DRAFT Prostate Cancer: Diagnosis, Referral and Follow-up in Primary Care

DRAFT FOR EXTERNAL REVIEW - The online questionnaire is available at https://survey.health.gov.bc.ca/prostate

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. 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.

Recommendations include clinical assessment, the management of prostate specific antigen (PSA) test results, and the appropriate referral of the patient to a specialist. This guideline also addresses follow-up after treatment, and post-treatment management including the numerous side effects associated with the treatment of prostate cancer, as well as how to detect and refer cases of possible recurrence.

Currently there is a lack of strong evidence to support unselected, population-wide PSA testing for prostate cancer screening because of the potential for overdiagnosis, overtreatment, and detrimental to quality of life. (Refer to Controversies in Care, below). However, men often present in primary care with questions about PSA testing and guidance is included for primary care practitioners to support conversations about the harms and benefits of PSA testing for asymptomatic men. The assessment and referral of asymptomatic men presenting with an elevated PSA test result is also addressed.

This guideline was developed in collaboration with the BC Cancer Primary Care Program (Family Practice Oncology Network), and was developed based on a guideline adaptation approach, including a recent systematic review of the evidence. Adapted recommendations were based on the following two publications: Referral of Suspected Prostate Cancer by Family Physicians and Other Primary Care Providers, and Follow-up Care and Psychosocial Needs of Survivors of Prostate Cancer.3,4

Key Recommendations

- In patients presenting with lower urinary tract symptoms, PSA testing should be avoided if the patient has signs or symptoms of acute prostatitis (e.g. dysuria, hematuria, pelvic/groin pain, fever/chills).
- In patients presenting with lower urinary tract symptoms, but without signs of acute prostatitis: antibiotics should not be used in an attempt to lower PSA. This practice may be detrimental.
- Currently there is a lack of strong evidence to support unselected, population-wide PSA screening because of the potential for overdiagnosis, overtreatment, and detriment to quality of life.
- For asymptomatic men asking about PSA testing, offer an informed discussion including a history of risk factors, current life expectancy, and the risks and benefits of PSA testing. Currently in B.C., the evidence supporting PSA testing of asymptomatic men is not strong enough to recommend a prostate cancer screening program for asymptomatic men. However, asymptomatic men in B.C. have the option to pursue PSA testing for screening purposes as patient paid, or through their third-party health insurers (when coverage is available).
- For men with PSA test results within the appropriate age-based reference range, further testing in less than 2 years is not indicated.
• In patients with otherwise unexplained lower back pain, bone pain, weight loss (especially in the elderly), consider the investigation of prostate cancer as part of the work-up.
• Patients with focal neurologic symptoms or spinal cord compression should be referred urgently to the emergency room.
• Primary care practitioners should be aware of potential long-lasting side effects of prostate cancer treatment that affect quality of life, and the management options available to combat them.

## Epidemiology

Prostate cancer accounts for 9% of all cancers diagnosed in men in British Columbia (B.C.)\(^5\) An expected 1 in 8 men will be diagnosed with prostate cancer in their lifetime. Of these men, 87% will be over the age of 60 when they are diagnosed.\(^5\) It is estimated that 1 in 26 men who are diagnosed with prostate cancer would be expected to die of the disease.\(^5\)

**Table 1: Age-standardized Relative Survival (1-, 3- and 5-year) for B.C. Adults (age 15-99) diagnosed with Prostate Cancer**\(^5\)

<table>
<thead>
<tr>
<th>Relative Survival Proportion %</th>
<th>1 year</th>
<th>3 year</th>
<th>5 year</th>
</tr>
</thead>
<tbody>
<tr>
<td>95% Confidence Interval</td>
<td>96.6</td>
<td>93.5</td>
<td>92.5</td>
</tr>
<tr>
<td></td>
<td>95.6 - 97.5</td>
<td>92.0 - 94.9</td>
<td>90.6 - 94.3</td>
</tr>
</tbody>
</table>

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.\(^6\)
- Family history of prostate cancer (paternal side; first-degree relatives).\(^7\)–\(^9\)
- High-risk hereditary gene mutations associated with prostate cancer (e.g., BRCA2 in a first-degree relative).\(^10\),\(^11\) 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.

## Diagnosis and Investigations

Prostate cancer develops slowly and the majority of patients will present with lower urinary tract symptoms. Less frequently, some patients may present with symptoms of advanced disease.

### Patients with Lower Urinary Tract Symptoms (LUTS) (Refer to Appendix A: Care Pathway A – Patients with Signs and Symptoms of Suspected Prostate Cancer including Lower Urinary Tract Symptoms and Asymptomatic Patients with Elevated PSA Results)

Lower urinary tract symptoms including voiding symptoms such as poor stream, hesitancy, urgency, frequency, intermittent flow, and/or straining to pass urine, are common symptoms in older men that may warrant investigation for suspected prostate cancer among other causes. Assessment should include diagnosing and treating acute prostatitis and evaluating for other causes of LUTS including benign prostatic hyperplasia (BPH).

1. **Acute Prostatitis**
   - **PSA testing is not indicated if the patient has signs or symptoms of acute prostatitis** (e.g. dysuria, hematuria, pelvic/groin pain, fever/chills).
     - Manage acute prostatitis as clinically appropriate.
     - If symptoms resolve, consider as asymptomatic patients.
     - In patients with unresolved symptoms, refer as clinically appropriate.
2. Benign prostatic hyperplasia (BPH) and other causes of LUTS

LUTS can also indicate benign prostatic hyperplasia (BPH), which may be an alternate or concurrent diagnosis with prostate cancer. Assessment for BPH includes assessment of symptoms and level of bother experienced by the patient, as well as a physical examination including a digital rectal examination (DRE). PSA testing is generally performed as appropriate for the detection of prostate cancer, and as a marker of prostate size and risk of BPH progression (see Assessing for potential prostate cancer below, for information about PSA testing for men with LUTS). Based on patient preferences and severity of symptoms, management of BPH can include watchful waiting and lifestyle changes, treatment with medications, and surgical therapy. Recommendations for the diagnosis and management of BPH and LUTS is beyond the scope of this guideline.

