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Prostate Cancer Part 2: Follow-up in Primary Care

Effective Date: April 15, 2020

Scope

This guideline provides recommendations for the follow-up of patients who have returned to their primary care provider following curative-intent treatment for prostate cancer. Recommendations include the management of potential long-lasting side-effects from treatment, surveillance for possible recurrence, and if needed best supportive care and the early involvement of palliative services.

Prostate Cancer Part 1: Diagnosis and Referral in Primary Care 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.

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

Key Recommendations

- PSA lab reports typically flag a PSA value of greater than the age-based reference range as abnormal, but a biochemical recurrence of the prostate cancer is detected at a much lower PSA value (for example > 0.2 µg/L for a patient after radical prostatectomy).
- Primary care providers should ***review the actual values*** and ensure patients are ***referred back to the oncologist if any measurable increase in PSA is detected*** (Refer to *Table 2 – PSA Profile Indicative of Recurrent Disease (Biochemical Relapse)*).
- Consider referral to the *Prostate Cancer Supportive Care Program*, which is a comprehensive survivorship program for prostate cancer patients, their partners and family from the time of initial diagnosis onwards (see *Resources*).

Follow-up Prostate Cancer Care

Primary care practitioners provide an essential role for the continuity of patient care in all settings, both directly and through the coordination of care with other health care professionals. This reduces the fragmentation of care, improves patient safety, and enhances the overall quality of patient care.

- **PSA Testing for Surveillance of Recurrent Disease**
  In the absence of specific evidence to guide prostate-specific antigen (PSA) testing intervals in patients who have completed treatment, the following recommendations were adapted with modifications from Cancer Care Ontario (CCO), and are based on working group clinical consensus.[1,2] These recommendations are intended for patients who have returned to their primary care practitioner for follow up.[1,2] Surveillance intensity should reflect the risk of recurrence, and practitioners should use clinical judgement to evaluate the benefits of surveillance in patients who are unlikely to benefit from additional salvage therapy. These recommendations are not exhaustive and should be used in accordance with other available resources.[2]
  If a patient develops biochemical relapse following treatment (refer to *Table 2 – PSA Profile Indicative of Recurrent Disease (Biochemical Relapse)* for definitions), then ***refer the patient back to their treating physician*** **(i.e., urology or radiation oncology)**.

Table 1 – Prostate Cancer Follow-up Care Surveillance for Patients who have Undergone Curative-Intent Treatment[2]

Prostate Cancer Follow-up Care Surveillance¥			
Recommendations	**Year 1**	**Year 2**	**Year 3**

Medical follow-up care appointments:¥
a) Medical history and physical examination where indicated
b) Any new and persistent or worsening signs/symptoms to watch for, especially:
• Severe and progressive axioskeletal bone pain
• Hematuria
• New urinary symptoms
  • Significant incontinence requiring changing of undergarments, pads, or diapers
  • Urgency
• Obstructive symptoms
  • Voiding discomfort
  • Nocturia
• New bowel symptoms
  • Rectal bleeding
  • Rectal pain
  • Urgency
  • Change in bowel movement
• Vague constitutional symptoms such as:
  • Fatique
  • Unexplained weight loss
Note: For patients that present with symptoms that could suggest recurrence, a prostate-specific antigen (PSA) text should be performed and a referral back to the appropriate specialist should be considered.
c) Health promotion and disease prevention counselling including (but not limited to):
• Diet, exercise, smoking status, alcohol, sun safety, mental health, sexual health, and other informational needs
	After first 3 months; then every 6 months	Every 6 months	Every 12 months

