Symptom Burden and Survivorship Care for Patients With Prostate Cancer on Androgen Deprivation Therapy

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Abstract

Prostate cancer survivors represent a growing population of patients with a diagnosis of prostate cancer, whether they were cured using local therapies or continue to receive systemic treatment of advanced disease. Many patients receive androgen deprivation therapy (ADT) during treatment, which is associated with many long-lasting physical and psychological effects. Identifying and addressing the needs of survivors is imperative for improving their health and well-being. This narrative review highlights the most common issues associated with ADT affecting survivorship in prostate cancer, including cardiovascular and metabolic effects, musculoskeletal health, sexual morbidity, and local therapy effects, as well as the mental and psychological toll. A special emphasis is placed on the existing literature examining specific interventions to alleviate these symptoms, along with describing existing gaps in knowledge, with the goal of promoting dedicated studies aimed at enhancing the survivorship experience of patients with prostate cancer.

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Prostate cancer is the most prevalent male cancer in the United States, affecting 1 in 8 men.[1] Due to a combination of increased screening awareness, improvement in surgery and radiation techniques, and more efficacious systemic treatments, most patients presenting with prostate cancer can expect to live many years with their disease, even in the metastatic setting. As such, identifying and addressing the needs of prostate cancer survivors, which comprise up to 20% of all cancer survivors, has gained significant attention from the medical community.[1–3]

The cornerstone of systemic treatment of prostate cancer is androgen deprivation therapy (ADT), generally with short-term use in the localized setting concurrent with radiation, followed by prolonged use in patients with advanced disease. Nowadays the preferred approach is reversible suppression via medications that target the gonadotropin releasing hormone (GnRH) axis. As more patients are exposed to ADT, there is a higher likelihood of long-lasting physical and psychological consequences.

The purpose of this review is to provide an overview of survivorship care for patients on ADT, focusing on the myriad health effects associated with long-term testosterone suppression. As prostate cancer survivorship becomes an increasingly recognized, guideline-driven objective,[3,4] discussing these issues with patients is paramount to improve their health and well-being.

Definition

Historically limited to patients cured from their cancer, survivorship is now recognized as encompassing all patients with a diagnosis of prostate cancer, whether they are on active surveillance, undergoing definitive surgery or radiation, or have advanced disease requiring systemic therapies indefinitely.[5,6] Therefore, prostate cancer survivors are a heterogeneous population that can range from asymptomatic patients who were never treated to patients near the end of life with high symptom burden.[2] Even among populations with a shared disease status, there can be differences in outcomes that disproportionately affect patients from lower socioeconomic status or non-White backgrounds.[7,8] Although determining the needs for all prostate cancer survivors is inherently challenging, there have been efforts to identify recurrent symptoms and develop tailored interventions.[4,6,9] In particular, patient-reported outcomes (PROs) implemented in clinical trials or routine practice are a tremendously useful tool that can directly elicit patient concerns derived from living with prostate cancer.[10]

This review describes the most common physical and psychological needs of prostate cancer survivors with prior ADT exposure, highlighting the areas lacking (or with limited) evidence that could benefit from dedicated research. While sometimes intensified ADT (ie, combination with androgen receptor synthesis inhibitors [ARSI]) is equated to ADT, the added side effects of ARSIs are beyond the scope of this review; however, the same principles of careful assessment of the risks and benefits of treatment intensification should be followed with each survivor.

Physical Effects

Cardiovascular and Metabolic

As the leading cause of noncancer mortality, cardiovascular disease (CVD) is a major concern for prostate cancer survivors. Men with prostate cancer are usually elderly adults (age >70 years) with comorbidities contributing to the risk of CVD or already have a history of CVD, such as prior myocardial infarction or ischemic stroke.[11] ADT affects body composition by increasing subcutaneous (but not visceral) fat, cholesterol and triglyceride levels, and insulin resistance within months of starting therapy.[12–15] Indeed, patients receiving ADT have been observed to have a higher incidence of diabetes,[16] and those with preexisting diabetes can experience worsening diabetic control.[17] Additionally, there are preclinical data suggestive of increased atherosclerotic plaque deposition in low testosterone states.[18,19]

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Prostate cancer survivors are prime candidates for interventions to prevent metabolic syndrome. However, there are no detailed screening guidelines for this population other than conventional monitoring of cholesterol and A1C levels.[13] In terms of lifestyle changes, low carbohydrate diets and low-intensity exercise have promising data for inducing weight loss and improving A1C, high-density lipoprotein, and triglyceride levels.[20,21] However, most of the data are derived from small studies because accrual is often slow for lifestyle studies.[14]

