Prostate Cancer Part 1: Diagnosis and Referral in Primary Care

Effective Date: April 15, 2020

Scope

This guideline provides recommendations for primary care providers for the investigation and management of adult male patients (≥19 years of age) who present with signs or symptoms that could lead to a diagnosis of prostate cancer. Recommendations include clinical assessment, the management of prostate specific antigen (PSA) test results, and the appropriate referral to a specialist. Risks and benefits of PSA testing for asymptomatic men are also addressed.

Transgender prostate cancer care is an emerging topic that is beyond the scope of this guideline.\(^1,2\) Refer to the TransCare BC Primary Care Toolkit and BC Cancer recommended resources.

Prostate Cancer Part 2: Follow-up in Primary Care addresses follow-up and post-treatment management including side effects associated with the treatment of prostate cancer, as well as how to detect and refer cases of possible recurrence.

This guideline was developed in collaboration with the BC Cancer Primary Care Program (Family Practice Oncology Network), and based on a guideline adaptation approach, including a recent systematic review of the evidence (Refer to Appendix A: Guideline Development Methodology).\(^3,4\)

Controversies in Care: There is significant debate both internationally and in British Columbia regarding the role and value of prostate cancer screening. This guideline acknowledges the divergent views and recommendations for current practice in the province. Controversies include:

- the role of PSA in prostate cancer screening (whether the benefits outweigh the harms of PSA testing of asymptomatic men), and
- the role of the digital rectal exam in prostate cancer screening.

For a more fulsome discussion, refer to the Controversies in Care section on page 5.

Key Recommendations

- The decision to use PSA testing for the early detection of prostate cancer should be individualized. Patients should be informed of the potential risks as well as the potential benefits of PSA testing.
- Not all men diagnosed with prostate cancer require immediate treatment and may undergo a program of active surveillance, which significantly reduces many harms associated with radical treatment.
- PSA testing of men without symptoms or other clinical suspicion of prostate cancer is not an insured benefit in BC under the Medical Services Plan.
- For men without a diagnosis of prostate cancer and PSA test results within the appropriate age-based reference range, further testing in less than 2 years is not indicated.
- Refer any patients with a hard or irregular prostate to urology regardless of PSA test results.
- For men taking 5-alpha reductase inhibitors (i.e., finasteride & dutasteride), PSA will drop by approximately 50%. For accurate interpretation relative to lab-reported aged-based ranges, adjust the reported result by a factor of 2.
- PSA testing should be avoided if the patient has signs or symptoms of acute prostatitis (e.g., dysuria, hematuria, pelvic/groin pain, fever/chills).
- Antibiotics should not be used in an attempt to lower PSA as this practice may be detrimental.
Epidemiology

Prostate cancer usually develops slowly. Many men with prostate cancer will not have clinical progression (i.e., symptoms or the need for additional therapies) of their cancer during their lifetime. At 10 years follow-up, 64% of men on active surveillance continue to avoid treatment. Autopsy studies suggest that prostate cancer is commonly found in men who have died of other causes (20% of men aged 50–59 and 33% in men 70–79%).

Prostate cancer accounts for 11% of all cancers diagnosed in men in BC. An expected 1 in 9 men will be diagnosed with prostate cancer in their lifetime. Of these men, 89% will be over the age of 60 when they are diagnosed and most men will survive their prostate cancer. It is estimated that 1 in 29 men who are diagnosed with prostate cancer would be expected to die of the disease.

The following risk factors are associated with an increased risk of prostate cancer and should be considered when assessing men who present with symptoms or with questions about testing:

- Men of African descent.
- Family history of prostate cancer (paternal side; first-degree relatives (i.e., father, siblings, children)).
- High-risk hereditary gene mutations associated with prostate cancer (e.g., BRCA2 genetic mutation in a first-degree relative). Refer to the BC Cancer Hereditary Cancer Program for more information about referral of men who suspect that they may have a hereditary gene mutation.

