *t*) but included in the sensitivity analysis. The literature on 'spillover effects' (e.g. when the illness of a child or family member has an economic or quality of life impact on the broader family or caregiver(s) is nascent and further work is required before these effects can be relied upon with confidence.[910,911]
- For every live birth with spina bifida avoided, an estimated 2.23 abortions would be avoided (Table 7, row *v*). The cost of an abortion is estimated at $609 (Table 7, row *w*).[912]
- Anencephaly is uniformly fatal. However, an estimated 11.4% of pregnancies with anencephaly result in live births (Table 1). These infants survive an average of 2.11 days.[913] According to the Canadian Institute for Health Information's *Patient Cost Estimator*, the average cost per day in BC in 2014 for CMG 599 (Neonate 2500+ grams, ages 0-28 days, other major problem) was $2,085.[914] We therefore calculated

[905] See http://www.londondrugs.com/search/?q=Folic+acid&lang=default. Accessed February 2017.
[906] Ouyang L, Grosse S, Armour B et al. Health care expenditures of children and adults with spina bifida in a privately insured US population. *Birth Defects Research Part A: Clinical and Molecular Teratology*. 2007; 79(7): 552-8.
[907] Tilford J, Grosse S, Goodman A et al. Labor market productivity costs for caregivers of children with spina bifida: a population-based analysis. *Medical Decision Making*. 2009; 29(1): 23-32.
[908] Grosse S, Berry R, Tilford J et al. Retrospective assessment of cost savings from prevention: folic acid fortification and spina bifida in the US. *American Journal of Preventive Medicine*. 2016; 50(5S1): S74-S80.
[909] Campbell and Cochrane Economics Methods Group. *CCEMG – EPPI-Centre Cost Converter*. 2016. Available at https://eppi.ioe.ac.uk/costconversion/. Accessed December 2016.
[910] Wittenberg E and Prosser L. Disutility of illness for caregivers and families: a systematic review of the literature. *Pharmacoeconomics*. 2013; 31(6): 489-500.
[911] Wittenberg E, Ritter G and Prosser L. Evidence of spillover of illness among household members EQ-5D scores from a US sample. *Medical Decision Making*. 2013; 33(2): 235-43.
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[913] Jaquier M, Klein A and Boltshauser E. Spontaneous pregnancy outcome after prenatal diagnosis of anencephaly. *British Journal of Obstetric and Gynaecology: An International Journal of Obstetrics & Gynaecology*. 2006; 113(8): 951-3.
[914] Canadian Institute for Health Information. *Patient Cost Estimator*. Available online at https://www.cihi.ca/en/spending-and-health-workforce/spending/patient-cost-estimator. Accessed January 2017

an avoided cost of $4,399 (2.11 * $2,085) per anencephaly live birth avoided (Table 7, row *p*).

- Other costs incurred or avoided and assumptions used in assessing cost-effectiveness are detailed in the Reference Document.
- Discount rate of 1.5%, varied from 0% to 3% in the sensitivity analysis.

Based on these assumptions, the CE associated with advising all women of reproductive age to take a daily supplement containing 0.4 to 0.8 mg (400-800µg) of folic acid is $195,379 / QALY (Table 7, row *ad*).

Table 7: CE Associated with Advising Women Ages 15 to 44 to Take a Daily Supplement Containing 0.4 to 0.8 mg of Folic Acid in a Birth Cohort of 40,000

Row Label	Variable	Base Case	Data Source
a	Life years lived between the ages of 15 and 44	594,110	Table 6, row b
b	Clinician adherence in offering advice re: folic acid supplementation	70%	Assumed
c	Frequency of offering advice re: folic acid supplementation (every x years)	3	Assumed
d	Life years covered by advice re: folic acid supplementation	415,877	= a * b
e	Proportion of women taking folic acid supplementation after receiving advice	76%	√
f	Life years covered by folic acid supplementation	316,067	= d * e
g	Annual cost of folic acid supplementation	$15.70	√
h	Cost of folic acid supplementation	$4,962,244	= f * g
i	Cost of 10-minute office visit	$34.85	√
j	Portion of 10-minute office visit for offering advice	50%	Assumed
k	Costs of office visits	$2,415,552	= (d / c) * i * j
l	Patient time required per office visit (hours)	2	Assumed
m	Value of patient time (per hour)	$29.69	√
n	Value of patient time and travel for intervention	$4,115,796	= (d / c) * l * m * j
o	**Estimated cost of the intervention**	**$11,493,593**	= h + k + n
p	Medical care costs avoided per anencephaly live birth avoided	-$4,399	√
q	Cases of anencephaly live births avoided with intervention	0.21	Table 4
r	Medical care costs avoided per case of spina bifida avoided	-$454,745	√
s	Special education and developmental service costs avoided per case of spina bifida avoided	-$79,203	√
t	Parental time costs avoided per case of spina bifida avoided	$0	√
u	Cases of spina bifida avoided with intervention	1.48	Table 6, row w + x
v	Abortions avoided per spina bifida live birth	2.23	√
w	Costs avoided per abortion avoided	-$609	√
	CE Calculation		
x	Cost of intervention over lifetime of birth cohort	$11,493,593	= o
y	Costs avoided over lifetime of birth cohort	-$793,981	= ((r + s + t) * u)+(u * v * w)+(p * q)
z	QALYs saved	95	Table 6, row ac
aa	Cost of intervention over lifetime of birth cohort (1.5% discount)	$11,493,593	Calculated
ab	Costs avoided over lifetime of birth cohort (1.5% discount)	-$697,164	Calculated
ac	QALYs saved (1.5% discount)	55	Calculated
ad	**CE ($/QALY saved)**	**$195,379**	= (aa + ab) / ac