- Note: common medications for BPH include 5 alpha-reductase inhibitors (finasteride and dutasteride) which have been shown to decrease PSA by approximately 50%. PSA values for men taking these medications should be adjusted to account for this decrease where appropriate.
- If urinary tract infection is suspected, refer to BCGuidelines: Macroscopic and Microscopic Urinalysis and the Investigation of Urinary Tract Infections (2009)

3. Assessing for potential prostate cancer

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, antibiotic resistance) and a drop in PSA on antibiotics does not correlate with the risk of harboring prostate cancer.

- PSA testing and DRE should be performed for all of these patients.
- Any patients with an abnormal prostate on DRE that is suspicious of prostate cancer should be referred 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, then prostate cancer is unlikely. Evaluate for other causes (refer to Table 2), and treat as appropriate. 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</td>
<td>0-2.5 ng/ml</td>
</tr>
<tr>
<td>50-59</td>
<td>0-3.5 ng/ml</td>
</tr>
<tr>
<td>60-69</td>
<td>0-4.5 ng/ml</td>
</tr>
<tr>
<td>≥70</td>
<td>0-6.5 ng/ml</td>
</tr>
</tbody>
</table>

Note: There is some variation in the currently reported lab specific PSA reference intervals, however, all clinical laboratories in B.C. agree with the merits of age specific PSA reference intervals, and are specifically supportive of the method independent reference intervals given in Table 1. The BC Agency of Pathology and Laboratory Medicine supports the provision of a consistent age specific reference range for PSA. If PSA testing is within age-based reference ranges, then prostate cancer is unlikely. This move to a consistent age-based reference range will help clarify the interpretation by the primary care provider of an individual's PSA levels and support appropriate referral for additional investigation if indicated.
Table 2 - Other Causes of Elevated PSA

<table>
<thead>
<tr>
<th>Cause</th>
</tr>
</thead>
<tbody>
<tr>
<td>Benign prostatic hyperplasia</td>
</tr>
<tr>
<td>Prostatitis (infection or inflammation)</td>
</tr>
<tr>
<td>Urinary retention</td>
</tr>
<tr>
<td>Bladder catheterization/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 significant risk of overdiagnosis and overtreatment of tumours that would not cause harm in a man’s lifetime.\(^{20,21}\) Potential harms include biopsy complications (i.e., pain, bleeding, infection), and treatment side-effects (i.e., erectile dysfunction and urinary incontinence) that affect quality of life.\(^{20,21}\) Refer to the *Controversies in Care* section below for more information about the harms and benefits of PSA testing in asymptomatic men. Currently in B.C., the evidence supporting PSA testing of asymptomatic men is not strong enough to recommend a prostate cancer screening program for asymptomatic men. However, asymptomatic men in B.C. have the option to pursue PSA testing for screening purposes as patient paid, or through their third-party health insurers (when coverage is available).

- **PSA testing is not indicated in asymptomatic patients <55 or >69 years of age who are without risk factors.**
- **Asymptomatic men age 55-69 years of age who have a greater than 10 years life expectancy, may decide to pursue PSA testing.** An informed discussion about the risk and benefits of testing is recommended.\(^{20,22}\)
- **Clinicians should include the issue of known risk factors to inform discussions with asymptomatic men who present with questions regarding possible PSA testing.** Additionally, refer to the *Associated Documents* section for prostate cancer risk calculators and patient decision aids.
- **There is insufficient evidence that asymptomatic men with risk factors** (African American origin, family history of prostate cancer) 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.
- **There is insufficient evidence that asymptomatic men with high risk hereditary gene mutations associated with prostate cancer (e.g., BRCA2 in a first-degree relative)\(^{10,11}\)** benefit from earlier PSA testing compared to those at normal risk. However, men with high risk hereditary gene mutations may consider PSA testing as early as 40 to 45 years of age. If the patient’s family history of close relatives reveals a possible familiar or inherited mutation, consider referral for genetic counselling. Refer to the BC Cancer [Hereditary Cancer Program](https://www.bccancer.ca) for more information.
- If an asymptomatic man 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.**
- Refer to *Controversies in Care* and *Resources* sections below for information to support discussions of the harms and benefits of PSA testing in asymptomatic men.

Use of the DRE for prostate cancer screening in asymptomatic men is also controversial and there are recommendations both for and against.\(^{15,16,22,23}\) DRE can lead to the identification of significant prostate cancer in asymptomatic men independent of PSA level,\(^{24}\) however there is insufficient evidence that the harms of overdiagnosis and overtreatment outweigh the benefits.\(^{23}\)

- **For asymptomatic men requesting a DRE, offer an informed discussion of the harms and benefits.** Refer any patients with a hard or irregular prostate to urology regardless of PSA test results.\(^{24}\)
Asymptomatic Patients with Known PSA Test Results (Refer to Appendix A: Care Pathway A – Patients with Signs and Symptoms of Suspected Prostate Cancer including Lower Urinary Tract Symptoms and Asymptomatic Patients with Elevated PSA Results)

For asymptomatic men presenting with known PSA test results:

- If PSA is above age-based reference ranges (refer to Table 1), consider DRE after discussion of harms and benefits to guide differential diagnosis. Any patients with hard or irregular prostate should be referred to urology.24
- 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. Such repeat PSA testing for men with PSA test result above age-based reference levels is MSP covered.
- Persistent elevation of PSA above age-based reference ranges should prompt a referral to urology.
- 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 (Refer to Appendix B: Care Pathway B – Patients with Possible Symptoms of Metastatic Prostate Cancer)

In 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.

- Patients with focal neurologic symptoms or spinal cord compression should be referred urgently to the emergency room.
- If there are no neurologic symptoms or signs of spinal cord compression, PSA testing and DRE should be performed in all patients. Additionally, consider a bone scan or other appropriate locally-available imaging.
- If prostate is hard or irregular on DRE, or PSA results are above the appropriate age-based reference range, then refer to urology.
- If DRE is normal and PSA is within the age-based range, then prostate cancer is unlikely; consider other metastatic cancers.

Diagnosis and Continuity of Care

Management of prostate cancer is beyond the scope of this guideline. For information on BC Cancer guidelines and details of the management of prostate cancer refer to http://www.bccancer.bc.ca/health-info/types-of-cancer/mens-cancer/prostate.

