Endocrine therapies for breast and prostate cancers

Essentials for primary care

Genevieve Chaput MD MA CCFP(PC) Nureen Sumar MSc MD CCFP

Breast and prostate cancers are the most common cancers in Canada, occurring in approximately 1 in 8 women and 1 in 8 men, respectively.[1] The predicted 5-year survival rate for patients with either cancer is approximately 90%.[1] Endocrine therapy is a mainstay treatment for the management of these hormone-sensitive cancers. Although endocrine therapies are associated with improved survival and prolonged time to disease progression, treatment-related side effects can be burdensome, leading to suboptimal adherence.[2,3] Primary care providers play an invaluable role in the care of cancer patients and survivors. This article provides an overview of endocrine therapy, with a focus on breast and prostate cancer agents, including indications, clinical pearls, and common side effects and their management.

What is endocrine therapy?

Endocrine therapy is used to treat cancers that use hormones or hormone signaling pathways for growth or survival. At the cellular level, endocrine signaling in cancer cells leads to increased cell proliferation, decreased time available for DNA repair, and increased risk of mutation.[4] Endocrine therapy primarily works by interfering with endocrine signaling, blocking hormone synthesis, or targeting hormone receptors.[5,6] In the adjuvant setting, these therapies can improve overall survival and decrease risk of cancer recurrence, whereas in the metastatic setting, they might reduce symptom burden.[7,8] The type and duration of endocrine therapy is determined by cancer stage at diagnosis, molecular characteristics, prognostic indicators, cancer genomics, endocrine resistance, and tolerance of adverse toxic effects.

Endocrine therapies include corticosteroids, thyroid hormones, somatostatin analogues, and reproductive hormones. Corticosteroids, frequently combined with chemotherapy to increase their effectiveness, are used in the treatment of hematologic cancers (ie, leukemias, lymphomas, and multiple myelomas).[5] Thyroid hormones (levothyroxine) are used to inhibit thyroid growth following surgery or radiotherapy for thyroid cancers, or as hormonal replacement therapy after thyroid gland resection.[9] Somatostatin analogues (octreotide) are a cornerstone treatment for neuroendocrine tumours and, in particular, reduce symptom burden associated with carcinoid syndrome.[8] Finally, and our focus here, reproductive hormones are frequently used to treat cancers requiring male or female hormones to grow, such as breast and prostate cancers.

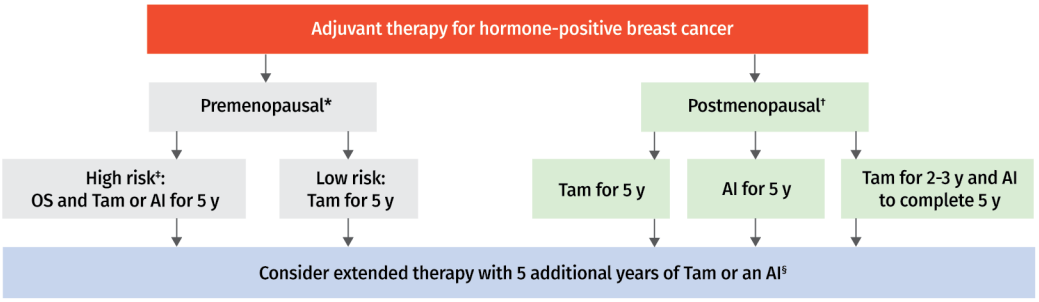
Endocrine therapy in breast cancer

More than 75% of breast cancers are driven by either estrogen or progesterone.[10] Compared with breast cancers that are not hormone receptor–positive, estrogen receptor–positive or progesterone receptor–positive breast cancers are usually associated with improved survival.[11] Endocrine therapy is a cornerstone treatment in both adjuvant and metastatic settings of hormone receptor–positive breast cancers; it is also sometimes used as a neoadjuvant therapy. Choice of endocrine regimen is typically determined by clinical, pathologic, and genetic factors, including menopausal status. The main breast cancer endocrine therapies are selective estrogen receptor modulators (eg, tamoxifen), aromatase inhibitors (eg, letrozole, anastrozole, exemestane), and ovarian suppression (ie, via gonadotropin-releasing hormone agonists or surgery). In the adjuvant setting, the choice of endocrine therapy is further determined by low-risk versus high-risk categories, with patients younger than 35 years at diagnosis or needing adjuvant chemotherapy following surgery categorized as high risk (**Figure 1**).[11] Other newer therapies, most used in the metastatic setting, include cyclin-dependent kinase 4 and cyclin-dependent kinase 6 inhibitors (eg, ribociclib, palbociclib), selective estrogen receptor degraders (eg, fulvestrant), and mTOR (mammalian target of rapamycin) inhibitors (eg, everolimus).