While there is little direct evidence to guide screening practices in asymptomatic men with the above risk factors, there is general consensus that these men at higher risk may consider PSA testing as early as 40 to 45 years of age and may consider re-testing every 2 years.

Diagnosis and Investigations

Most patients with early stage prostate cancer do not experience clinical symptoms. While there is an absence of highly predictive signs and symptoms of prostate cancer, lower urinary tract symptoms (LUTS) including voiding symptoms (e.g., poor stream, hesitancy, urgency, frequency, intermittent flow, and/or straining to pass urine), are common symptoms in older men and warrant investigation to rule out possible prostate cancer.

Patients with Lower Urinary Tract Symptoms (LUTS)

(Refer to Appendix B: Care Pathway – Patients with Signs and Symptoms of Possible Prostate Cancer)

1. Benign prostatic hyperplasia (BPH)

LUTS commonly indicate benign prostatic hyperplasia (BPH). Assessment for BPH includes digital rectal examination (DRE). Refer any patients with a hard or irregular prostate to urology. Primary care practitioners are encouraged to consult with specialist colleagues or the RACE line if they are in doubt regarding need for and timing of referral.

- PSA testing is a standard component of the evaluation of men with LUTS in order to rule out prostate cancer as a possible cause of LUTS, and as a relative marker of prostate size to assess the risk of BPH progression over time.
- Definitive recommendations for the diagnosis and management of BPH and LUTS are beyond the scope of this guideline.
- For men taking 5-alpha reductase inhibitors (i.e., finasteride & dutasteride), PSA will drop by approximately 50%. For accurate interpretation relative to lab-reported aged-based ranges, adjust the reported result by a factor of 2.

2. Other benign causes of LUTS

Acute Prostatitis

- PSA testing should be avoided if the patient has signs or symptoms of acute prostatitis (e.g., dysuria, hematuria, pelvic/groin pain, fever/chills).

Urinary Tract infections

- Refer to BCGuidelines: Urinary Tract Infections in the Primary Care Setting – Investigations

LUTS that are considered benign should be reconsidered when new or worsening symptoms occur.

Note: In patients presenting with LUTS, but without signs of acute prostatitis, antibiotics should not be used in attempt to lower the PSA. This practice may be detrimental (e.g., increased risk of infection after subsequent biopsy, Clostridium difficile infection, and antibiotic resistance). A drop in PSA on antibiotics does not rule out concurrent prostate cancer.
3. Potential prostate cancer
   - DRE and PSA testing should be performed for all patients initially presenting with LUTS, in the absence of more likely alternate diagnoses (e.g., acute prostatitis, urinary tract infection).
   - Refer any patients with a hard or irregular prostate to urology.
   - If PSA results are above the age-based reference ranges (refer to Table 1), and DRE is normal, consider other causes of elevated PSA (refer to Table 2), and repeat PSA testing in 4–12 weeks.
   - Persistent elevation of PSA above the age-based reference ranges should prompt a referral to urology.
   - If PSA is within age-based reference ranges and DRE is normal or consistent with BPH, then prostate cancer is unlikely.
   - Further PSA testing in less than 2 years is not indicated.

Table 1 – Age-based Reference Ranges for PSA Test Results

<table>
<thead>
<tr>
<th>Age</th>
<th>PSA Reference Ranges</th>
</tr>
</thead>
<tbody>
<tr>
<td>0–49 years</td>
<td>0–2.5 μg/L</td>
</tr>
<tr>
<td>50–59 years</td>
<td>0–3.5 μg/L</td>
</tr>
<tr>
<td>60–69 years</td>
<td>0–4.5 μg/L</td>
</tr>
<tr>
<td>≥70 years</td>
<td>0–6.5 μg/L</td>
</tr>
</tbody>
</table>