Transrectal ultrasound guided core needle biopsy is the standard method used to confirm the diagnosis of prostate cancer in B.C.25 Potential biopsy related harms include pain, bleeding, and infection.21

The use of multi-paramagnetic magnetic resonance imaging (mpMRI) is an emerging technology for prostate cancer diagnosis26,27 and is not currently recommended as the standard of care.15,27

The role of primary care practitioners in providing continuity of care to their patients in all settings, both directly and by coordination of care with other health care professionals, reduces the fragmentation of care and thus improves patient safety and the overall quality of care.

Coordination of patient care between primary care and specialist physicians throughout the cancer journey, from diagnosis through treatment and post-treatment care, is fundamental to the delivery of effective health care, especially for more complex patient populations.
Follow-up Prostate Cancer Care

Patients who have completed treatment for prostate cancer are usually returned to the care of their primary care provider who will be asked to manage their follow-up care. Follow-up care may include the following:

- Surveillance for recurrent disease, or late effects of treatment,
- Monitoring and treating complications and/or side effects, and
- Symptom management, best supportive care, and the early involvement of palliative services, if needed.

PSA Testing for Surveillance for Recurrent Disease

In patients who have completed definitive therapy with curative intent, surveillance for recurrent disease is typically done by testing the serum PSA – Refer to Table 3 for information on biochemical relapse and when to refer.

In the absence of evidence to guide PSA testing intervals, the following recommendations for monitoring recurrence are based on clinical opinion and are considered reasonable. The intensity of surveillance will depend on the risk of recurrence. Practitioners should use clinical judgement to evaluate the benefits of surveillance in patients who are unlikely to benefit from additional salvage therapy. Please note that the recommended intervals are different following surgery versus non-surgery.

PSA Testing for surveillance for recurrent disease following surgery:

- Year 1 – every 3 months
- Year 2 to 5 – every 6 months
- Year ≥5 to 10 – annually, if still undetectable
- If PSA levels become detectable, more frequent surveillance may be appropriate

PSA Testing for surveillance for recurrent disease following non-surgery primary therapy (e.g., radiation therapy, cryotherapy, or high-intensity focused ultrasound):

- First test – 6 weeks post-treatment completion
- Every 6 months until the end of year 5
- Annually thereafter

Table 3 - Biochemical Relapse/PSA Recurrence

<table>
<thead>
<tr>
<th>Treatment</th>
<th>PSA Profile Indicative of Recurrent Disease</th>
</tr>
</thead>
<tbody>
<tr>
<td>Radical prostatectomy</td>
<td>• 2 successive increases to a level of &gt;0.2ng/ml.</td>
</tr>
</tbody>
</table>
| External beam radiation therapy         | • After external beam radiation therapy, relapse may occur following achievement of nadir (the lowest post-therapy PSA value).  
  • Biochemical relapse is defined as nadir plus 2.                                                      |
| Brachytherapy                           | • Biochemical relapse is defined as nadir plus 2.                                                        |
|                                         | • The PSA level may ‘bounce’ typically as much as 1-3 years post-therapy.                                 |
|                                         | • PSA levels may temporarily rise to ≥4ng/ml                                                            |
|                                         | • In brachytherapy, because of the risk of bowel injury, prostate biopsy should not be performed; seek consultation with a radiation oncologist. |

Follow-up of Patients with Symptoms Following Treatment

A PSA test should be performed if the symptoms listed in Table 4 develop. Diagnostic imaging specific to the patient’s symptom(s) may be indicated:
Table 4 - Possible Symptoms Following Treatment

<table>
<thead>
<tr>
<th>Possible Symptoms Following Treatment</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>New urinary symptoms</td>
<td>• significant incontinence requiring changing of undergarments, pads, or diapers</td>
</tr>
<tr>
<td></td>
<td>• urgency</td>
</tr>
<tr>
<td></td>
<td>• obstructive symptoms</td>
</tr>
<tr>
<td></td>
<td>• voiding discomfort</td>
</tr>
<tr>
<td></td>
<td>• nocturia</td>
</tr>
<tr>
<td></td>
<td>• hematuria</td>
</tr>
<tr>
<td>Swelling of legs</td>
<td></td>
</tr>
<tr>
<td>New bowel symptoms</td>
<td>• rectal bleeding</td>
</tr>
<tr>
<td></td>
<td>• rectal pain</td>
</tr>
<tr>
<td></td>
<td>• urgency</td>
</tr>
<tr>
<td></td>
<td>• change in bowel movement</td>
</tr>
<tr>
<td>Fatigue</td>
<td>• tiredness unrelated to sleep disturbance</td>
</tr>
<tr>
<td></td>
<td>• lack of energy</td>
</tr>
<tr>
<td></td>
<td>• weakness or lack of muscle strength</td>
</tr>
<tr>
<td></td>
<td>• physical, emotional or cognitive exhaustion</td>
</tr>
<tr>
<td>Severe and progressive axial skeletal bone pain</td>
<td></td>
</tr>
<tr>
<td>Unexplained weight loss</td>
<td></td>
</tr>
</tbody>
</table>

Management of Patients with Long-lasting Symptoms

Men experience very specific and oftentimes long-lasting effects after their primary therapy, usually occurring more than three months after surgery or radiation, or during/after androgen deprivation therapy (ADT) (Refer to Table 5).³ Follow-up healthcare providers should be aware of the domains of quality of life potentially affected by treatment for prostate cancer, and the management options available to combat them.²⁹ Research surrounding management options is lacking.²⁹ The symptoms listed are based on known profiles; however, individual men respond differently to treatments, resulting in individual side-effect profiles.³ To ensure optimal quality of life in these men, individual patient-reported outcomes should be measured.³,²⁹