Premenopausal patients. In the adjuvant setting, for premenopausal patients at standard risk, tamoxifen is the first-line recommended agent at an oral dose of 20 mg daily for a minimum of 5 years.[11] Adjuvant tamoxifen therapy for 5 to 10 years is associated with a statistically significant absolute breast cancer mortality reduction at 15 years (mean [SD] 9.2% [1%]).[12,13] For premenopausal patients at high risk of recurrence, tamoxifen or an aromatase inhibitor is recommended in addition to ovarian suppression based on a discussion of risks and benefits with the patient.[11]

Clinical pearl: Given the risk of inducing estrogen production due to ovarian stimulation, aromatase inhibitors should not be used as a single agent in premenopausal patients. In high-risk patients, aromatase inhibitors coupled with ovarian suppression might be used. Recurrence of menstrual periods during aromatase inhibitor therapy

Figure 1. Algorithm for choice of endocrine therapy for breast cancer in the adjuvant setting



AI—aromatase inhibitor (letrozole, anastrozole, exemestane), OS—ovarian suppression, Tam—tamoxifen.
*Menopause: Defined as any patient younger than 60 y of age who previously underwent bilateral oophorectomy or who has not had any menstrual periods for 12 mo or more in the absence of tamoxifen, chemotherapy, or ovarian suppression, and whose serum estradiol level is in the postmenopausal range or who is amenorrheic on tamoxifen, with follicle-stimulating hormone and serum estradiol levels in the postmenopausal range.
†Any patient 60 y of age or older.
‡Any patient younger than 35 y of age or any premenopausal patient who has received chemotherapy in the adjuvant setting.
§Additional treatments to be decided in conjunction with an oncologist on a case-by-case basis.
Adapted from Awan and Esfahani (Creative Commons—Attribution 4.0 International—CC BY 4.0: **https://creativecommons.org/licenses/by/4.0/**).[11]

warrants measurement of serum estradiol levels and urgent referral back to an oncology specialist.

Postmenopausal patients. In the adjuvant setting, aromatase inhibitors are the endocrine therapy of choice in postmenopausal patients, for a minimum duration of 5 years. A daily oral dose of letrozole at 2.5 mg, anastrozole at 1 mg, or exemestane at 25 mg can be used. In comparison with tamoxifen, aromatase inhibitors are associated with a statistically significant absolute risk reduction of recurrence at 10 years (3.6%) and an increase in overall survival (2.1%).[14]

Clinical pearl: Breast cancer recurrence reduction has been demonstrated in patients who switch from tamoxifen to an aromatase inhibitor within the first couple of years of endocrine therapy (2.0%).[14] Therefore, patients who reach menopause after 2 to 3 years of taking tamoxifen should be considered for a substitution in their endocrine regimen to aromatase inhibitors.

Endocrine therapy duration. The duration of adjuvant endocrine therapy is typically 5 years.[14] Endocrine therapy extension for up to 10 years with either tamoxifen or an aromatase inhibitor might further reduce the risk of breast cancer recurrence in high-risk patients.[14] Potential benefits versus potential adverse effects of extended therapy should be carefully assessed by an oncology specialist.[11]