√ = Estimates from the literature

For our sensitivity analysis, we modified a number of major assumptions and recalculated the CE as follows:

- Assume that the loss in QoL associated with a sacral lesion is reduced from 34% to 6% (Table 6, row *j*), the loss in QoL associated with a lower lumbar lesion is reduced from 42% to 22% (Table 6, row *k*) and the loss in QoL associated with an upper lumbar lesion is reduced from 52% to 25% (Table 6, row *l*): CE = $223,110.

- Assume that the loss in QoL associated with a sacral lesion is increased from 34% to 62% (Table 6, row *j*), the loss in QoL associated with a lower lumbar lesion is increased from 42% to 62% (Table 76 row *k*) and the loss in QoL associated with an upper lumbar lesion is increased from 52% to 78% (Table 6, row *l*): CE = $173,945.
- Assume that the reduction in life expectancy with either a sacral and lumbar lesion is increased by 25% (Table 6, rows *m* & *n*): CE = $175,564.
- Reduce the incidence of NTDs from 5.8 to 4.0 / 10,000 live births: CE = $88,410.
- Assume that clinician adherence in offering advice re: folic acid supplementation is reduced from 70% to 60% (Table 7, row *b*): CE = $165,666.
- Assume that clinician adherence in offering advice re: folic acid supplementation is increased from 70% to 80% (Table 7, row *b*): CE = $225,093.
- Assume that the frequency of offering advice re: folic acid supplementation is increased from every 3 years to every year (Table 7, row *c*): CE = $431,720.
- Assume that the frequency of offering advice re: folic acid supplementation is decreased from every 3 years to every 5 years (Table 7, row *c*): CE = $148,101.
- Assume the proportion of women taking folic acid supplementation after receiving advice is decreased from 76% to 66% (Table 7, row *e*): CE = $183,563.
- Assume the proportion of women taking folic acid supplementation after receiving advice is increased from 76% to 86% (Table 7, row *e*): CE = $207,195.
- Assume that the portion of 10-minute office visit required for offering advice is reduced from 50% to 33% (Table 7, row *j*): CE = $155,193.
- Assume that the portion of 10-minute office visit required for offering advice is increased from 50% to 66% (Table 7, row *j*): CE = $233,202.
- Include parental time costs avoided per case of spina bifida avoided (Table 7, row *t*): CE = $189,069

Summary

Applying a 1.5% discount rate, the clinically preventable burden (CPB) associated with advising all women of reproductive age to take a daily supplement containing 0.4 to 0.8 mg (400-800µg) of folic acid is estimated to be 55 quality-adjusted life years (QALYs) while the cost-effectiveness (CE) is estimated to result in cost savings of $195,379 per QALY (see Table 8).

Table 8: Advising Women Ages 15 to 44 to Take a Daily Supplement Containing 0.4 to 0.8 mg of Folic Acid in a Birth Cohort of 40,000

Summary

	Base Case	Range	
CPB (Potential QALYs Gained)			
1.5% Discount Rate	**55**	48	114
3% Discount Rate	35	31	72
0% Discount Rate	95	83	195
CE ($/QALY) **including** patient* time costs			
1.5% Discount Rate	**$195,379**	$88,410	$431,770
3% Discount Rate	$310,525	$141,800	$683,392
0% Discount Rate	$113,155	$50,643	$251,301
CE ($/QALY) **excluding** patient time costs			
1.5% Discount Rate	$120,897	$52,233	$208,324
3% Discount Rate	$193,042	$84,736	$330,943
0% Discount Rate	$69,628	$29,501	$120,720

** Patient time costs do not normally include caregiver time costs (spillover effects). In this model, however, we have included caregiver time costs but only in the sensitivity analysis and not in the base case analysis.*

While the approach modelled above involving regular clinic-based reminders for women ages 15 to 44 to take a daily supplement containing folic acid is not cost-effective, folic acid supplementation is still highly recommended before conception and throughout pregnancy. The BC Perinatal Health Program's *Maternity Care Pathway*, for example, recommends "supplementation with folic acid before conception and throughout pregnancy. Folic acid supplementation as per patient risk (0.4 mg – 5 mg per day pre pregnancy)."[915]

[915] BC Perinatal Health Program, *Maternity Care Pathway*, February 2010. Available online at http://www.perinatalservicesbc.ca/Documents/Guidelines-Standards/Maternal/MaternityCarePathway.pdf. Accessed July 2017.