There is ongoing controversy regarding whether ADT independently contributes to CVD, because many studies were not designed to assess CVD outcomes, and instead indirectly evaluated cardiovascular toxicity in preselected populations.[6,12] Large observational studies and meta-analyses have suggested either no relationship between ADT and CVD,[14,16] increased risk in patients with preexisting CVD,[22,23] or an independent association.[11,24,25] The only prospective study that included CVD events as a primary endpoint was the PRONOUNCE trial, which compared CVD events between patients on gonadotropin-releasing hormone (GnRH) agonists and the GnRH antagonist degarelix. Ultimately the study did not find a difference between approaches to ADT and CVD events and was deemed inconclusive, possibly due to a lower-than-predicted CVD event rate and close follow-up of study participants by cardiology providers that is not mirrored in real-world settings.[26] Dedicated prospective studies evaluating the CVD effects of ADT are desperately needed. Thus far, the contradictory evidence likely reflects the effect of multiple variables, including baseline risk factors, different types of ADT (eg, GnRH agonist vs antagonist), or duration of treatment.

Nevertheless, there is general agreement that patients on ADT should be counseled on addressing reversible risk factors of CVD and should be closely monitored for new or recurrent cardiac events.[13,27] In particular, patients with preexisting CVD require dedicated follow-up by cardiology and/or cardio-oncology providers, if available. For this reason, the ABCDE framework (Awareness/Aspirin, Blood Pressure, Cholesterol/Cigarettes, Diet/Diabetes, Exercise) is a systemic approach recommended for counseling survivors in order to encourage a healthy lifestyle and work closely with their providers (including physicians, dietitians, and physical therapists) to mitigate CVD risks[28] (Table 1).

Muscle and Bone Health

Androgen hormones are necessary for maintaining normal muscle bulk and bone mineral density. Loss of muscle mass is postulated to occur from dysregulation of anabolic pathways.[29] Sarcopenia is a known side effect of ADT and a contributor to frailty, and has been linked with increased likelihood of non-cancer mortality in patients with prostate cancer.[30] ADT use, particularly prolonged courses, is associated with a 20% increased risk of osteoporosis within the first year,[31] as well as fractures.[32] Moreover, patients with advanced prostate cancer often have metastatic disease to the bone, which further puts them at risk for pathologic fractures.[6] The mechanism behind bone loss from androgen suppression is thought to involve increased bone resorption with a decrease in bone deposition.[33]

To combat muscle loss, resistance exercise is linked with improving muscle mass and preserving strength.[34,35] The effect of supervised versus self-directed exercise on survival is being compared in the ongoing phase III INTERVAL trial in patients with metastatic castration-resistant prostate cancer.[36]

In terms of bone health, a baseline dual-energy x-ray absorptiometry (DEXA) scan is strongly recommended for patients embarking on treatment plans including long-term ADT, especially patients with preexisting risk factors for osteoporosis.[27,37] Still, real-world implementation of bone density screening in prostate cancer survivors has been disappointingly low.[32] A follow-up scan approximately 2 years after initiating treatment is also recommended in patients receiving bone resorption agents. Importantly, because this algorithm was borrowed from primary osteoporosis and adapted to prostate cancer, it is possible that some patients at risk for fracture may not be identified due to confounding issues, including overestimated bone density when measuring through blastic metastatic lesions.[38]

To preserve bone health, patients should be counseled on lifestyle changes (smoking cessation, reduced alcohol consumption) and on calcium (up to 1,200 mg daily) and vitamin D (≥800 IU) intake, with supplementation as necessary. Weight-bearing exercise and low-impact training are considered adjunctive interventions to prevent bone loss, with inconsistent results.[39] Additionally, patients with osteoporosis or at risk for fracture (FRAX score ≥3% risk of hip fracture or ≥20% risk of major osteoporotic fracture in 10 years) should be offered bone resorption agents. Engaging patients to practice good dental hygiene and receive periodic dental evaluations is essential to avoid the rare but preventable side effect of osteonecrosis of the jaw. RANK-L inhibitors (eg, subcutaneous denosumab) are associated with fracture prevention,[40] whereas bisphosphonates (eg, oral alendronate or intravenous zoledronic acid) are associated with improved bone mineral density but have less robustly demonstrated a reduced fracture risk across all patient populations.[41]