Side effects and management. An overwhelming majority of patients experience burdensome side effects, causing suboptimal adherence or therapy discontinuation in approximately 30% of patients.[3] Primary care providers' role in active screening and management of these side effects is imperative to alleviate symptom burden, optimize adherence, and prevent rare but potentially serious complications.[11] Hot flashes are one of the most frequently reported side effects of tamoxifen, occurring in nearly 80% of patients.[15] The mainstay of management includes promotion of lifestyle changes (diet, dressing, bedding) and use of a selective serotonin reuptake inhibitor or a serotonin-norepinephrine reuptake inhibitor.[11] Half of patients experience bothersome arthralgias caused by aromatase inhibitors.[11] Regular physical exercise, massage therapy, and acupuncture can help alleviate these side effects; the substitution of another aromatase inhibitor might also be helpful.[11] Osteoporosis can also result from aromatase inhibitor therapy; supplemental calcium and vitamin D, as well as routine bone mineral density tests, are the mainstay of management.[11] **Table 1** provides a summary of common side effects of breast cancer endocrine therapies and their respective management.[11]

Endocrine therapy in prostate cancer

Approximately 75% of prostate cancer cases are diagnosed at an early stage; the remainder present either with regional nodal disease or as metastatic upon diagnosis.[1] Androgen deprivation therapy is a mainstay treatment of prostate cancer and has resulted in a considerable decline in associated mortality rates since 1994.[1] More specifically, androgen deprivation therapy is used as the primary systemic therapy for regional or advanced disease and is combined with radiotherapy as neoadjuvant, concurrent, or adjuvant therapy in localized or locally advanced prostate cancers.[16] Treatment agents can block the action or the production of androgen throughout the body, or reduce its production from the testicles, thereby reducing cancer cell growth.[17] Androgen deprivation can be achieved

Table 1. Breast endocrine therapy: adverse effects and their management

ENDOCRINE AGENT AND ADVERSE EFFECTS	MANAGEMENT
Tamoxifen	
• Hot flashes	• Lifestyle changes in dressing and bedding • For severe symptoms try SSRIs or SNRIs (venlafaxine, citalopram, escitalopram, sertraline) • Avoid paroxetine and fluoxetine
• VTE	• Use caution in patients with factor V Leiden heterozygosity or homozygosity, recent fracture, recent surgery, immobilization, or prior history of VTE • Treat VTE per guidelines
• Endometrial cancer	• No routine surveillance for standard-risk patients • Premenopausal patients: any irregular vaginal bleeding to be investigated with endometrial biopsy • Postmenopausal patients: all vaginal bleeding to be investigated with endometrial biopsy; otherwise, only normal routine gynecologic examination per standard guidelines
• Ocular pathologies	• Consider yearly eye examination
• Fatty liver disease	• No routine screening recommended • If fatty liver documented, obtain liver enzyme levels every 3-6 mo • Stop tamoxifen if liver enzyme levels exceed twice the upper limit of normal
Aromatase inhibitors	
• Osteoporosis	• Bone mineral density measurement at baseline and every 2 y • Vitamin D: 800 IU/d • Total calcium (diet and supplement): 1200 mg/d • Manage as per osteoporosis guidelines
• Arthralgias and musculoskeletal symptoms	• Switch the aromatase inhibitor • Consider exercise, massage, acupuncture, or NSAIDs
• Sexual dysfunction	• Biopsychosocial approach • Education and counseling • Sexual aids (eg, lubricants, lidocaine preparations)
• Cardiovascular disease	• Routine screening for hypertension, hypercholesterolemia, and metabolic syndrome

NSAID—nonsteroidal anti-inflammatory drug, SNRI—serotonin-norepinephrine reuptake inhibitor, SSRI—selective serotonin reuptake inhibitor, VTE—venous thromboembolism.

either surgically (orchiectomy) or medically. Medical therapies include gonadal androgen ablation through luteinizing hormone–releasing hormone agonists (eg, leuprolide, triptorelin, goserelin) or luteinizing hormone–releasing hormone antagonists (eg, degarelix, relugolix); androgen receptor antagonists (eg, bicalutamide, enzalutamide, apalutamide, darolutamide); and adrenal androgen synthesis inhibitors (abiraterone acetate, ketoconazole).[18] Medical castration is monitored by assessing circulating testosterone levels. Choice of prostate cancer treatments is determined by a multitude of factors, including stage and grade of cancer at diagnosis, risk of disease progression, expected survival, comorbidities, and family history, as well as patient preference and the side effect profiles of proposed treatments.[16,17] Moreover, as initiation of luteinizing hormone–releasing hormone agonists is associated with a testosterone flare, the use of an androgen receptor antagonist is recommended in the first 2 to 4 weeks of therapy.[16,18]