Note: There is some variation in lab reporting practices in BC, but all report a normal reference interval based on expected values in a healthy North American population. PSA values may vary significantly with regard to obesity (slightly lower than non-obese), and African American ethnicity (slightly higher than white North American ethnicity), so that these characteristics should be factored into the comparison with the reported reference intervals. The method of measurement may also cause lab to lab fluctuations of approximately 15% on the same sample and therefore the reported reference intervals should be viewed as guideposts rather than absolute delimiters of normal. In practice, if a patient result is well below the reference interval, they do not have an increased risk of prostate cancer as compared to the general population. For those with a result near the upper limit of normal, a repeat test at the same laboratory is helpful to evaluate for a significant increase (>20%) over the short term. For those patients who wish more precise information on positive and negative predictive value for prostate cancer, which takes into account ethnicity and other factors (e.g., family history & DRE findings) which may affect interpretation, use of an online calculator to determine positive predictive value is recommended.

Table 2 – Causes of Elevated PSA Other than Cancer

<table>
<thead>
<tr>
<th>Cause</th>
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<tbody>
<tr>
<td>Benign prostatic hyperplasia</td>
</tr>
<tr>
<td>Prostatitis (infection or inflammation)</td>
</tr>
<tr>
<td>Acute urinary retention</td>
</tr>
<tr>
<td>Bladder catheterization or instrumentation</td>
</tr>
</tbody>
</table>

Note: PSA levels are not significantly altered after cycling, intercourse, or digital rectal exam.
Asymptomatic Patients Presenting for Consideration of PSA Testing

PSA testing in asymptomatic men for the purpose of prostate cancer screening is controversial because of the risk of overdiagnosis and overtreatment of tumours that would not cause harm in a person's lifetime.\textsuperscript{5,27} Potential harms include biopsy complications (e.g., pain, bleeding, and infection), and treatment side-effects (e.g., erectile dysfunction and urinary incontinence) that affect quality of life.\textsuperscript{5,27} Refer to the Controversies in Care section below for more information about the risks and benefits of PSA testing in asymptomatic men.

Asymptomatic men at average risk

Asymptomatic men aged 55-69 years, who have greater than 10 years life expectancy, may decide to pursue PSA testing. An informed discussion about the risks and benefits of testing is recommended.\textsuperscript{14,27}

Refer to the Informed Discussion and Resources sections below for prostate cancer risk calculators and patient decision aids to support an informed discussion.

If an asymptomatic patient decides to undergo PSA testing and results are within the appropriate age-based reference range, further testing in less than 2 years is not indicated. This is not an insured benefit in BC under the Medical Services Plan (patient-pay, a cost of approximately $35). If a patient-pay PSA level is abnormal, repeat PSA testing is an insured benefit.

PSA testing is not indicated in asymptomatic patients <55 or >69 years of age who are without risk factors. The value of screening in men <55 years has not been adequately addressed in the large screening trials. There is likely little benefit to screening in men 70 years or older.

Asymptomatic men with risk factors

- Clinicians should consider known risk factors including African descent, family history of prostate cancer, high risk hereditary gene mutations associated with prostate cancer (e.g., BRCA2 genetic mutation in a first-degree relative)\textsuperscript{13,28,29} to inform discussions with asymptomatic men.
- There is a lack of clear evidence that asymptomatic men with risk factors benefit from earlier PSA testing compared to those at normal risk. However, men at higher risk may consider PSA testing as early as 40 to 45 years of age and may consider re-testing every 2 years.
- If the patient's family history of close relatives reveals a possible familial or inherited mutation, consider referral for genetic counselling. Refer to the BC Cancer Hereditary Cancer Program for more information.