Prostate-specific antigen (PSA) test:¥ **a) For patients following curative-intent treatment with surgery***	Every 3 months	Every 6 months	Every 6 months (until end of year 3; then annually thereafter)
b) For patients following curative-intent treatment with non-surgery primary therapy (e.g., radiation therapy, cryotherapy, or high-intensity focused ultrasound)*	Every 6 months	Every 6 months	Every 12 months
*Caution: **PSA lab test results:** PSA lab reports typically flag a PSA value of greater than the age-based reference range as abnormal, but a biochemical recurrence of the prostate cancer is detected at a much lower PSA value (for example >0.2 µg/L for a patient after radical prostatectomy). Therefore, primary care providers should ***review the actual values*** and ensure patients are ***referred back to the oncologist if any measurable increase in PSA is detected*** (Refer to *Table 2 – PSA Profile Indicative of Recurrent Disease (Biochemical Relapse)*).			
For patients on androgen deprivation therapy (ADT): Consider a complete blood count (CBC) annually to monitor hemoglobin levels, particularly in men presenting with symptoms suggestive of anemia. Asses risk of fracture for men treated with ADT through baseline DEXA (dual energy x-ray absorptiometry) scan and calculation of a FRAX® (fracture risk assessment score). Recommend calcium and vitamin D supplementation.			
¥ *Adapted with permission from CCO with modifications: Ontario Prostate Cancer Follow-up Care Clinical Guidance Summary*[2]			
Special Considerations¥			
Digital rectal exam (DRE): Routine DRE is not required after treatment of localized prostate cancer unless there is evidence of a PSA recurrence, or for the evaluation of symptoms (e.g., obstructive voiding symptoms, change in bowel habits or pelvic pain).			
¥ *Adapted with permission from CCO with modifications: Ontario Prostate Cancer Follow-up Care Clinical Guidance Summary*[2]			

Table 2 – PSA Profile Indicative of Recurrent Disease (*Biochemical Relapse*)[3]

Treatment	PSA Profile Indicating Possible Recurrent Disease
Note: If a patient develops a PSA profile indicative of recurrent disease, they should be referred back to their treating physician (i.e., urology or radiation oncology).	
Radical prostatectomy	• 2 successive increases to a level of >0.2 µg/L.
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 long as 1-3 years post-therapy. PSA levels may temporarily rise to ≥4 µg/L.

Management of Patients with Long-lasting Symptoms

Men can experience specific and often long-lasting effects usually occurring more than three months after surgery or radiation, or during/after androgen deprivation therapy.[1,2] Refer to *Table 3 – Common Long-term and Late Effects of Prostate Cancer Treatment*, to identify common long-term and late effects of treatment including sexual, urinary, or bowel dysfunction, and other physical and/or psychological effects.[1,2] For additional information on the management of common prostate cancer side effects in primary care refer to *Appendix B: Long-term Side Effects and Recommendations for Management* and *Appendix C: Medications for the Management of Prostate Cancer Side Effects in Primary Care*. To address individual variability in response to treatments, and to ensure optimal quality of life, individual patient-reported outcomes should be measured.[1,4]

Table 3 – Common Long-term and Late Effects of Prostate Cancer Treatment

Common Long-term and Late Effects[¥]

Physical:
• Sexual dysfunction (for all treatments)
  • Erectile dysfunction
  • Loss of libido
  • Anorgasmia
  • Dry ejaculate
  • Climacturia
  • Penile shortening or curvature
  • Infertility
• Urinary dysfunction (for those treated with surgery or RT)
  • Obstructive symptoms
  • Urgency symptoms
  • Hematuria
  • Incontinence
• Bowel dysfunction (for those treated with RT)
  • Rectal bleeding
  • Urgency and frequency sysmptoms
• Other (mostly for those treated with ADT)
  • Anemia
  • Body composition alterations
  • Fatique (for all treatments)
  • Gynecomastia/mastodynia
  • Hot flashes
  • Bone health

Psychosocial: • Psychological distress (e.g., depression, anxiety, worry, fear of recurrence) • Cognitive side-effects • Changes in sexual function/fertility • Challenges with body and/or self-image, relationships, and other social role difficulties • Return to work concerns and financial challenges
¥ *Adapted with permission from CCO with modifications: Ontario Prostate Cancer Follow-up Care Clinical Guidance Summary*[2]

Survivorship

Survivorship care is a fundamental component of post-treatment care. It is the link between treatment and recovery, and a key point of continuity of care bridging the connections 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.[1] Consider referral to the *Prostate Cancer Supportive Care Program*, which is a comprehensive survivorship program for prostate cancer patients, their partners and family from the time of initial diagnosis onwards (see *Resources*).

Palliative Care and 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 (ACP) that incorporates the patient's values and personal goals, indicates potential outcomes, and identifies linkages with other health care professionals that would be involved in the care, as well as their expected roles. The ACP is an opportunity to also identify the patient's alternate substitute decision-maker or legal health representative. For information and tools on advance care planning refer to the *Resources* section below. For information on palliative care, including tools for identifying patients who would benefit from palliative care at earlier stages of the illness, refer to the *Resources – Palliative Care and Advanced Care Planning* section below.