In patients with intermediate- to high-risk disease, androgen deprivation therapy combined with radiotherapy has been shown to improve survival. Duration of therapy is typically 4 to 6 months for those with intermediate risk, whereas those at higher risk receive continuous androgen deprivation therapy to treat occult systemic disease and reduce the risk of recurrence.[16,19] However, androgen deprivation therapy is most often used in the metastatic prostate cancer setting in an intermittent or continuous fashion.[19] Worthy of mention, abiraterone has been shown to increase the level of adrenocorticotropic hormone owing to decreased production of cortisol, leading to substantial adverse effects from mineralocorticoid excess (eg, hypertension, fluid retention, hypokalemia).[20] To mitigate these adverse effects, glucocorticoids are administered in combination with abiraterone: 5 mg of oral prednisone twice daily is the standard formulation.[16,20] **Table 2** provides a summary of prostate cancer agents, including their mechanism of action and indications.[20]

Clinical pearl: Androgen deprivation therapy is not recommended as monotherapy in localized prostate cancer, except in the presence of a contraindication to curative local therapy, such as comorbidities or a prognosis of less than 5 years.[16]

Table 2. Prostate cancer treatments, mechanism of action, and indications

CLASS*	TARGET	AGENT	MECHANISM OF ACTION	INDICATIONS	NOTABLE SIDE EFFECTS
Nonsteroidal AR antagonist (first generation)	AR	Bicalutamide, flutamide, nilutamide	Competitively and reversibly inhibit binding of testosterone and DHT to ligand binding domain of AR	In combination with GnRH agonists in metastatic disease	Hot flashes, pain, infection, abdominal pain
Nonsteroidal AR antagonist (second generation)	AR	Apalutamide, darolutamide, enzalutamide	Competitively and reversibly inhibit binding of testosterone and DHT to ligand binding domain of AR; and downstream inhibition of AR translocation to nucleus from cytoplasm, recruitment of coactivators, and binding to DNA	CRPC, mCSPC, nmCRPC (in combination with ADT)	Fatigue, hypertension, seizures (enzalutamide), arthralgia, nausea, hot flashes
Androgen biosynthesis inhibitor	Steroidal enzyme CYP17A1 (17α-hydroxylase and C17,20-lyase)	Abiraterone	Abiraterone acetate (prodrug) converted in vivo to abiraterone which inhibits CYP17A1 expression in adrenal, testicular, and prostate tumours	mCRPC, mCSPC (in combination with prednisone and ADT)	Hypokalemia, hypertension, edema, adrenal insufficiency, hepatotoxicity
GnRH antagonists	GnRH receptor	Degarelix, relugolix	Competitively and reversibly inhibit GnRH receptors in pituitary gland, which blocks release of FSH and LH	Advanced prostate cancer	Injection site reaction (degarelix), hot flashes, fatigue, weight gain, hepatotoxicity
GnRH agonists	GnRH receptor	Histrelin, goserelin, leuprolide, triptorelin	Continuous stimulation of GnRH receptor that leads to initial surge in FSH, LH, testosterone, and DHT levels followed by reductions	Advanced prostate cancer (including mCRPC)	General pain, hot flashes and sweating, gastrointestinal disorders

ADT—androgen deprivation therapy, AR—androgen receptor, CRPC—castration-resistant prostate cancer, CYP—cytochrome P450, DHT—5α-dihydrotestosterone, FSH—follicle-stimulating hormone, GnRH—gonadotropin-releasing hormone, LH—luteinizing hormone, mCSPC—metastatic castration-sensitive prostate cancer, nmCSPC—nonmetastatic castration-resistant prostate cancer.
*Not all agents in a given class are approved for all indications of their class.
Reproduced from Desai et al[20] by permission of Oxford University Press on behalf of the Endocrine Society.