Table 5 - Long-term Side Effects and Recommendations for Management

<table>
<thead>
<tr>
<th>Side Effect</th>
<th>Management Options</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Sexual Dysfunction</strong> <em>(Patients with primary treatment of surgery, radiation therapy, or androgen deprivation therapy)</em></td>
<td></td>
</tr>
<tr>
<td>Erectile dysfunction</td>
<td>• Men may be prescribed phosphodiesterase type 5 (PDE5) inhibitors as first line treatment.*</td>
</tr>
<tr>
<td></td>
<td>• Men who do not respond to PDE5 inhibitors will need more advanced treatments and should be referred to a urologist or sexual health expert.*</td>
</tr>
<tr>
<td></td>
<td>• Men may be referred to penile rehabilitation programs, which include PDE5 inhibitors, vacuum constriction devices, intracorporal or intraurethral therapy, or placement of penile prostheses.*</td>
</tr>
<tr>
<td>Side Effect</td>
<td>Management Options</td>
</tr>
<tr>
<td>-------------------------------------------</td>
<td>---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------</td>
</tr>
<tr>
<td><strong>Sexual Dysfunction - continued</strong></td>
<td><em>Patients with primary treatment of surgery, radiation therapy, or androgen deprivation therapy</em></td>
</tr>
<tr>
<td>Loss of libido</td>
<td>• Men and their partners should be referred to a healthcare professional with training in sexual health counselling, when available.</td>
</tr>
<tr>
<td></td>
<td>• Testosterone therapy can be considered in men with signs and symptoms of testosterone deficiency and documented low serum testosterone levels, provided their cancer is treated and without evidence of persistent or recurrent disease, and if prescribed by the treating oncologist/urologist after extensive review of the potential risks.*</td>
</tr>
<tr>
<td>Anorgasmia</td>
<td>• Men and their partners should be referred to a healthcare professional with training in sexual health counselling, when available.*</td>
</tr>
<tr>
<td>Dry ejaculate</td>
<td>• Men should be educated on dry ejaculate.*</td>
</tr>
<tr>
<td>Climaturia</td>
<td>• Men should be provided education on self-management strategies, such as emptying the bladder before sexual relations, use of a condom, use of a penile constriction band, and Kegel exercises.*</td>
</tr>
<tr>
<td>Penile shortening or curvature</td>
<td>• Regular sexual stimulation may prevent penile shortening.</td>
</tr>
<tr>
<td></td>
<td>• If there is significant penile curvature impairing sexual function, refer patient to a urologist.</td>
</tr>
<tr>
<td>Infertility</td>
<td>• Men and their partner should be informed that:</td>
</tr>
<tr>
<td></td>
<td>• men treated with radical prostatectomy will become infertile, and</td>
</tr>
<tr>
<td></td>
<td>• some men treated with radiation therapy may remain fertile, even when experiencing sexual dysfunction symptoms.*</td>
</tr>
<tr>
<td>Urinary Dysfunction</td>
<td><em>Patients with primary treatment of surgery and/or radiation therapy</em></td>
</tr>
<tr>
<td>Obstructive symptoms</td>
<td>• Selective alpha-antagonists may be prescribed for patients who have not undergone radical prostatectomy.</td>
</tr>
<tr>
<td></td>
<td>• Refer to a urologist to evaluate for bladder neck contracture or urethral stricture.</td>
</tr>
<tr>
<td>Urgency symptoms</td>
<td>• If the patient is able to completely empty his bladder (i.e., post-void residual of &lt;100cc), anticholinergic medications may be appropriate.</td>
</tr>
<tr>
<td></td>
<td>• All refractory symptoms should result in a referral to a urologist for evaluation and escalation of therapy if appropriate*</td>
</tr>
<tr>
<td>Hematuria</td>
<td>• Men with hematuria should be referred to a urologist for evaluation*</td>
</tr>
<tr>
<td>Incontinence requiring urinary pads</td>
<td>• Men with persistent leakage impacting quality of life should be referred to a urologist to evaluate the cause of incontinence.*</td>
</tr>
<tr>
<td></td>
<td>• Exercise intervention such as Kegel exercises may improve continence.\textsuperscript{30} Specialized physiotherapists and nurse continence advisors may help patients with stress incontinence following radical prostatectomy.</td>
</tr>
<tr>
<td></td>
<td>• In men with post-prostatectomy incontinence &gt;1 year, consider referral for assessment for urethral slings or artificial urinary sphincters.</td>
</tr>
</tbody>
</table>
### Table 5 - Long-term Side Effects and Recommendations for Management

**Bowel Dysfunction**  
*patients with primary treatment of radiation therapy*

<table>
<thead>
<tr>
<th>Side Effect</th>
<th>Management Options</th>
</tr>
</thead>
</table>
| Rectal Bleeding | - All men with rectal bleeding should be referred for a colonoscopy.*  
- For men with rectal bleeding post-radiation therapy, referral to a gastroenterologist who has experience in managing radiation therapy proctitis is recommended. **The anterior rectum should not be biopsied due to the risk of a fistula of the rectum**.*  
- For men with bleeding secondary to radiation proctitis, the following strategies may be considered:*  
  - Dietary changes to bulk stool.  
  - Hydration education.  
  - Referral for assessment for other medical treatments, if primary management strategies are unsuccessful. |
| Urgency and frequency symptoms | For men with urgency and frequency symptoms, the following options may be considered:*  
  - Dietary changes to bulk stool.  
  - Hydration education.  
  - Medical treatments (antidiarrheals, anticholinergics).  
  - Pelvic floor muscle therapy. |

**Other Physical Side-effects**  
*Patients with primary treatment of surgery, radiation therapy, or androgen deprivation therapy*

<table>
<thead>
<tr>
<th>Side Effect</th>
<th>Management Options</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anemia</td>
<td>- Investigation for common sources of anemia should be considered.*</td>
</tr>
<tr>
<td>Body composition alterations</td>
<td>- Men should be encouraged to participate in an exercise program.</td>
</tr>
<tr>
<td>Fatigue</td>
<td>- Men should be encouraged to participate in an exercise program.</td>
</tr>
<tr>
<td>Gynecomastia/Mastodynia</td>
<td>- In severe cases, surgical excision can be considered; patients should be referred to a specialist.*</td>
</tr>
<tr>
<td>Hot flushes</td>
<td>- Treatment with transdermal estrogen, gabapentin, diethylstilbestrol, megestrol acetate, venlafaxine, cyproterone acetate, and medroxyprogesterone have been shown to decrease the number of hot flushes and can be considered. Use with caution because treatment with these medications has been associated with adverse side-effects (e.g., gynecomastia, depression, weight gain, muscle spasms, insomnia, nausea, and elevated blood pressure).</td>
</tr>
<tr>
<td>Physical activity</td>
<td>- Men should be encouraged to participate in an exercise program.</td>
</tr>
<tr>
<td>Bone health</td>
<td>- For recommendations on maintaining bone health, refer to Osteoporosis: Diagnosis, Treatment and Fracture Prevention at <a href="https://www.bcguidelines.ca">BCGuidelines.ca</a>.</td>
</tr>
<tr>
<td>Cognitive side-effects</td>
<td>- Rule out other reversible cognitive problems.</td>
</tr>
</tbody>
</table>
Table 5 - Long-term Side Effects and Recommendations for Management\(^3\) - Continued