Table 1. ABCDE Framework for CVD Reduction in Prostate Cancer Survivors

Awareness and aspirin	• Increasing patient awareness about signs and symptoms of CVD • Inform usual care providers (PCP, cardiologist) of ADT start • Aspirin 81 mg daily for primary or secondary prevention
Blood pressure	• Targeting blood pressure <130/90 mmHg
Cholesterol and cigarettes	• Starting high intensity statin for preexisting CVD or hyperlipidemia • Smoking cessation counseling and therapy
Diet and diabetes	• Monitoring blood glucose and starting metformin if necessary • Diet rich in fruits, vegetables, and whole grain and low in saturated fat; alcohol in moderation • Referral to dietitian for advice on maintaining or losing weight as appropriate
Exercise	• Aerobic exercise 150 min/wk with moderate intensity or 75 min/wk vigorously • Concurrent resistant training 2–3 times a week • Consider consultation with physical therapist

Abbreviations: ADT, androgen deprivation therapy; CVD, cardiovascular disease; PCP, primary care physician.
Adapted from Bhatia N, Santos M, Jones LW, et al. Cardiovascular effects of androgen deprivation therapy for the treatment of prostate cancer. Circulation 2016;133:537–541.

Important considerations that remain largely unresolved in prostate cancer include the optimal duration of bone resorption agents and the possibility of rebound bone density loss with discontinuation of denosumab.[42]

Sexual Health

Sexual health encompasses physical symptoms, including erectile dysfunction (ED) and inability to orgasm, and psychological symptoms, including diminished libido and level of sexual desire, and is a crucial aspect of survivorship care in patients with prostate cancer following ADT.[3,43] A qualitative study assessing longitudinal sexual function in patients who received ADT compared with those who had a prostatectomy and healthy men, found that immediately after treatment, patients receiving ADT or prostatectomy had worse function and bother from sexual function compared with healthy men; however, at 12 months, patients receiving ADT had worse function and bother than both postprostatectomy and healthy men.[44] The findings of EORTC 22991 suggest that shorter durations of hormone therapy may result in a leveling off of sexual dysfunction at 2 years.[45]

Conversations about sexual health should be initiated early to allow patients to express concerns and seek support. Sexual health clinicians, either in person or online, can be tremendously helpful in discussing strategies, such as exercise and mindfulness techniques, to enhance libido while on ADT. Psychological counseling is invaluable in helping patients navigate the complexities of sexual dysfunction. Although medications such as phosphodiesterase-5 inhibitors can offer meaningful improvements in managing ED, they may not completely restore pre-ADT sexual function.[4,43] Other approaches, such as vacuum erection devices and intracavernosal injections, present viable alternatives for select patients.[46] Testosterone therapy is contraindicated in men undergoing active surveillance or active therapy, and is controversial in survivors of localized prostate cancer.[43] Studies evaluating the safety of testosterone supplementation in patients previously treated for localized disease who remain with persistently low testosterone levels are ongoing (ClinicalTrials.gov identifier: NCT03716739).

Gynecomastia is a common physical change with hormone therapy, particularly bicalutamide-based monotherapy, that can be associated with strong negative impact on patients' overall quality of life, self-perception, psychological well-being, and sexual health.[44] The reported "loss of male appearance" can precipitate early discontinuation of hormone therapy in up 15% of patients.[47] Prophylaxis typically consists of tamoxifen started with and continued throughout hormone therapy.[48] Radiotherapy (RT), govern in 1 to 5 fractions using low-dose radiation to bilateral breasts, can also decrease rates of gynecomastia.[49]

Toxicity of Local Therapy

Surgery and RT have expanded beyond their traditional definitive roles in prostate cancer, and are now options for patients with locally advanced, oligometastatic, or even advanced symptomatic disease, most of which are on long-term ADT. Modern studies suggest the addition of local therapy to ADT is not associated with significantly worse long-term health-related quality of life.[45]

Urinary toxicity is a prevalent and distressing side effect among prostate cancer survivors who previously received local therapy.[50] Common symptoms include increased urinary frequency, urgency, and nocturia. Addressing urinary toxicity necessitates a multifaceted approach. Lifestyle adjustments encompassing moderation in fluid intake, avoidance of bladder irritants such as caffeine and alcohol, and regular voiding, are recommended. Pelvic floor exercises have shown promise in enhancing bladder control. Additionally, pharmacologic interventions, including alpha-blockers and anticholinergics, should be tailored to individual patients to alleviate urinary symptoms effectively.[3,4]