Side effects and management. Although androgen deprivation therapies have improved oncological outcomes, they are nonetheless associated with several frequently debilitating side effects that adversely affect quality of life.[17-19] In turn, care of patients on androgen deprivation therapy is best provided by a multidisciplinary approach that includes active collaboration between the treating specialists and primary care providers.[18,19] Androgen deprivation therapy can adversely impact various organ systems and affect bone health, sexual function, and mental health, and lead to cardiovascular disease and metabolic consequences.[18,19] Routine screening and prompt management of these potential side effects are of primary importance.[18] **Table 3** outlines common adverse effects of prostate cancer endocrine therapies and the management of each.[18]

Conclusion

Endocrine therapy is a cornerstone treatment for breast and prostate cancers. While associated with improved survival and reduced risk of cancer recurrence, endocrine therapy treatments are also associated with taxing psychosocial and physical side effects.[1,3,12-15,17,18] Family physicians are integral providers of care to cancer patients and survivors: their contributions to the identification and management of endocrine-related side effects are of utmost importance to supporting and optimizing these patients' overall health and quality of life. **Box 1** provides additional useful resources to help guide primary care providers in this important work.[18,21-25]

Dr Genevieve Chaput is Assistant Professor at McGill University in Montreal, Que, an attending physician in the departments of family medicine and secondary care and oncology at the McGill University Health Centre, and Medical Director of the Vaudreuil-Soulanges Palliative Care Residence in Hudson, Que. **Dr Nureen Sumar** is Clinical Assistant Professor in the Department of Family Medicine at the University of Calgary in Alberta, a faculty member in the Department of Haematology-Oncology at Aga Khan University in Nairobi, Kenya, and Clinical Associate at the Tom Baker Cancer Centre in Calgary.

Competing interests
None declared

References

1. Canadian Cancer Statistics Advisory Committee, Canadian Cancer Society, Statistics Canada, Public Health Agency of Canada. *Canadian cancer statistics 2021*. Toronto, ON: Canadian Cancer Society; 2021. Available from: **https://cdn.cancer.ca/-/media/files/research/cancer-statistics/2021-statistics/2021-pdf-en-final.pdf**. Accessed 2022 Jan 29.

Table 3. Summary of adverse effects of prostate cancer endocrine therapy and their management

COMPLICATION	SUMMARY OF EVENTS	MANAGEMENT
Cardiovascular disease	• Increased risk of cardiac events • Increased risk of stroke • Increased risk of DVT/PE	• Lifestyle changes to promote healthy diet and weight • Smoking cessation • Exercise therapy • Monitoring and medical optimization of blood glucose, blood pressure, lipid profiles • Consider use of GnRH antagonist in patients with significant cardiac comorbidities • Consider referral to cardiac oncology
Change in body composition	• Increased BMI • Increased percentage body fat • Decreased muscle mass	• Lifestyle changes to promote healthy diet and weight • Exercise therapy • Monitoring and medical optimization of blood glucose, blood pressure, lipid profiles
Change in metabolic parameters	• Insulin resistance/ glucose intolerance • Increased risk for incident diabetes • Worse glycemic control • Altered lipid profiles • Increased risk for metabolic syndrome	• Lifestyle changes to promote healthy diet and weight • Exercise therapy • Monitoring and medical optimization of blood glucose, blood pressure, lipid profiles
Bone health	• Decreased BMD • Increased risk for osteoporosis • Increased risk for clinical fractures	• Smoking and alcohol cessation • Adequate calcium intake (1200 mg/d) and vitamin D supplementation (800-1000 IU/d) • Exercise therapy • Pharmacologic therapy with a bisphosphonate or denosumab for men with risk factors for bone fracture (ie, previous history of low trauma fracture, diagnosis of osteoporosis, moderate or high 10-year fracture risk)
Hot flashes	NA	• Avoidance of triggers • Pharmacologic therapy • Consider acupuncture • Consider intermittent ADT
Breast events	• Gynecomastia • Mastodynia	• Treatment with tamoxifen or low-dose RT (tamoxifen preferred) • Surgical management for select patients
Cognitive function	• Concentration • Memory • Dementia • Depression	• Evidence for causality is weak • Appropriate patient education and monitoring of symptoms
Fatigue and anemia	NA	• Exercise therapy for fatigue • Workup secondary causes of anemia and referral to hematology when indicated
Impaired sexual function	• Decreased penile and testicular size • Loss of libido • Decreased sensitivity to sexual stimulation • Erectile dysfunction	• Appropriate pretreatment counseling • Sex therapy • PDE5 inhibitor and other ED therapies where appropriate • Consider intermittent ADT
Quality of life	• Multiple domains	• Exercise therapy • Consider intermittent ADT

ADT—androgen deprivation therapy, BMD—bone mineral density, BMI—body mass index, DVT—deep-vein thrombosis, ED—erectile dysfunction, GnRH—gonadotropin-releasing hormone, NA—not applicable, PDE5—phosphodiesterase 5, PE—pulmonary embolism, RT—radiation therapy.