<table>
<thead>
<tr>
<th>Side Effect</th>
<th>Management Options</th>
</tr>
</thead>
<tbody>
<tr>
<td>Other Physical Side-effects - continued (Patients with primary treatment of surgery, radiation therapy, or androgen deprivation therapy)</td>
<td></td>
</tr>
</tbody>
</table>
| Psychological distress (depression and anxiety) | • Offer in-office psychological therapy and pharmacotherapy as appropriate.  
• Referral to a local support group and/or patient self-help group (see Resources, below). |
| General quality of life and psychosocial sequelae | • Men should be encouraged to participate in an exercise program.  
• Advise patients on strategies for achieving and maintaining a healthy weight using diet and exercise.  
• During scheduled follow-up clinical visits, assess men’s psychosocial status; if distress is evident, refer to specialized care to address social and emotional quality of life, as well as support groups for coping training for couples when applicable.\(^32\)  
• Use of standardized assessment tools is recommended (e.g., EPIC or PHQ9). |

* Recommendations were adapted from CCO and are based on expert consensus; additional clinical references are outlined as indicated. Abbreviations: PDE5 - phosphodiesterase type 5, QoL - quality of life, EPIC - expanded prostate cancer index composite, PHQ9 - Patient Health Questionnaire 9

### Survivorship

Survivorship care is a key and fundamental component of post-treatment care, in addition to and beyond follow-up care. It is the link between treatment and recovery, and a key point of continuity of care through the connections formed between the patient, BC Cancer, and the patient’s primary care team.

Patient quality of life and satisfaction have been shown to be higher in prostate cancer survivors who have access to survivorship care, and this suggests that disease-specific survivorship clinics that incorporate quality-of-life reporting may have better outcomes.\(^32\)

### Advance Care Planning

While the majority of prostate cancers advance slowly and/or are potentially curable, some will be discovered in late stages or will be aggressive and treatment resistant. Patients with a potentially life-limiting disease or illness may benefit from the development of an advance care plan that incorporates the patient’s values and personal goals, indicates potential outcomes, and outlines linkages with other health care professionals that would be involved in the care as well as their expected roles. The advance care plan is an opportunity to also identify the patient’s alternate substitute decision-maker or legal health representative.


For more information on palliative care, including identifying patients who would benefit from palliative care early in the illness trajectory refer to BCGuidelines.ca – Palliative Care for the Patient with Incurable Cancer or Advanced Disease.
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, however, the use of PSA testing for prostate cancer screening is controversial because of the significant risk of overdiagnosis and overtreatment of tumours that would not cause harm in a man’s lifetime.20,21 Potential harms include biopsy complications (i.e., pain, bleeding, infection), and treatment side-effects (i.e., erectile dysfunction and urinary incontinence) that affect quality of life.20,21 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% in the incidence of metastatic disease, in men aged 55-69 who were randomized to screening.20,33 The absolute 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 (median follow-up of 13 years), and
- a reduction in the incidence of metastatic disease of 3.1 per 1000 men screened (median follow-up of 12 years).33

Recently, a 16 year ESPRC follow-up was released showing increased absolute benefit of screening compared to 13 years follow-up.34 Modelling 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.35 Furthermore, increased use of active surveillance in prostate cancer management may mitigate some of the harms associated with treatment.21

Although a PSA result serves as a prognostic marker that is useful to identify clinically significant disease, it has both a significant false positive and false negative predictive rate. PSA testing lacks sensitivity at lower ranges as elevations may be due to other causes (e.g. BPH).36 PSA values increase with age, and there is currently no 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.37,38

Digital Rectal Exam

The ERSPC protocol initially included DRE for men with PSA levels greater that 3 ng/uL, however there was variation in the application of DRE among the study centres.39,40 DRE can lead to the identification of significant prostate cancer in asymptomatic men independent of PSA level.24 However, there are concerns that there is insufficient evidence that the harms of overdiagnosis and overtreatment outweigh the benefits,23 and use of DRE in asymptomatic men remains controversial with recommendations both for and against.15,16,22,23

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.23 As a predictor of prostate cancer in symptomatic patients in primary care, positive and negative predictive values were 42% and 84% respectively.41

While the role of DRE in the initial assessment of a man 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.

Informed decision-making

It is imperative that men understand the harms and benefits of PSA testing and DRE. Primary care providers play an important role in supporting informed discussions with patients. Refer to the Resources section below for examples of decision aids that support informed decision-making. These guidelines are intended to support rational utilization of PSA testing, and to reduce over-testing for asymptomatic individuals who may decide to have a PSA test.
Methodology

This guideline was developed based on the ADAPTE Collaboration guideline adaption 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 included 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, using the following two publications: Referral of Suspected Prostate Cancer by Family Physicians and Other Primary Care Providers, and Follow-up Care and Psychosocial Needs of Survivors of Prostate Cancer.

This guideline includes a systematic review of the evidence 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).

Resources

References


Appendices

- Appendix A: Care Pathway A - Patients with Signs and Symptoms of Suspected Prostate Cancer Including Lower Urinary Tract Symptoms (LUTS) and Elevated PSA Results
- Appendix B: Care Pathway B - Patients with Possible Symptoms of Metastatic Prostate Cancer
- Appendix C: Medication Table for Management of Prostate Cancer Side Effects in Primary Care

Associated Documents

- PSA testing Decision Aids – for Asymptomatic Men Who Ask About PSA Testing
  - HealthLinkBC - Prostate Cancer Screening: Should I have a PSA Test? - https://www.healthlinkbc.ca/health-topics/aa38144#zx3721
  - Canadian Task Force on Preventative Health Care
    - Benefits and Harms of PSA Screening (1000 People Tool)
    - PSA Screening: Patient FAQ
- Prostate Cancer Risk Calculators
  - Patient Health Questionnaire (PHQ-9) - www2.gov.bc.ca/assets/gov/health/practitioner-bc-guidelines/depression_patient_health_questionnaire.pdf
  - Expanded Prostate Cancer Index Composite (EPIC) - https://medicine.umich.edu/dept/urology/research/epic