Digital rectal exam

The use of the DRE for prostate cancer screening in asymptomatic men is also controversial. There are recommendations both for and against.\textsuperscript{14,30} DRE can lead to the identification of significant prostate cancer in asymptomatic men independent of PSA level.\textsuperscript{31} However, DRE has poor sensitivity and specificity, high inter-observer variability, and may contribute to unnecessary biopsies (Refer to Controversies in Care section, below).\textsuperscript{30}

- For asymptomatic men requesting a DRE, offer an informed discussion of the harms and benefits. Consider DRE at the same time PSA testing is considered.
- Refer any patients with a hard or irregular prostate to urology regardless of PSA test results.
Asymptomatic Patients with Known PSA Test Results
(Refer to Appendix B: Care Pathway – Patients with Signs and Symptoms of Suspected Prostate Cancer)

- If PSA is above age-based reference ranges (refer to Table 1), consider DRE to guide a differential diagnosis. Any patients with hard or irregular prostate should be referred to urology.
- If PSA is above age-based reference ranges (refer to Table 1), and DRE is not suspicious of prostate cancer, consider other causes of elevated PSA (refer Table 2), and repeat PSA testing in 4–12 weeks.
- Persistent elevation of PSA above age-based reference ranges should prompt a referral to urology.
- If a patient has decided to pursue screening after an informed discussion, and if PSA is within the appropriate age-based reference range, further testing in less than 2 years is not indicated.

Patients with Possible Symptoms of Metastatic Prostate Cancer
For patients with signs or symptoms of possible metastatic cancer of indeterminant cause (e.g., weight loss, bone pain, etc), rule out advanced prostate cancer with DRE and PSA. Refer to Appendix C: Care Pathway – Patients with Suspected Metastatic Prostate Cancer.

Diagnosis

Transrectal ultrasound guided core needle biopsy is the standard method used in B.C. to confirm the diagnosis of prostate cancer. Potential biopsy-related harms include pain, bleeding, and infection.

The use of multi-parametric magnetic resonance imaging (mpMRI) for prostate cancer diagnosis can reduce harms associated with over-biopsying. However, mpMRI is an emerging technology in B.C. that is not yet the standard of care.

Management of prostate cancer is beyond the scope of this guideline. It is important to note that not all men diagnosed with prostate cancer require immediate treatment and may undergo a program of active surveillance which significantly reduces many harms associated with radical treatment.


Controversies in Care

- PSA testing of asymptomatic men

The role of PSA testing in the diagnostic work-up of men with symptoms and in follow-up of confirmed prostate cancer is well defined. Nevertheless, the use of PSA testing for prostate cancer screening is controversial because of the risk of overdiagnosis and overtreatment of tumours that would not cause harm in a man’s lifetime. Potential harms include biopsy complications (e.g., pain, bleeding, infection), and treatment side-effects (e.g., erectile dysfunction and urinary incontinence) that affect quality of life. These harms should be considered along with the potential benefit of PSA testing of asymptomatic men.

The result of the European Randomised Study of Screening for Prostate Cancer (ERSPC) showed a relative risk reduction of 27% in prostate cancer mortality and 30% reduction in the incidence of metastatic disease in men aged 55-69 who were randomized to screening. The benefits of screening in the ERSPC were shown to be:

- a reduction in prostate cancer mortality of 1.28 prostate cancer deaths per 1000 men screened during the 13 year median observation period of the trial. However, modelling studies suggest that the reduction of prostate cancer mortality may be as high as 5.9 per 1000 men screened if extrapolated to the expected lifetime of the patient population, and
- a reduction in the incidence of metastatic disease of 3.1 per 1000 men screened during the 12 year median observation period of the trial; this number will also be higher when projected to the expected lifetime of the patient population.

Recently, a 16 year ERSPC follow-up showed increased benefit of screening compared to 13 years follow-up. After 16 years of follow-up, the number needed to screen to prevent one prostate cancer death was 570 and the number needed to diagnose was 18. These numbers have continued to improve with increased duration of follow-up. Modeling studies suggest that the benefit with respect to reduced prostate cancer mortality and incidence of metastatic disease may be greater when extrapolated to the lifetime of the patient. Furthermore, increased use of active surveillance in prostate cancer management mitigates some of the harms associated with treatment.
Although the serum PSA level serves as a risk factor for the presence of clinically significant prostate cancer, it has both a significant false positive and false negative rate for prostate cancer detection. PSA testing lacks sensitivity at lower ranges (many men with a PSA in the age-specific reference range have prostate cancer), and lacks specificity at higher ranges as elevations may be due to other causes (e.g., BPH).\footnote{40} PSA values increase with age and there is currently no single cut-off value with a corresponding high sensitivity and specificity for prostate cancer, but rather a continuum for which it serves as an indicator for further investigations.\footnote{41,42}