2. Pilon D, LaMori J, Rossi C, Durkin M, Ghelerter I, Ke X, et al. Medication adherence among patients with advanced prostate cancer using oral therapies. *Future Oncol* 2022;18(2):231-43. Epub 2021 Nov 3.
3. Berkowitz MJ, Thompson CK, Zibecchi LT, Lee MK, Streja E, Berkowitz JS, et al. How patients experience endocrine therapy for breast cancer: an online survey of side effects, adherence, and medical team support. *J Cancer Surviv* 2021;15(1):29-39. Epub 2020 Aug 17.
4. Cleator SJ, Ahamed E, Coombes RC, Palmieri C. A 2009 update on the treatment of patients with hormone receptor-positive breast cancer. *Clin Breast Cancer* 2009;9(Suppl 1):S6-17.
5. *Hormone therapy to treat cancer*. Bethesda, MD: National Cancer Institute. Available from: **https://www.cancer.gov/about-cancer/treatment/types/hormone-therapy**. Accessed 2022 Jan 8.

Box 1. Useful resources for primary care providers

Breast cancer

- Evidence-based approaches for the management of side effects of adjuvant endocrine therapy in patients with breast cancer[21]: **https://www.sciencedirect.com/science/article/abs/pii/S1470204520306665**
- American Society of Clinical Oncology guideline. Neoadjuvant chemotherapy, endocrine therapy, and targeted therapy for breast cancer[22]: **https://pubmed.ncbi.nlm.nih.gov/33507815/**

Prostate cancer

- BCGuidelines.ca. Medications for the management of prostate cancer side effects in primary care[23]: **https://www2.gov.bc.ca/assets/gov/health/practitioner-pro/bc-guidelines/prostatecancer-part2_appendixc.pdf**
- Canadian Urological Association guideline on androgen deprivation therapy. Adverse events and management strategies[18]: **https://www.cua.org/system/files/Guideline-Files/7355_v8.pdf**
- Cancer Care Ontario. Managing symptoms, side effects, and well-being[24]: **https://www.cancercareontario.ca/en/symptom-management**

Cardiovascular effects of breast and prostate cancer endocrine therapies

- American Heart Association. Impact of hormonal therapies for treatment of hormone-dependent cancers (breast and prostate) on the cardiovascular system[25]: **https://www.ahajournals.org/doi/epub/10.1161/HCG.0000000000000082**