Resources

- Canadian Cancer Society, www.cancer.ca
- HealthLinkBC - www.healthlinkbc.ca or by telephone (toll free in B.C.) 8-1-1, or 7-1-1 (for the hearing impaired)
- Prostate Cancer Foundation of BC - If I Were Tom | Prostate Cancer Tips, Advice, and Support - www.ifiweretom.ca
- Prostate Centre Canada | Research, Advocacy, Education, Support and Awareness -
www.prostatecancer.ca

- Vancouver Prostate Centre - www.prostatecentre.com

- Advance Care Planning Resources
  - Ministry of Health - Advance Care Planning, www.gov.bc.ca/advancecare
  - BC Guidelines - Advance Care Planning Resource Guide for Patients and Caregivers

- Diagnostic Code: 185 (malignant neoplasm of prostate)

- Abbreviations

  ACP - advance care plan
  ADT - androgen deprivation therapy
  BRCA2 - breast cancer 2 human tumour suppressor gene
  CCO - Cancer Care Ontario
  DRE - digital rectal exam
  EPIC - Expanded Prostate Cancer Index Composite
  ERSPC - European Randomized Study of Screening for Prostate Cancer
  LUTS - lower urinary tract symptoms
  PDE5 - phosphodiesterase type 5
  PHQ9 - Patient Health Questionnaire 9
  PSA - prostate specific antigen
  QoL - quality of life

This guideline is based on scientific evidence current as of November 2017 (refer to Methodology).

The guideline was developed by the BC Cancer Primary Care Program (Family Practice Oncology Network), and the Guidelines and Protocols Advisory Committee.

THE GUIDELINES AND PROTOCOLS ADVISORY COMMITTEE

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

Contact Information:
Guidelines and Protocols Advisory Committee
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Victoria, BC V8W 9P1
Email: hlth.guidelines@gov.bc.ca
Website: www.BCGuidelines.ca

Disclaimer
The Clinical Practice Guidelines (the guidelines) have been developed by 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.
Care Pathway A - Patients with Signs and Symptoms of Suspected Prostate Cancer including Lower Urinary Tract Symptoms (LUTS) and Asymptomatic Men with Elevated PSA results

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

Consider DRE after discussion of harms and benefits

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

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

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

Prostate hard or irregular on DRE?

Yes

Psychiatric not indicated prior to treatment.

No

PSA elevated above age-adjusted reference range?

Yes

Consider other causes of elevated PSA. Repeat PSA at 4-12 weeks.

No

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.

Repeat PSA above age-adjusted reference range?

Yes

Refer to urology.

*Age-based PSA Reference Ranges:
- 0-49 yrs: 0.2-5.0 ng/ml
- 50-59 yrs: 0.3-5.0 ng/ml
- 60-69 yrs: 0.4-5.0 ng/ml
- ≥70 yrs: 0.6-5.0 ng/ml

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.

BC Guidelines - Prostate Cancer, Diagnosis, Referral and Follow-up in Primary Care
DRAFT for External Review - April 18 2019
16
Care Pathway B - 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.

Focal neurologic symptoms or spinal compression?

No

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

Yes

Refer to Emergency Room.

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

No

Prostate cancer is unlikely. Consider other metastatic cancers.

Yes

Refer to urology.

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

Other Causes of Elevated PSA
- Benign prostatic hyperplasia (BPH)
- Prostatitis
- Urinary retention
- Bladder catheterization/instrumentation

PSA levels are not significantly altered after cycling, intercourse, or digital rectal exam.
# Appendix C: Medication Table for Management of Prostate Cancer Side Effects in Primary Care

## Drugs for Management of Prostate Cancer Side Effects in Primary Care

<table>
<thead>
<tr>
<th>Generic Name</th>
<th>Trade name</th>
<th>Dosage form and strengths</th>
<th>Recommended Adult Dose</th>
<th>Adverse Effects</th>
<th>Drug Interactions</th>
<th>PharmaCare Coverage</th>
<th>Approx. Cost</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Management of Erectile Dysfunction</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sildenafil</td>
<td>Viagra, G</td>
<td>Tabs: 25, 50, 100 mg</td>
<td>As needed dosing: 50 to 100 mg 30-60 min before sexual activity Maximum: 100 mg/24 h</td>
<td>Headache, flushing, dyspepsia, nasal congestion, transient visual disturbances, dizziness, skin rash Rare: priapism, permanent vision loss</td>
<td>Decrease dose in patients taking CYP3A4 inhibitors (e.g., cimetidine, clarithromycin, grapefruit juice, ketoconazole) Decreased efficacy in patients taking CYP3A4 inducers (e.g., carbamazepine, phenytoin) Nitrates are contraindicated within 24 hours of sildenafil or vardenafil and 48 hours of tadalafil. May cause hypotension if used with nonselective alpha-blockers, e.g., doxazosin, prazosin, CYP3A4 inhibitors</td>
<td>Non-benefit</td>
<td>$7-10/tab</td>
</tr>
<tr>
<td>Tadalafil</td>
<td>Cialis, G</td>
<td>Tabs: 2.5, 5, 10, 20 mg</td>
<td>Once daily dosing: 2.5 to 5 mg daily PO As needed dosing: 10 to 20 mg 60 min before sexual activity Maximum: 20 mg/36-48h</td>
<td>Orthostatic hypotension, dizziness, headache, asthenia and nasal congestion; syncope The &quot;first-dose effect&quot; of orthostatic hypotension with a severe drop in blood pressure and sudden syncope may occur when beginning therapy. Risk is increased during dose adjustments, with concurrent use of antihypertensive drugs, or ethanol, and in elderly and sodium-depleted patients.</td>
<td>Regular Benefit</td>
<td>$13-14/tab OR $120/month</td>
<td></td>
</tr>
<tr>
<td>Vardenafil</td>
<td>Levitra, G</td>
<td>Tabs: 5, 10, 20 mg</td>
<td>Tablets: As needed dosing: 10 to 20 mg 30-60 min before sexual activity Maximum: 20 mg/24h ODT: As needed dosing: 10 mg dissolved on tongue 45-90 min before sexual activity Maximum: 10 mg/24h</td>
<td>Orthostatic hypotension, dizziness, retrograde ejaculation, orthostatic hypotension May precipitate significant hypotension when used in conjunction with other alpha-blockers, antihypertensives, nitrates or PDE5 inhibitors. Concurrent use with strong CYP3A4 or CYP2D6 inhibitors may increase serum concentration of tamsulosin</td>
<td>Regular Benefit</td>
<td>$8-13/tab</td>
<td></td>
</tr>
<tr>
<td>Doxazosin</td>
<td>Cardura, G</td>
<td>Tabs: 1, 2, 4 mg</td>
<td>Initial: 1 mg qHS Usual: 1-8 mg once daily Maximum: 8 mg per day</td>
<td>Dizziness, retrograde ejaculation, orthostatic hypotension May precipitate significant hypotension when used in conjunction with other alpha-blockers, antihypertensives, nitrates or PDE5 inhibitors. Concurrent use with strong CYP3A4 or CYP2D6 inhibitors may increase serum concentration of tamsulosin</td>
<td>Regular Benefit</td>
<td>$5-8/m</td>
<td></td>
</tr>
<tr>
<td>Tamsulosin</td>
<td>Flomax, Uflo, G</td>
<td>CR tabs: 0.4 mg once daily SR caps: 0.4 mg once daily Maximum: 0.8 mg per day</td>
<td>Dizziness, retrograde ejaculation, orthostatic hypotension May precipitate significant hypotension when used in conjunction with other alpha-blockers, antihypertensives, nitrates or PDE5 inhibitors. Concurrent use with strong CYP3A4 or CYP2D6 inhibitors may increase serum concentration of tamsulosin</td>
<td>Regular Benefit</td>
<td>$6-12/m</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
### Management of bladder and bowel dysfunction