\section*{Digital Rectal Exam}

The ERSPC protocol initially included DRE for men with PSA levels greater than 3 $\mu$g/L. However there was variation in the application of DRE among the study centres and it is not clear how it impacted the results of the trial demonstrating a reduction in the risk of death from prostate cancer.\footnote{43,44} DRE can lead to the identification of significant prostate cancer in asymptomatic men independent of PSA level (e.g., a secondary study of the screening arm of the PLCO (Prostate Lung Colorectal Ovarian) trial found that only 15\% of suspicious DRE screening results were also abnormal for age-based PSA levels).\footnote{31} However, it is uncertain that the harms of overdiagnosis and overtreatment outweigh the benefits, and a recent systematic review highlighted the lack of evidence supporting the effectiveness of the DRE as a screening tool in primary care.\footnote{30} The accuracy of DRE as a diagnostic tool for prostate cancer has limited applications when evaluated by systematic review due to its low predictive values, with positive predictive values of 41\% and negative predictive values of 64\% when evaluated against biopsy for patients in primary care.\footnote{30} As a predictor of prostate cancer in symptomatic patients in primary care, positive and negative predictive values were 42\% and 84\% respectively. The role of DRE in asymptomatic men remains controversial with recommendations both for and against.\footnote{18,19,30,45}

While the role of DRE in the initial assessment of a patient without symptoms or a known PSA result may be limited, when a patient presents with symptoms and/or an elevated PSA, the DRE may have a clinical role to help formulate a differential diagnosis.

\section*{Informed Discussion}

These guidelines are intended to support rational utilization of PSA testing and to reduce over-testing for asymptomatic individuals.

It is imperative that patients understand the harms and benefits of PSA testing and DRE. Primary care providers play an important role in supporting informed discussions with patients. Informed discussion can be challenging to support effectively. Although many decision aids have been developed and may improve patient understanding and ability to make a decision, the effect of decision aids on prostate cancer screening choice is not consistent and additional research is needed. Refer below for aids that support informed decision-making.
Example of discussion topics to support informed decision-making*

For men aged 55-69, there are both benefits and harms to having a PSA test to screen for prostate cancer. Before having a PSA test it is important to understand the pros and cons of having a PSA test.

1. A PSA test may be positive for reasons other than prostate cancer. High levels of PSA in blood may indicate the presence of prostate cancer, but frequently are due to other non-cancer causes such as benign prostatic hyperplasia (BPH, enlargement of the prostate) or prostatitis (inflammation or infection of the prostate).

2. Most men who have prostate cancer do not die of prostate cancer. Most prostate cancers are slow-growing and many will not need treatment during a man’s life.

3. PSA Screening reduces the relative risk of death due to prostate cancer by 20%. For 1000 men undergoing PSA screening (based on 13 year observation period*):
   - 5 or 6 men die of prostate cancer during the 13 year observation period
   - 1 man avoids death from prostate cancer during the 13 year observation period
   - Computer modeling studies suggest that potential benefit may be higher over a patient’s lifetime. Studies are ongoing and we will learn more as more time passes.

4. PSA testing reduces the risk of developing metastatic disease (prostate cancer spreading to other organs).

5. PSA testing of asymptomatic men may lead to investigation and treatment, which have known potential risks and harms.
   - 20%-50% of men diagnosed with prostate cancer have a cancer that would not cause harm in their lifetime. Much of the controversy surrounding prostate cancer screening is derived from treatment of these men, which is considered over-treatment. However, active surveillance has become a much more widely adopted practice for men with low risk prostate cancer, so that the harms of overtreatment have been reduced.