Resources

References

1. A. Matthew, L.H. Souter, R.H. Breau, C. Canil, M. Haider, L. Jamnicky, R. Morash, D. Smith, M. Surchin, A. Loblaw , Prostate Cancer Follow-up Expert Panel. Follow-up Care and Psychosocial Needs of Survivors of Prostate Cancer [Internet]. Cancer Care Ontario. [cited 2020 Jul 2]. Available from: https://www.cancercareontario.ca/en/guidelines-advice/types-of-cancer/266
2. Cancer Care Ontario – Prostate Cancer Follow-up Care Pathway Map Version 2018.03 [Internet]. Available from: https://www.cancercareontario.ca/sites/ccocancercare/files/assets/CCOProstateFollowUpPathway.pdf
3. BC Cancer. Prostate – Chapter 5 Management – Follow-up: Definitions of Biochemical Relapse. [Internet]. [cited 2020 Jul 2]. Available from: http://www.bccancer.bc.ca/health-professionals/clinical-resources/cancer-management-guidelines/genitourinary/prostate#Management-prostate
4. Gilbert SM, Dunn RL, Wittmann D, Montgomery JS, Hollingsworth JM, Miller DC, et al. Quality of life and satisfaction among prostate cancer patients followed in a dedicated survivorship clinic. Cancer. 2015 May 1;121(9):1484–91.

Appendices

- Appendix A: Guideline Development Methodology
- Appendix B: Long-term Side Effects and Recommendations for Management
- Appendix C: Medications for the Management of Prostate Cancer Side Effects in Primary Care

Associated Documents

- BC Guidelines: Prostate Cancer Part 1: Diagnosis and Referral in Primary Care, www.BCguidelines.ca
- Patient Health Questionnaire (PHQ-9), www2.gov.bc.ca/assets/gov/health/practitioner-pro/bc-guidelines/depression_patient_health_questionnaire.pdf
- Expanded Prostate Cancer Index Composite (EPIC), https://medicine.umich.edu/dept/urology/research/epic

Resources

- **BC Cancer**
  - Prostate, www.bccancer.bc.ca/health-info/types-of-cancer/mens-cancer/prostate
  - Hereditary Cancer Program, www.bccancer.ca/our-services/services/hereditary-cancer
  - Lesbian, Gay, Bisexual and Transgender with Cancer Websites, www.bccancer.bc.ca/our-services/services/library/recommended-websites/living-with-cancer-websites/lgbt-with-cancer-websites