Bowel dysfunction, characterized by symptoms including diarrhea and urgency, is a common challenge among prostate cancer survivors who have received high-dose RT together with ADT. Although modern techniques such as intensity-modulated RT and rectal spacer have significantly decreased incidence of bowel toxicity, patients who have adverse events may continue to experience symptoms well after treatment.[51,52] Dietary adjustments may be most effective in patients, with emphasis on increasing fiber intake, hydration, and avoiding foods that trigger bowel symptoms and maintain bowel regularity. Medical management with antidiarrheal medications, such as loperamide, can provide benefit. For patients with refractory symptoms, multidisciplinary management with gastroenterologists is recommended.[3] Even though the population of patients with prostate cancer receiving only ADT alongside RT at the localized stage is diminishing as ARSIs enter this space, it is worth considering that the risk of toxicity applies at other time points, such as the salvage or adjuvant settings, and thus careful assessment of potential bowel issues should also be considered at those stages.

Mental and Psychological Effects

Fatigue and Cognition

The burden of fatigue from low testosterone can be quite significant and compounded by prior RT or concurrent systemic therapies.[53] Although it is unclear how much contribution is derived from organic causes like ADT-induced anemia,[54] fatigue remains prevalent and can persist months after testosterone recovery. There is a large body of evidence linking aerobic and/or resistance exercise with improvement in fatigue from ADT.[55] Thus, encouraging survivors to participate in some form of regular exercise routine can help mitigate the fatigue associated with cancer treatments.

The cognitive effects of ADT can similarly be influenced by systemic treatment (particularly androgen receptor inhibitors) or confounded by the presence of fatigue.[6] The mechanisms behind memory impairment, specifically affecting spatial memory, remain elusive, but preclinical studies suggest that there are androgen receptors in several brain regions, including the hippocampus and amygdala.[56] Observational data are mixed—some studies have suggested that ADT is associated with early onset of dementia, particularly with ADT use for more than 1 year and in men aged >70 years,[57,58] whereas other studies have not found a relationship with cognitive decline.[59,60] Because of the lack of conclusive evidence linking ADT with cognitive impairment, there is no screening recommendation for prostate cancer survivors.

Mood Changes and Vasomotor Symptoms

Mood disorders such as anxiety and depression are common in prostate cancer survivors. Although confounded by fatigue and worries about recurrence or progression, depression is believed to affect one-fourth to one-third of patients, and is linked with

Table 2. Examples of Lifestyle Recommendations for Prostate Cancer Survivors Based on Limited Evidence and/or Expert Opinion

Category	Advice	Goal
Physical activity	Participate in daily physical activity that you feel comfortable doing, and slowly increase the demands on your body until you feel tired	90–150 min per week of aerobic exercise combined with 2–3 resistance workouts
	Try standing up if you have been sitting down for a prolonged period of time	Frequent breaks to avoid sedentary habits
Nutrition	Substitute processed grains with whole or enriched grains	Decrease diabetogenic sugars
	Aim to eat 5 servings of fruits and vegetables every day	Natural vitamin supplementation
	Have low-fat yogurt or similar dairy for breakfast	Recommended dietary intake of calcium and vitamin D
	Substitute fat from red meat for fish, nuts, or soy	Increase omega-3 rich fatty acid intake
Smoking	Avoid cigarettes and other tobacco products	Complete cessation or on stable pharmacotherapy or behavioral therapy
Alcohol	If you drink alcohol, limit yourself to not more than 2 drinks a day, preferably wine over spirits	Moderate or eliminate alcohol use habits

twice the risk of suicide compared with men without prostate cancer.[61] ADT is linked with depression, with both continuous versus intermittent ADT use similarly associated.[62] Patients experiencing depression are less likely to be adherent to routine care and to require more urgent care.[63] Early detection of anxiety and depression can help connect survivors with appropriate support services, with some proposing PROs as screening tools.[64] Some evidence suggests that many patients meeting criteria for depression are not receiving appropriate interventions,[65] further stressing the importance of screening every survivor regardless of their disease stage or risk factors.

Hot flashes are a prevalent side effect of blocking the androgen hormonal axis that can severely affect quality of life, interrupt daily activities, and disturb sleep. Unfortunately, there are limited randomized data to assess the true efficacy of treatments compared with natural resolution; most approaches borrow from treatment of hot flashes in women.[3] The best evidence in prostate cancer supports estrogen supplementation (eg, estradiol patches) or venlafaxine,[66] as well as some observational data on acupuncture for patients who would prefer nonpharmacologic approaches.[67] Naturally, the side effects of therapies trialed (eg, risk of venous thromboembolism and gynecomastia with estrogen products) should be carefully balanced with the benefit gained.