6. PSA screening may lead to needless biopsy. Risks associated with biopsy include pain, bleeding, and infection.

7. Treatment can have side effects, such as erectile dysfunction and urinary incontinence:
   For 1000 men undergoing PSA screening, 80 will receive surgery or radiation treatment (either immediately or after active surveillance), and a proportion of these men will experience side effects of treatment (based on a 13 year observation period*):
   - 50 men will have erectile dysfunction during the 13 year observation period
   - 15 men will have urinary incontinence during 13 year observation period

8. A man diagnosed with low-risk prostate cancer may be monitored by active surveillance, which can avoid or delay treatment and reduce associated harms.
   - At 10 years follow-up, 64% of men on active surveillance continue to avoid treatment.6

*Information in this example adapted from US Preventative Task Force Patient Handout ‘Is Prostate Cancer Screening Right for You?’ based on 13 year ERSPC trial for men aged 55 to 69 years, and treatment harms derived from pooled absolute rates in the treatment group of the ProtecT, PIVOT, and SPCG-4 trials as described in an infographic and table:
   - Table: https://www.uspreventiveservicestaskforce.org/Page/Document/RecommendationStatementFinal/prostate-cancer-screening1

PSA testing Decision Aids
   - HealthLinkBC – Prostate Cancer Screening: Should I Have a PSA Test? – https://www.healthlinkbc.ca/health-topics/aa381444#zx3721
   - Canadian Task Force on Preventative Health Care Prostate Cancer Recommendations (2014):
     - Benefits and Harms of PSA Screening (1000 People Tool)
     - PSA Screening: Patient FAQ
References


Appendices

- Appendix A: Guideline Development Methodology
- Appendix B: Care Pathway – Patients with Signs and Symptoms of Suspected Prostate Cancer
- Appendix C: Care Pathway – Patients with Possible Symptoms of Metastatic Prostate Cancer

Associated Documents


PSA Testing Decision Aids – for Asymptomatic Men Who Ask About PSA Testing
- HealthLinkBC
- Prostate Cancer Screening: Should I Have a PSA Test? – www.healthlinkbc.ca/health-topics/aa38144#zx3721
- Canadian Task Force on Preventive Health Care
- Prostate Cancer Recommendations (2014): Benefits and Harms of PSA Screening (1000 People Tool)
- Prostate Cancer Recommendations (2014): PSA Screening: Patient FAQ

Prostate Cancer Risk Calculators
- Prostate Cancer Prevention Trial Risk Calculator Version 2.0
  - http://riskcalc.org:3838/PCPTRC/
- European Randomised Study of Screening for Prostate Cancer Prostate Cancer Risk Calculator
Resources

- **BC Cancer**

- **Family Practice Oncology Network (FPON) UBC- Continuing Professional Development**
  - Online Prostate Cancer Module – [https://ubccpd.ca/courses/oncology](https://ubccpd.ca/courses/oncology)

- **Communication with Specialists**
  - Primary care practitioners are encouraged to consult with specialist colleagues or the RACE line if they are in doubt regarding need for and timing of referral.
  - RACE Line: [raceconnect.ca 1-877-696-2131](http://raceconnect.ca 1-877-696-2131)
  - The provincial RACE line provides specialist consultation to physicians and nurse practitioners. Available Monday to Friday from 8 am to 5 pm. Calls not answered immediately are returned within 2 hours. There is also a free RACE line app for smartphone or desktop. Note urology consultation is only available via RACEapp.
  - There are a variety of incentive fees available to support communications between primary care and specialty providers. As these do change over time, please check the [MSC Payment Schedule](http://www.msc.ca), the [General Practice Services Committee](http://www.bccma.ca), or with your relevant Section at the Doctors of BC.