- **Family Practice Oncology Network (FPON) UBC - Continuing Professional Development**
  - Online Prostate Cancer Module – 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
  - 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, the General Practice Services Committee, or with your relevant Section at the Doctors of BC.
- Canadian Cancer Society – www.cancer.ca
- Prostate Cancer Canada – Research, advocacy, education, support and awareness, www.prostatecancer.ca
- Survivorship
  - BC Cancer – Emotional support, exercise support, complementary and alternative therapies, and life after cancer resources:
    - Advance Care Planning, www.bccancer.bc.ca/health-info/coping-with-cancer/advance-care-planning
    - Complementary & Alternative Therapies, www.bccancer.bc.ca/health-info/coping-with-cancer/complementary-alternative-therapies
    - Coping with Cancer, www.bccancer.bc.ca/health-info/coping-with-cancer
    - Emotional Support, www.bccancer.bc.ca/health-info/coping-with-cancer/emotional-support
    - Exercise Support, www.bccancer.bc.ca/health-info/coping-with-cancer/exercise-support#More--Resources
    - Life After Cancer, www.bccancer.bc.ca/health-info/coping-with-cancer/life-after-cancer
  - HealthLink BC, 8-1-1 (toll free in B.C.), or 7-1-1 (for the hearing impaired)
    - Dietitian Services, www.healthlinkbc.ca/dietitian-services
    - Eating Guidelines for After a Prostate Cancer Diagnosis, www.healthlinkbc.ca/healthy-eating/prostate-cancer-diagnosis
    - Nutrition for People with Cancer, www.healthlinkbc.ca/healthy-eating/your-condition/cancer
    - Physical Activity Services, www.healthlinkbc.ca/physical-activity-services
  - Prostate Cancer Foundation of BC – www.prostatecancerbc.ca
    - If I Were Tom – Prostate Cancer Tips, Advice, and Support – www.ifiweretom.ca
  - Vancouver Prostate Centre – www.prostatecentre.com
    - Prostate Cancer Supportive Care (PCSC) Program, https://pcscprogram.ca
- Palliative Care and Advance Care Planning
  - BC Guidelines, www.BCguidelines.ca
    - Advance Care Planning: Resource Guide for Patients and Caregivers, www2.gov.bc.ca/assets/gov/health/practitioner-pro/bc-guidelines/advance-care-guide.pdf
    - Palliative Care for the Patient with Incurable Cancer or Advanced Disease – Parts 1-3, www2.gov.bc.ca/gov/content/health/practitioner-professional-resources/bc-guidelines/palliative-care-approach
  - B.C. Ministry of Health – Advance Care Planning, www.gov.bc.ca/advancecare
    - My Voice – Expressing My Wishes for Future Health Care Treatment, www.gov.bc.ca/advancecare
  - Cancer Care Ontario, www.cancercareontario.ca/en
    - A Palliative Care Approach for Primary Care, www.ccohealth.ca/sites/CCOHealth/files/assets/CCOPalliativePrimaryApproach.pdf
  - HealthLinkBC – Advance Care Planning, www.healthlinkbc.ca/health-feature/advance-care-planning
- Provincial Health Services Authority
  - Trans Care BC – A Primary Care Toolkit – Gender-affirming Care for Trans, Two-spirit, and Gender Diverse Patients in BC, http://www.phsa.ca/transcarebc/Documents/HealthProf/Primary-Care-Toolkit.pdf

Diagnostic Code: 185 (malignant neoplasm of prostate)

Abbreviations

ACP - advance care plan
ADT - androgen deprivation therapy
AGREE - appraisal of guidelines for research and evaluation
CBC - complete blood count
CCO - Cancer Care Ontario
DEXA - dual-energy x-ray absorptiometry
DRE - digital rectal exam
EPIC - Expanded Prostate Cancer Index Composite
FRAX® - fracture risk assessment score
PHQ-9 - Patient Health Questionnaire
PSA - prostate specific antigen
RT - Radiation Therapy

The guideline was developed by the BC Cancer Primary Care Program (Family Practice Oncology Network), and the Guidelines and Protocols Advisory Committee. This guideline is based on scientific evidence current as of November 2017. For more information about how this guideline was developed, refer to *Appendix A: Guideline Development Methodology*. For more information about how BC Guidelines are developed in general, refer to the GPAC Handbook available at BCGuidelines.ca: GPAC Handbook.

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

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Appendix A: Guideline Development Methodology

The BCGuideline, *Prostate Cancer – Part 2: Follow-up in Primary Care*, was developed by a working group of practicing BC physicians, based on the ADAPTE Collaboration guideline adaption methodology.[1] 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.[2]

The recommendations in this guideline were adapted with permission from Cancer Care Ontario's Program in Evidence Based Care, *Follow-up Care and Psychosocial Needs of Survivors of Prostate Cancer, and Ontario Prostate Cancer Follow-up Care Clinical Guidance Summary*.[3,4]

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

1. ADAPTE Collaboration. ADAPTE Resource Toolkit for Guideline Adaptation. Version 1.0: 2007. [Internet]. Available from: https://g-i-n.net/document-store/working-groups-documents/adaptation/adapte-resource-toolkit-guideline-adaptation-2-0.pdf/view.
2. AGREE Next Steps Consortium. The AGREE II Instrument [Electronic version]. [Internet]. 2017 [cited 2018 Aug 29]. Available from: http://www.agreetrust.org.
3. A. Matthew, L.H. Souter, R.H. Breau, C. Canil, M. Haider, L. Jamnicky, R. Morash, D. Smith, M. Surchin, A. Loblaw , Prostate Cancer Follow-up Expert Panel. Follow-up Care and Psychosocial Needs of Survivors of Prostate Cancer [Internet]. Cancer Care Ontario. [cited 2020 Jul 2]. Available from: https://www.cancercareontario.ca/en/guidelines-advice/types-of-cancer/266
4. Cancer Care Ontario – Prostate Cancer Follow-up Care Pathway Map Version 2018.03 [Internet]. Available from: https://www.cancercareontario.ca/sites/ccocancercare/files/assets/CCOProstateFollowUpPathway.pdf

Appendix B: Long-term Side Effects and Recommendations for Management

This table accompanies the BC Guideline *Prostate Cancer – Follow up in Primary Care* and is adapted with permission from Cancer Care Ontario's *Follow-up Care and Psychosocial Needs of Survivors of Prostate Cancer*.[1] Refer also to *Appendix C:* Medications for the Management of Prostate Cancer Side Effects in Primary Care.