#### Antidiarrheals

<table>
<thead>
<tr>
<th>Medicine</th>
<th>Dose and Administration</th>
<th>Side Effects</th>
<th>Contraindications</th>
<th>Coverage</th>
<th>Cost</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Loperamide</strong>&lt;br&gt;Imodium, G&lt;br&gt;Caps/Tabs: 2 mg</td>
<td>4 mg after 1st loose stool then 2 mg after each subsequent loose stool&lt;br&gt;<strong>Maximum:</strong> 16 mg per day</td>
<td>Abdominal cramps or discomfort, drowsiness, dizziness, dry mouth, skin rash. Higher than recommended doses can lead to cardiac dysrhythmia and death</td>
<td>Concomitant administration with quinidine or ritonavir may increase plasma levels of loperamide</td>
<td>Limited coverage</td>
<td>$30/ 42 pills</td>
</tr>
<tr>
<td><strong>Atropine/diphenoxylate</strong>&lt;br&gt;Lozotil, G&lt;br&gt;Tabs: 0.025/2.5 mg</td>
<td>2 tablets (0.05/5mg) initially, then 1 tablet after each loose stool&lt;br&gt;<strong>Maximum:</strong> 8 tablets per day</td>
<td>Sedation, nausea, abdominal cramps, dry skin and mucous membranes (from atropine), some addiction potential.</td>
<td>Additive anticholinergic effects with other anticholinergic agents</td>
<td>Limited coverage</td>
<td>$35/ 50 tablets</td>
</tr>
</tbody>
</table>

#### Osmotic Laxatives

<table>
<thead>
<tr>
<th>Medicine</th>
<th>Dose and Administration</th>
<th>Side Effects</th>
<th>Contraindications</th>
<th>Coverage</th>
<th>Cost</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Glycerin</strong>&lt;br&gt;G&lt;br&gt;Suppositories: 2.6 mg</td>
<td>1 suppository once or twice daily or as needed&lt;br&gt;Onset: 15-60 mins</td>
<td>Rectal discomfort or burning.</td>
<td>No known drug interactions</td>
<td>Non-benefit</td>
<td>$5-10/ 24 supps</td>
</tr>
<tr>
<td><strong>Lactulose</strong>&lt;br&gt;G&lt;br&gt;Solution: 667 mg/ml</td>
<td>15-30 ml once or twice daily or as needed&lt;br&gt;Onset: 24-48 hours&lt;br&gt;<strong>Maximum:</strong> 60 ml per day</td>
<td>Bloating, flatulence, cramps, diarrhea.</td>
<td>Monitor INR with concomitant warfarin therapy when initiating or discontinuing lactulose</td>
<td>Non-benefit</td>
<td>$10/ 500 ml</td>
</tr>
<tr>
<td><strong>Polyethylene glycol 3350</strong>&lt;br&gt;Lax-A-Day, Pegalax, Resotralax, G&lt;br&gt;Powder</td>
<td>17 g once daily&lt;br&gt;Onset: 2-4 days</td>
<td>Common: nausea, cramping, diarrhea. Rare: hives, skin rash.</td>
<td>May decrease the absorption of other drugs, separate by 2 hours.</td>
<td>Non-benefit (Regular benefit: Plan W)</td>
<td>$25/ month</td>
</tr>
<tr>
<td><strong>Bisacodyl</strong>&lt;br&gt;Dulcolax, G&lt;br&gt;Tabs: 5 mg&lt;br&gt;Suppositories: 10 mg</td>
<td>Oral: 5-10 mg once daily or as needed&lt;br&gt;Onset: 6-12 hours&lt;br&gt;Suppository: 10 mg daily or as needed&lt;br&gt;Onset: 15-60 mins</td>
<td>Abdominal pain, cramps, cathartic colon. Rectal microscopic mucosal changes with suppository</td>
<td>Milk, antacids or PPIs may cause premature dissolution of the enteric coating</td>
<td>Non-benefit (Regular benefit: Plan P and Plan W)</td>
<td>$5/ 30 tabs</td>
</tr>
<tr>
<td><strong>Seneca</strong>&lt;br&gt;Senokot Preparations, G&lt;br&gt;Tabs: 8.6, 12 mg&lt;br&gt;Syrup: 1.7 mg/ml</td>
<td>8.6-17.2 mg once or twice daily&lt;br&gt;Onset: 6-12 hours&lt;br&gt;<strong>Maximum:</strong> 68.8 mg per day</td>
<td>Abdominal pain, cramps, cathartic colon.</td>
<td>No known drug interactions</td>
<td>Non-benefit (Regular benefit: Plan P and Plan W)</td>
<td>$10/ 100 tabs</td>
</tr>
</tbody>
</table>