Fear of Recurrence

Many survivors live with the persistent stress of cancer recurrence or disease progression. This anxiety has been best described in patients with early-stage disease on active surveillance,[68] but it is applicable to other stages. A prospective study identified significant fear of recurrence in patients ahead of surgery, with younger age and lower education linked with higher stress levels.[69] In turn, a separate study linked lower levels of education or African American ethnicity with a greater sense of uncertainty about the future among patients in remission.[70] There is mixed evidence on whether fear of recurrence decreases with time. A good deal of anxiety centers around prostate-specific antigen (PSA) levels.[68]

Although a small, randomized study found lower cancer-specific anxiety and concern regarding progression among patients participating in an exercise group compared with usual care,[71] this is an area of prostate cancer survivorship with limited evidence-based interventions. Recent[68] and ongoing studies (ClinicalTrials.gov identifier: NCT05099679) evaluating cognitive behavioral therapy and other mindfulness techniques can hopefully shed some light, particularly for at-risk populations.

Surveillance and Follow-up Care

Patients in remission or who have sustained cancer control (eg, biochemical relapse with slow PSA doubling time) need to engage with their providers to establish and maintain healthy living habits to prevent other illnesses from impacting their survivorship. To that end, professional societies have recommendations focused on physical activity, nutrition, smoking cessation, and alcohol consumption[3,4] (Table 2).

With regard to PSA monitoring, national guidelines recommend checking PSA levels every 6 to 12 months for the first 5 years. After that time point, care is generally transitioned back to primary care doctors who can monitor PSA levels annually.[3] The roles of digital rectal examination and imaging have changed over time, currently reserved for suspicion of recurrence.[27]

Monitoring for second malignancies should be an important part of survivorship care. In particular, patients who received radiation to the prostate have a slightly increased risk of bladder and colorectal cancers.[72] There are no specific screening recommendations for these patients, or all prostate cancer survivors for that matter, other than age-appropriate cancer screening and maintaining a healthy level of suspicion for unexplained hematuria or rectal bleeding.[3,4]

In summary, cancer specialists are essential in providing survivorship care plans, including treatment summary, interventions for managing persistent side effects from therapies, and follow-up recommendations, to the primary care doctors who assume the care of survivors after prolonged periods of stability.[3] Real-world examples have revealed good adoption of care plans, although with some gaps in implementation.[73] As patients are able to live longer with their cancer diagnosis, it is imperative that comprehensive care plans become standard of care across health care settings and readily available to all stakeholders.

Conclusions

Men affected by prostate cancer are a diverse and growing segment of the US population. Dedicated attention to their needs can prevent myriad issues that stem from pervasive and underrecognized side effects from ADT and other cancer-directed therapies (Figure 1). Survivorship care attempts to deliver evidence-based recommendations to patients with prostate cancer, albeit with diminishing but remaining gaps in knowledge. Future studies aimed at solving these existing limitations can continue to enhance the well-being of prostate cancer survivors.

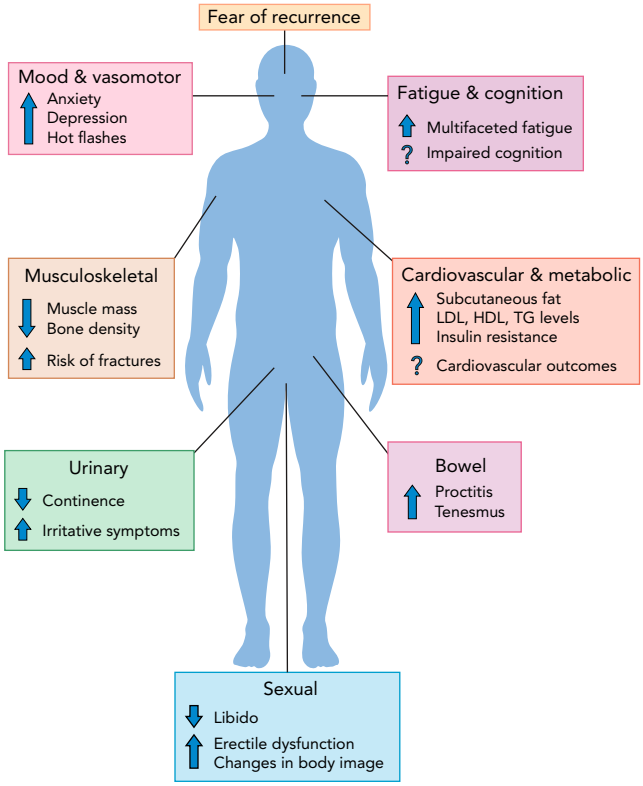

Figure 1. Symptom burden linked with androgen deprivation and associated local therapies.
Abbreviations: HDL, high-density lipoprotein; LDL, low-density lipoprotein; TG, triglyceride.