Side Effect	Management Options*
Sexual Dysfunction *Patients with primary treatment of surgery, radiation therapy, or androgen deprivation therapy*	
Erectile dysfunction	• Men may be prescribed phosphodiesterase type 5 (PDE5) inhibitors as first line treatment.* • Men who do not respond to PDE5 inhibitors will need more advanced treatments and should be referred to a urologist or sexual health expert.* • Men may be referred to penile rehabilitation programs, which include PDE5 inhibitors, vacuum constriction devices, intracorporal or intraurethral therapy, or placement of penile prostheses.*
Loss of libido	• Men and their partners should be referred to a healthcare professional with training in sexual health counselling, when available. • 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.*
Anorgasmia	• Men and their partners should be referred to a healthcare professional with training in sexual health counselling, when available.*
Dry ejaculate	• Men should be educated on dry ejaculate.*
Climacturia	• 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.*
Penile shortening or curvature	• Regular sexual stimulation may prevent penile shortening. • If there is significant penile curvature impairing sexual function, refer patient to a urologist.

Infertility	• Men and their partner should be informed that:
	  • men treated with radical prostatectomy ***will become*** infertile, and
	  • some men treated with radiation therapy ***may remain*** fertile, even when experiencing sexual dysfunction symptoms.*

Side Effect	Management Options*
Urinary Dysfunction *(Patients with primary treatment of surgery and/or radiation therapy)*	
Obstructive symptoms	• Selective alpha-antagonists may be prescribed for patients who ***have not*** undergone radical prostatectomy. • Refer to a urologist to evaluate for bladder neck contracture or urethral stricture.
Urgency symptoms	• If the patient is able to completely empty his bladder (i.e., post-void residual of <200cc), bladder antispasmodic medications (anticholinergics or beta-3 agonists) may be appropriate. • All refractory symptoms should result in a referral to a urologist for evaluation and escalation of therapy if appropriate*
Hematuria	• Men with hematuria should be referred to a urologist for evaluation*
Incontinence requiring urinary pads	• Men with persistent leakage impacting quality of life should be referred to a urologist to evaluate the cause of incontinence.* • Exercise intervention such as Kegel exercises may improve continence. Specialized physiotherapists and nurse continence advisors may help patients with stress incontinence following radical prostatectomy. • In men with post-prostatectomy incontinence >1 year, consider referral back to treating urologist for assessment for urethral slings or artificial urinary sphincters.
Bowel Dysfunction *Patients with primary treatment of radiation therapy*	

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.

Side Effect	Management Options*
Other Physical Side-effects *– continued* *Patients with primary treatment of surgery, radiation therapy, or androgen deprivation therapy*	
Anemia	• Investigation for common sources of anemia should be considered.*
Body composition alterations	• Men should be encouraged to participate in an exercise program.
Fatigue	• Men should be encouraged to participate in an exercise program.
Gynecomastia/ mastodynia	• In severe cases, surgical excision can be considered; patients should be referred to a specialist.*
Hot Flashes	• Treatment with transdermal estrogen, megestrol acetate, venlafaxine, cyproterone acetate, and medroxyprogesterone can be considered, however, use for this indication is off-label.** Longer-term prospective studies are required to determine whether these medications can alleviate hot flashes without increased harms. Use with caution because treatment with these medications has been associated with serious adverse effects. Consult the product monograph for a full list of adverse effects.
Physical activity levels	• Men should be encouraged to participate in an exercise program.
Bone health	• For recommendations on maintaining bone health, refer to *Osteoporosis: Diagnosis, Treatment and Fracture Prevention* at BCGuidelines.ca
Cognitive side-effects	• Rule out other reversible cognitive problems.
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. • Use of standardized assessment tools is recommended (e.g., EPIC or PHQ9).