- **HealthLinkBC** – Prostate Cancer Health Topic: [www.healthlinkbc.ca/health-topics/hw78220](http://www.healthlinkbc.ca/health-topics/hw78220)

- **Vancouver Prostate Centre** – [www.prostatecentre.com](http://www.prostatecentre.com)

- **Prostate Cancer Foundation of BC** – If I Were Tom | Prostate Cancer Tips, Advice, and Support – [www.ifiweretom.ca](http://www.ifiweretom.ca)

- **Prostate Centre Canada** – [www.prostatecancer.ca](http://www.prostatecancer.ca)

- **Canadian Cancer Society** – [www.cancer.ca](http://www.cancer.ca)

### Diagnostic Code: 185 (malignant neoplasm of prostate)

### Abbreviations

- **CCO** - Cancer Care Ontario
- **DRE** - digital rectal exam
- **ERSPC** - European Randomized Study of Screening for Prostate Cancer
- **LUTS** - lower urinary tract symptoms
- **PSA** - prostate specific antigen
The principles of the Guidelines and Protocols Advisory Committee are to:

- encourage appropriate responses to common medical situations
- recommend actions that are sufficient and efficient, neither excessive nor deficient
- permit exceptions when justified by clinical circumstances

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Disclaimer
The Clinical Practice Guidelines (the guidelines) have been developed by the BC Cancer Primary Care Program, Family Practice Oncology Network and the Guidelines and Protocols Advisory Committee, on behalf of the Medical Services Commission. The guidelines are intended to give an understanding of a clinical problem, and outline one or more preferred approaches to the investigation and management of the problem. The guidelines are not intended as a substitute for the advice or professional judgment of a health care professional, nor are they intended to be the only approach to the management of clinical problem. We cannot respond to patients or patient advocates requesting advice on issues related to medical conditions. If you need medical advice, please contact a health care professional.
Appendix A: Guideline Development Methodology

The BCGuideline, Prostate Cancer – Part 1: Diagnosis and Referral in Primary Care, was developed by a working group of practicing BC physicians, based on the ADAPTE Collaboration guideline adaptation methodology. Clinical recommendations were developed based on the sourced guidelines, an updated systematic review of the clinical literature, as well as expert clinical consensus where evidence was insufficient or unavailable.

The source guidelines were chosen following an environmental scan of internationally available guidelines. Inclusion criteria for potential adaptation included guidelines published after 2010 and a systematic review of the literature that included at least one outcome of interest. Guidelines were chosen for adaptation following an evaluation using the AGREE tool.

The recommendations in this guideline were adapted with permission from Cancer Care Ontario's Program in Evidence Based Care, Referral of Suspected Prostate Cancer by Family Physicians.

This guideline includes a systematic review of the evidence addressing specific clinical questions and expands upon Cancer Care Ontario's evidence strategy, which addressed the primary care management and follow-up of prostate cancer in symptomatic men. Clinical databases searched included MEDLINE (OVID, 2016 Sept 01–2017 Nov 05) and Embase (OVID, 2016 week 41–2017 week 45), which included the Cochrane Library, for clinical questions related to the referral of suspected prostate cancer. The databases MEDLINE (OVID, 2014 September 01–2017 Dec 01) and Embase (OVID, 2014 week 33–2017 week 47), for questions related to follow-up in men after curative treatment for prostate cancer. Additionally, a full literature search was completed to address investigation of prostate cancer in asymptomatic men. Databases searched included MEDLINE (OVID, 2000 Jan 01–2016 Aug 31), and Embase (OVID, 2000 week 1–2016 week 40). No attempt was made to search unpublished literature. The complete search strategy, clinical questions, outcomes of interest, and inclusion/exclusion criteria are available upon request by contacting the BC Cancer Primary Care Program (Family Practice Oncology Network).

The guideline development process included significant engagement and consultation with primary care providers, specialists and key stakeholders, including with BC's Agency of Pathology and Laboratory Medicine, the Population Oncology and the Genitourinary Tumour Groups at BC Cancer, and the Ministry of Health Lifetime Prevention Schedule Expert Committee. For more information about GPAC guideline development processes, refer to the GPAC handbook available at BCGuidelines.ca.