6. Sleightholm R, Neilsen BK, Elkhatib S, Flores L, Dukkipati S, Zhao R, et al. Percentage of hormone receptor positivity in breast cancer provides prognostic value: a single-institute study. *J Clin Med Res* 2021;13(1):9-19. Epub 2021 Jan 12.
7. Cao L, Sugumar K, Keller E, Li P, Rock L, Simpson A, et al. Neoadjuvant endocrine therapy as an alternative to neoadjuvant chemotherapy among hormone receptor-positive breast cancer patients: pathologic and surgical outcomes. *Ann Surg Oncol* 2021;28(10):5730-41. Epub 2021 Aug 3.
8. Hofland J, Herrera-Martínez AD, Zandee WT, de Herder WW. Management of carcinoid syndrome: a systematic review and meta-analysis. *Endocr Relat Cancer* 2019;26(3):R145-56.
9. Schlumberger M, Leboulleux S. Current practice in patients with differentiated thyroid cancer. *Nat Rev Endocrinol* 2021;17(3):176-88. Epub 2020 Dec 18.
10. Howlader N, Altekruse SF, Li CI, Chen VW, Clarke CA, Ries LA, et al. US incidence of breast cancer subtypes defined by joint hormone receptor and HER2 status. *J Natl Cancer Inst* 2014;106(5):dju055.
11. Awan A, Esfahani K. Endocrine therapy for breast cancer in the primary care setting. *Curr Oncol* 2018;25(4):285-91. Epub 2018 Aug 14.
12. Early Breast Cancer Trialists' Collaborative Group. Effects of chemotherapy and hormonal therapy for early breast cancer on recurrence and 15-year survival: an overview of the randomised trials. *Lancet* 2005;365(9472):1687-717.
13. Early Breast Cancer Trialists' Collaborative Group. Aromatase inhibitors versus tamoxifen in early breast cancer: patient-level meta-analysis of the randomised trials. *Lancet* 2015;386(10001):1341-52. Epub 2015 Jul 23.
14. Loibl S, Poortmans P, Morrow M, Denkert C, Curigliano G. Breast cancer. *Lancet* 2021;397(10286):1750-69. Epub 2021 Apr 1. Erratum in: *Lancet* 2021;397(10286):1710.
15. Day R. Quality of life and tamoxifen in a breast cancer prevention trial: a summary of findings from the NSABP P-1 study. National Surgical Adjuvant Breast and Bowel Project. *Ann N Y Acad Sci* 2001;949:143-50.
16. *NCCN clinical practice guidelines in oncology: prostate cancer*. Plymouth Meeting, PA: National Comprehensive Cancer Network; 2022.
17. Edmunds K, Tuffaha H, Galvão DA, Scuffham P, Newton RU. Incidence of the adverse effects of androgen deprivation therapy for prostate cancer: a systematic literature review. *Support Care Cancer* 2020;28(5):2079-93. Epub 2020 Jan 7.
18. Kokorovic A, So AI, Serag H, French C, Hamilton RJ, Izard JP, et al. Canadian Urological Association guideline on androgen deprivation therapy: adverse events and management strategies. *Can Urol Assoc J* 2021;15(6):E307-22. Erratum in: *Can Urol Assoc J* 2021;15(7):E383.
19. Magee DE, Singal RK. Androgen deprivation therapy: indications, methods of utilization, side effects and their management. *Can J Urol* 2020;27(Suppl 1):11-6.
20. Desai K, McManus JM, Sharifi N. Hormonal therapy for prostate cancer. *Endocr Rev* 2021;42(3):354-73.
21. Franzoi MA, Agostinetto E, Perachino M, Del Mastro L, de Azambuja E, Vaz-Luis I, et al. Evidence-based approaches for the management of side-effects of adjuvant endocrine therapy in patients with breast cancer. *Lancet Oncol* 2021;22(7):e303-13. Epub 2021 Apr 20.
22. Korde LA, Somerfield MR, Carey LA, Crews JR, Denduluri N, Hwang ES, et al. Neoadjuvant chemotherapy, endocrine therapy, and targeted therapy for breast cancer: ASCO guideline. *J Clin Oncol* 2021;39(13):1485-505. Epub 2021 Jan 28.
23. BCGuidelines.ca. *Appendix C: medications for the management of prostate cancer side effects in primary care*. Vancouver, BC: Guidelines and Protocols and Advisory Committee, Government of British Columbia; 2020. Available from: **https://www2.gov.bc.ca/assets/gov/health/practitioner-pro/bc-guidelines/prostatecancer-part2_appendixc.pdf**. Accessed 2022 Jan 15.
24. *Managing symptoms, side effects & well-being*. Toronto, ON: Cancer Care Ontario. Available from: **https://www.cancercareontario.ca/en/symptom-management**. Accessed 2022 Jan 6.
25. Okwuosa TM, Morgans A, Rhee JW, Reding KW, Maliski S, Plana JC, et al. Impact of hormonal therapies for treatment of hormone-dependent cancers (breast and prostate) on the cardiovascular system: effects and modifications: a scientific statement from the American Heart Association. *Circ Genom Precis Med* 2021;14(3):e000082. Epub 2021 Apr 26.

This article is eligible for Mainpro+ certified Self-Learning credits. To earn credits, go to **https://www.cfp.ca** and click on the Mainpro+ link.
Can Fam Physician 2022;68:271-6. DOI: 10.46747/cfp.6804271
La traduction en français de cet article se trouve à **https://www.cfp.ca** dans la table des matières du numéro **d'avril 2022** à la **page e120**.