* *Recommendations were adapted with modifications from CCO and are based on expert consensus; additional clinical references are outlined as indicated.*

** *Off-label: the prescription of a registered medicine for a use that is not included in the product information.*

Abbreviations: *PDE5 – phosphodiesterase type 5; QoL – quality of life; EPIC – expanded prostate cancer index composite; PHQ9 – Patient Health Questionnaire 9*

References

1. Matthew A, Souter LH, Breau RH, Canil C, Haider M,, Jamnicky R, et al. Follow-up care and psychosocial needs of survivors of prostate cancer. Toronto (ON): Cancer Care Ontario; 2015 June 16. Program in Evidence-based Care Guideline No.: 26-4.
2. Frisk J. Managing hot flushes in men after prostate cancer—A systematic review. Mauritas. 2010 Jan;65(1):15-22.
3. Gazarian M, Kelly M, McPhee JR, et al. Off-label use of medicines: consensus recommendations for evaluating appropriateness. MJA. 2006;185:544-8.

Appendix C: Medications for the Management of Prostate Cancer Side Effects in Primary Care

Medications for the Management of Prostate Cancer Side Effects in Primary Care

Generic Name *Trade* name Dosage form and strengths	Recommended Adult Dose[A]	Adverse Effects[B]	Drug Interactions[B]	PharmaCare Coverage[C]	Approx. Cost per month[D]
Management of Erectile Dysfunction					
Phosphodiesterase type 5 inhibitors					
sildenafil *Viagra, G* Tabs: 25, 50, 100 mg	**As needed dosing:** 50 to 100 mg 30-60 min before sexual activity **Duration:** up to 12 hours **Maximum:** 100 mg per day	Headache, flushing, dyspepsia, nasal congestion, transient visual disturbances, dizziness, skin rash Rare: priapism, vision loss	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	Non-benefit	$7-10/tab
tadalafil *Cialis, G* Tabs: 2.5, 5, 10, 20 mg	**Once daily dosing:** 2.5 to 5 mg daily **As needed dosing:** 10 to 20 mg 30-60 min before sexual activity **Duration:** Up to 36 hours **Maximum:** 20 mg per day			Non-benefit	$13-14/tab OR $120/month
vardenafil *Levitra, G* Tabs: 5, 10, 20 mg *Staxyn* Oral disintegrating tablets (ODT): 10 mg	Tablets: **As needed dosing:** 10 to 20 mg 30-60 min before sexual activity **Duration:** up to 12 hours **Maximum:** 20 mg/24h *ODT:* **As needed dosing:** 10 mg dissolved on tongue 45-90 min before sexual activity **Maximum:** 10 mg per day			Non-benefit	$8-13/tab

Generic Name *Trade* name Dosage form and strengths	Recommended Adult Dose[A]	Adverse Effects[B]	Drug Interactions[B]	PharmaCare Coverage[C]	Approx. Cost per month[D]
Management of bladder and bowel dysfunction					
Alpha1-adrenergic Receptor Antagonists					
doxazosin[E] *Cardura, G* Tabs: 1, 2, 4 mg	Initial: 1 mg once daily Usual: 1-8 mg once daily **Maximum:** 8 mg per day	Orthostatic hypotension, dizziness, headache, asthenia, nasal congestion, syncope. The "first-dose effect" 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.	May precipitate significant hypotension when used in conjunction with other alpha-blockers, antihypertensives, nitrates or PDE5 inhibitors.	Regular Benefit	$5-8
tamsulosin[E] *Flomax, Uflo, G* CR tabs: 0.4 mg SR caps: 0.4 mg	CR tab: 0.4 mg once daily SR caps: 0.4 mg once daily **Maximum:** 0.8 mg per day	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	Regular Benefit	$6-12
Antidiarrheals					
loperamide *Immodium, G* Caps/Tabs: 2 mg	4 mg after 1st loose stool then 2 mg after each subsequent loose stool **Maximum:** 16 mg per day	Abdominal cramps or discomfort, drowsiness, dizziness, dry mouth, skin rash. Higher than recommended doses can lead to cardiac dysrhythmia and death	Concomitant administration with quinidine or ritonavir may increase plasma levels of loperamide	Limited coverage	$30/ 42 pills
atropine/diphenoxylate *Lomotil, G* Tabs: 0.025/2.5 mg	2 tablets (0.05/5mg) initially, then 1 tablet after each loose stool **Maximum:** 8 tablets per day	Sedation, nausea, abdominal cramps, dry skin and mucous membranes (from atropine), some addiction potential.	Additive anticholinergic effects with other anticholinergic agents	Limited coverage	$35/ 50 tablets
Osmotic Laxatives					
glycerin *G* Suppositories: 2.6 mg	1 suppository once or twice daily or as needed *Onset:* 15-60 mins	Rectal discomfort or burning.	No known drug interactions	Non-benefit	$10-20
lactulose *G* Solution: 667 mg/ml	15-30 ml once or twice daily or as needed *Onset:* 24-48 hours **Maximum:** 60 ml per day	Bloating, flatulence, cramps, diarrhea.	Monitor INR with concomitant warfarin therapy when initiating or discontinuing lactulose	Non-benefit	$30
polyethylene glycol 3350 *Lax-A-Day, Pegalax, ResotraLax, G* Powder	17 g once daily *Onset:* 2-4 days	Common: nausea, cramping, diarrhea. Rare: hives, skin rash.	May decrease the absorption of other drugs, separate by 2 hours.	Non-benefit (Regular benefit: Plan W)	$25
Stimulant Laxatives					