References
Appendix B: Care Pathway I – Patients with Signs and Symptoms of Suspected Prostate Cancer

- Asymptomatic patients presenting with PSA elevated above age-adjusted reference range

  - Consider DRE after discussion of harms and benefits

  - Antibiotics contraindicated and may be detrimental (e.g., biopsy infection, C. difficile, antibiotic resistance)
    - DRE for all patients.
    - PSA for all patients.

  - Prostate hard or irregular on DRE?
    - Yes
    - When DRE and PSA are normal, prostate cancer is unlikely. Evaluate for other causes and treat as appropriate. Repeat PSA/DRE in less than 2 years is not indicated.
    - No

  - PSA elevated above age-adjusted reference range?
    - Yes
    - Consider other causes of elevated PSA. Repeat PSA at 4-12 weeks.
    - No

- Patients with LUTS (Voiding symptoms: poor stream, hesitancy, urgency, frequency, intermittent flow, and straining to pass urine)

  - Signs/symptoms of acute prostatitis? (e.g., dysuria, hematuria, pelvic/groin pain, fever/chills)
    - Yes
    - PSA not indicated prior to treatment.
      - Manage as clinically appropriate.
      - If symptoms resolve, discuss role of DRE/PSA as per asymptomatic patients.
      - If symptoms do not resolve, refer as clinically appropriate.
    - No

- Other Causes of Elevated PSA
  - Urinary retention
  - Prostatitis
  - Benign prostatic hyperplasia (BPH)
  - Bladder catheterization/instrumentation
  - PSA levels are not significantly altered after cycling, intercourse, or digital rectal exam.

* Age-based PSA Reference Ranges:
  - 0-49 yrs 0-2.50 µg/L
  - 50-59 yrs 0-3.50 µg/L
  - 60-69 yrs 0-4.50 µg/L
  - ≥70 yrs 0-6.50 µg/L

Note: For men taking 5-alpha reductase inhibitors (i.e., finasteride & dutasteride), PSA will drop by approximately 50%. For accurate interpretation relative to lab-reported aged-based ranges, adjust the reported result by a factor of 2.

Abbreviation: BPH - benign prostatic hyperplasia; DRE - digital rectal exam; PSA - prostate specific antigen.
Appendix C: Care Pathway II – Patients with Possible Symptoms of Metastatic Prostate Cancer

Patients with *otherwise unexplained*:
- lower back pain
- bone pain
- weight loss, especially in the elderly
Consider the investigation of prostate cancer as part of your work-up.

- DRE for all patients
- PSA test for all patients
- Consider bone scan, or other appropriate, locally-available imaging

Focal neurologic symptoms or spinal compression?

No
- Prostate cancer is unlikely. Consider other metastatic cancers.

Yes
- Refer to urology.

DRE hard or irregular, or PSA above age-based* reference range?

No

Yes
- Refer to Emergency Room.

- **Age-based PSA Reference Ranges:**
  - 0-49 yrs: 0-2.50 µg/L
  - 50-59 yrs: 0-3.50 µg/L
  - 60-69 yrs: 0-4.50 µg/L
  - ≥70 yrs: 0-6.50 µg/L

**Other Causes of Elevated PSA**
- Urinary retention
- Prostatitis
- Benign prostatic hyperplasia (BPH)
- Bladder catheterization/instrumentation
PSA levels are not significantly altered after cycling, intercourse, or digital rectal exam.

**Note:** For men taking 5-alpha reductase inhibitors (i.e., finasteride & dutasteride), PSA will drop by approximately 50%. For accurate interpretation relative to lab-reported aged-based ranges, adjust the reported result by a factor of 2.

**Abbreviations:** BPH - benign prostatic hyperplasia; DRE - digital rectal exam; PSA - prostate specific antigen.