#### Stimulant Laxatives

<table>
<thead>
<tr>
<th>Medicine</th>
<th>Dose and Administration</th>
<th>Side Effects</th>
<th>Contraindications</th>
<th>Coverage</th>
<th>Cost</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Psyllium</strong>&lt;br&gt;Metamucil, G&lt;br&gt;Multiple</td>
<td>Initial: 15 mg BID with meals&lt;br&gt;(instructions vary with product)</td>
<td>Bloating, flatulence, abdominal discomfort. Rare: allergic reactions, esophageal and colonic obstruction.</td>
<td>May decrease the absorption of other drugs, separate by 3 hours.</td>
<td>Non-benefit</td>
<td>$25/m</td>
</tr>
</tbody>
</table>
### Anticholinergics

<table>
<thead>
<tr>
<th>Medication</th>
<th>Description</th>
<th>Dose</th>
<th>Side Effects</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>oxybutynin \n<em>Ditropan, G</em></td>
<td>IR tabs: 2.5, 5 mg \nSyrup: 1 mg/ml</td>
<td>2.5-5 mg daily to QID \nXL:5-30 mg daily</td>
<td>Dry mouth, constipation, tachycardia.</td>
<td>Potential additive effects with other anticholinergic drugs.</td>
</tr>
<tr>
<td>oxybutynin \n<em>Ditropan XL</em></td>
<td>XL tabs: 5, 10 mg</td>
<td>5-30 mg daily</td>
<td></td>
<td></td>
</tr>
<tr>
<td>solifenacin \n<em>Vesicare, G</em></td>
<td>Tabs: 5, 10 mg</td>
<td>5 mg daily \nMay increase to 10 mg daily</td>
<td>Dry mouth, constipation, tachycardia.</td>
<td>Limited Coverage $11/m</td>
</tr>
<tr>
<td>tolterodine \n<em>Detrol, Detrol LA, G</em></td>
<td>IR tabs: 1, 2 mg \nLA caps: 2, 4 mg</td>
<td>1-2 mg BID \nLA: 2-4 mg once daily</td>
<td>Primarily anticholinergic effects (dry mouth, constipation, tachycardia).</td>
<td>Non-benefit $60/m</td>
</tr>
<tr>
<td>mirabegron \n<em>Myrbetriq</em></td>
<td>Tabs: 25, 50 mg</td>
<td>25 to 50 mg once daily</td>
<td>Hypertension, nasopharyngitis, urinary tract infection, tachycardia</td>
<td>May increase serum concentration of substrates of CYP2D6 (desipramine, metoprolol) and Pgp (digoxin, dabigatran). Coadministration with antimuscarinic agents may increase risk of urinary retention. In patients with severe renal impairment or moderate hepatic impairment do not exceed 25 mg once daily PO.</td>
</tr>
<tr>
<td>17B-estradiol, gel \n<em>Divigel 0.1%, Estrogel 0.06%</em></td>
<td>Packet: 1 packet (0.25, 0.5, 1 mg) once daily \nPump: 1 or 2 actuations once daily</td>
<td>Bloating, headache, nausea, chloasma, breast tenderness. Increased risk of VTE, CVD, breast cancer. Redness, skin irritation.</td>
<td>Estrogens may diminish the effectiveness of anticoagulant, antidiabetic and antihypertensive agents.</td>
<td></td>
</tr>
<tr>
<td>17B-estradiol, patch \n<em>Climara, Estradot, Oesclim, G</em> 25, 37.5, 50, 75, 100 mcg/patch</td>
<td>Climara: 1 patch applied once weekly \nOthers: 1 patch applied twice weekly</td>
<td></td>
<td>Limited Coverage $22-44/m</td>
<td></td>
</tr>
<tr>
<td>cyproterone acetate \n<em>Androcur, G</em></td>
<td>Tabs: 50 mg</td>
<td>Usual: 50 mg BID \nMaximum: 300 mg per day</td>
<td>Decreased libido, edema, gynecomastia, impotence, osteoporosis. Serious: hepatic toxicity, benign and malignant liver tumors and thromboembolic events</td>
<td>CYP3A4 inhibitors (e.g., ketoconazole, clotrimazole, ritonavir) may increase cyproterone levels. CYP3A4 inducers (e.g., rifampicin, phenytoin, St Johns wort) may decrease cyproterone levels. Use with HMGCoA inhibitors (statins) may increase the risk of myopathy or rhabdomyolysis.</td>
</tr>
<tr>
<td>Medication</td>
<td>Dose</td>
<td>Side Effects</td>
<td>Interactions</td>
<td>Cost</td>
</tr>
<tr>
<td>------------</td>
<td>------</td>
<td>--------------</td>
<td>--------------</td>
<td>------</td>
</tr>
<tr>
<td>medroxyprogesterone (Provera, G)</td>
<td>20 mg once daily</td>
<td>Bloating, irritability, weight gain, mood swings.</td>
<td>May diminish therapeutic effect of Anticoagulants</td>
<td>Regular Benefit $12/m</td>
</tr>
<tr>
<td>megestrol acetate (Megace, G)</td>
<td>20 mg once or twice daily</td>
<td>Bloating, irritability, weight gain, mood swings.</td>
<td>May diminish therapeutic effect of Anticoagulants</td>
<td>Regular Benefit $50/m</td>
</tr>
<tr>
<td>venlafaxine (Effexor XR, G)</td>
<td>Initial: 37.5 mg once daily Usual: 37.5 to 150 mg once daily Maximum: 225 mg per day</td>
<td>Nausea, sleep disturbance, drowsiness, nervousness, dizziness, dry mouth. Rare: dose-related hypertension</td>
<td>Use with MAOIs may lead to potentially fatal reaction initially presenting with tremor, agitation, hypomania, hyperthermia and/or hypertension. Inhibitors of CYP2D6 or CYP3A4 may increase venlafaxine levels.</td>
<td>Regular Benefit $4-8/m</td>
</tr>
</tbody>
</table>

Abbreviations: G generics; LCA low cost alternative program; max maximum dose; SL sublingual; XR extended release, XL extended release, LA long active.

* Not an exhaustive list. Check the product monographic or an interaction checker (e.g., Lexicomp®) before prescribing

* PharmaCare coverage as of March 31, 2019 (subject to revision). Obtain current coverage, eligibility, and coverage information from the PharmaCare Formulary Search website at https://pharmacareformularysearch.gov.bc.ca/

* Cost as of March 31, 2019 and does not include retail markups or pharmacy fees.