Generic Name *Trade* name Dosage form and strengths	Recommended Adult Dose[A]	Adverse Effects[B]	Drug Interactions[B]	PharmaCare Coverage[C]	Approx. Cost per month[D]
bisacodyl *Dulcolax, G* Tabs: 5 mg Suppositories: 10 mg	Oral: 5-10 mg once daily or as needed *Onset:* 6-12 hours Suppository: 10 mg daily or as needed *Onset:* 15-60 mins	Abdominal pain, cramps, cathartic colon. Rectal microscopic mucosal changes with suppository	Milk, antacids or PPIs may cause premature dissolution of the enteric coating	Non-benefit (Regular benefit: Plan P and Plan W)	$5/ 30 tabs $30/ 30 supps
senna *Senokot Preparations, G* Tabs: 8.6, 12 mg Syrup: 1.7 mg/ml	8.6-34.4 mg once or twice daily *Onset:* 6-12 hours **Maximum:** 68.8 mg per day	Abdominal pain, cramps, cathartic colon.	No known drug interactions	Non-benefit (Regular benefit: Plan P and Plan W)	$10/ 100 tabs
Other					
psyllium *Metamucil, G* Multiple	Initial: 15 mg BID with meals (instructions vary with product)	Bloating, flatulence, abdominal discomfort. Rare: allergic reactions, esophageal and colonic obstruction.	May decrease the absorption of other drugs, separate by 3 hours.	Non-benefit	$25
Anticholinergics					
oxybutynin *Ditropan, Ditropan XL, G* IR tabs: 2.5, 5 mg Syrup: 1 mg/ml XL tabs: 5, 10 mg	IR: 2.5-5 mg once daily to four times a day XL: 5-30 mg daily	Dry mouth, constipation, tachycardia.	Potential additive effects with other anticholinergic drugs. **solifenacin:** do not exceed 5 mg daily with potent CYP3A4 inhibitors, e.g., erythromycin, itraconazole, nelfinavir, ritonavir. **tolterodine:** maximum dose of 2 mg/day in patients taking potent inhibitors of CYP3A4 (e.g., erythromycin, itraconazole, ketoconazole, nelfinavir, ritonavir). Coadministration of Detrol LA with antacid results in increased Cmax and the potential for "dose-dumping." Tolterodine extended-release products may also be affected by PPI treatment	IR: Regular benefit XL: Non-benefit	IR: $11-85 XL: $90-280
oxybutynin *Oxytrol Patch* 36mg	1 patch (3.9 mg/d) twice weekly			Non-benefit	$60
solifenacin *Vesicare, G* Tabs: 5, 10 mg	5 mg daily May increase to 10 mg daily	Dry mouth, constipation, tachycardia.		Limited Coverage	$11
tolterodine *Detrol, Detrol LA, G* IR tabs: 1, 2 mg LA caps: 2, 4 mg	IR: 1-2 mg BID LA: 2-4 mg once daily	Primarily anticholinergic effects (dry mouth, constipation, tachycardia).		Non-benefit	$17-60
Beta-3-adrenergic agonists					
mirabegron *Myrbetriq* Tabs: 25, 50 mg	25 to 50 mg once daily	Hypertension, nasopharyngitis, urinary tract infection, tachycardia	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.	Non-benefit	$60

Generic Name *Trade* name Dosage form and strengths	Recommended Adult Dose[A]	Adverse Effects[B]	Drug Interactions[B]	PharmaCare Coverage[C]	Approx. Cost per month[D]
Management of hot flashes[F]					
17B-estradiol, gel[E] *Divigel 0.1%, Estrogel 0.06%* Packet: 0.25, 0.5, 1 mg Pump: 0.75 mg/ actuation	Packet: 1 packet (0.25, 0.5, 1 mg) once daily Pump: 1 or 2 actuations once daily	Bloating, headache, nausea, chloasma, breast tenderness. Redness, skin irritation. Serious: Increased risk of VTE, CVD, breast cancer.	Estrogens may diminish the effectiveness of anticoagulant, antidiabetic and antihypertensive agents.	Limited Coverage	$22-44
17B-estradiol, patch[E] *Climara, Estradot, Oesclim, G* 25, 37.5, 50, 75, 100 mcg/ patch	Climara: 1 patch applied once weekly Others: 1 patch applied twice weekly			Limited Coverage	$20-25
cyproterone acetate[E] *Androcur, G* Tabs: 50 mg	Usual: 50 mg BID **Maximum:** 300 mg per day	Decreased libido, edema, gynecomastia, impotence, osteoporosis. Serious: hepatic toxicity, benign and malignant liver tumors and thromboembolic events	CYP3A4 inhibitors (e.g., ketoconazole, clotrimazole, ritonavir) may increase cyproterone levels CYP3A4 inducers (e.g., rifampicin, phenytoin, St. John's Wort) may decrease cyproterone levels Use with HMGCoA inhibitors (statins) may increase the risk of myopathy or rhabdomyolysis	Non-benefit	$100
medroxyprogesterone[E] *Provera, G* Tabs: 2.5, 5, 10 mg	20 mg once daily	Bloating, irritability, weight gain, mood swings. Serious: hepatic dysfunction, thromboembolic events	May diminish therapeutic effect of Anticoagulants	Regular Benefit	$12
megestrol acetate[E] *Megace, G* Tab: 40, 160 mg	20 mg once or twice daily			Regular Benefit	$50
venlafaxine[E] *Effexor XR, G* Caps: 37.5, 75, 150 mg	Initial: 37.5 mg once daily Usual: 37.5 to 150 mg once daily **Maximum:** 225 mg per day	Nausea, sleep disturbance, drowsiness, nervousness, dizziness, dry mouth. Discontinuation symptoms. Serious: dose-related hypertension, suicidal ideation, severe agitation	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.	Regular Benefit	$4-8

Abbreviations: BID twice a day; **CAP** capsules; **CR** controlled release; **G** generics; **IR** immediate release; **ODT** oral dissolving tablet; ; **LA** long acting; **MAOIs** – monoamine oxidase inhibitors; **SR** sustained release; **Tab** tablets; **XR** extended release

[A] For normal renal and hepatic function. Consult product monograph for detailed dosing instructions and dose adjustments for unique patient populations

[B] Not an exhaustive list. Check the product monograph (https://health-products.canada.ca/dpd-bdpp/index-eng.jsp) or an interaction checker (e.g., Lexicomp©) before prescribing

[C] PharmaCare coverage as of April 2019 (subject to revision). Regular Benefit: Eligible for full reimbursement*. Limited Coverage: Requires Special Authority to be eligible for reimbursement*. Non-benefit: Not eligible for reimbursement. *Reimbursement is subject to the rules of a patient's PharmaCare plan, including any deductibles. In all cases, coverage is subject to drug price limits set by PharmaCare. See: www.health.gov.bc.ca/pharmacare/plans/index.html and www.health.gov.bc.ca/pharmacare/policy.html for further information.

[D] Drugs costs are average retail cost of the generic, when available. Current as of April 2019 and does not include retail markups or pharmacy fees.

[E] Off-label: Prescription of a registered medicine for a use that is not included in the product information.

[F] Longer-term prospective studies are required to determine whether these medications can alleviate hot flushes, without increased toxicity.

References

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