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References

1. Siegel RL, Miller KD, Wagle NS, Jemal A. Cancer statistics, 2023. CA Cancer J Clin 2023;73:17–48.
2. Mollica MA, Tesauro G, Gallicchio L, et al. Survivorship science at the National Institutes of Health 2017-2021. J Cancer Surviv 2024;18:1443–1452.
3. Skolarus TA, Wolf AMD, Erb NL, et al. American Cancer Society prostate cancer survivorship care guidelines. CA Cancer J Clin 2014;64:225–249.
4. Resnick MJ, Lacchetti C, Bergman J, et al. Prostate cancer survivorship care guideline: American Society of Clinical Oncology clinical practice guideline endorsement. J Clin Oncol 2015;33:1078–1085.
5. Morgans A. Prostate cancer survivorship today: support that spans the journey. Eur Urol Focus 2023;9:403–404.
6. Narayan V, Harrison M, Cheng H, et al. Improving research for prostate cancer survivorship: a statement from the Survivorship Research in Prostate Cancer (SuRECaP) working group. Urol Oncol 2020;38:83–93.
7. Chamie K, Connor SE, Maliski SL, et al. Prostate cancer survivorship: lessons from caring for the uninsured. Urol Oncol 2012;30:102–108.
8. Moss JL, Pinto CN, Srinivasan S, et al. Enduring cancer disparities by persistent poverty, rurality, and race: 1990-1992 to 2014-2018. J Natl Cancer Inst 2022;114:829–836.
9. Crawford-Williams F, March S, Goodwin BC, et al. Interventions for prostate cancer survivorship: a systematic review of reviews. Psychooncology 2018;27:2339–2348.
10. Briggs LG, Sentana-Lledo D, Lage DE, et al. Optimal assessment of quality of life for patients with prostate cancer. Ther Adv Med Oncol 2022;14:17588359221141306.
11. Bosco C, Bosnyak Z, Malmberg A, et al. Quantifying observational evidence for risk of fatal and nonfatal cardiovascular disease following androgen deprivation therapy for prostate cancer: a meta-analysis. Eur Urol 2015;68:386–396.
12. Gupta D, Lee Chuy K, Yang JC, et al. Cardiovascular and metabolic effects of androgen-deprivation therapy for prostate cancer. J Oncol Pract 2018;14:580–587.
13. Levine GN, D'Amico AV, Berger P, et al. Androgen-deprivation therapy in prostate cancer and cardiovascular risk. Circulation 2010;121:833–840.
14. Nguyen PL, Je Y, Schutz FAB, et al. Association of androgen deprivation therapy with cardiovascular death in patients with prostate cancer: a meta-analysis of randomized trials. JAMA 2011;306:2359–2366.
15. Saylor PJ, Smith MR. Metabolic complications of androgen deprivation therapy for prostate cancer. J Urol 2013;189:S34–44.
16. Alibhai SMH, Duong-Hua M, Sutradhar R, et al. Impact of androgen deprivation therapy on cardiovascular disease and diabetes. J Clin Oncol 2009;27:3452–3458.
17. Keating NL, Liu PH, O'Malley AJ, et al. Androgen deprivation therapy and diabetes control among diabetic men with prostate cancer. Eur Urol 2014;66:e51–52.
18. Bourghardt J, Wilhelmson ASK, Alexanderson C, et al. Androgen receptor-dependent and independent atheroprotection by testosterone in male mice. Endocrinology 2010;151:5428–5437.
19. Nathan L, Shi W, Dinh H, et al. Testosterone inhibits early atherogenesis by conversion to estradiol: critical role of aromatase. Proc Natl Acad Sci U S A 2001;98:3589–3593.

20. Freedland SJ, Howard L, Allen J, et al. A lifestyle intervention of weight loss via a low-carbohydrate diet plus walking to reduce metabolic disturbances caused by androgen deprivation therapy among prostate cancer patients: carbohydrate and prostate study 1 (CAPS1) randomized controlled trial. Prostate Cancer Prostatic Dis 2019;22:428–437.
21. Pernar CH, Fall K, Rider JR, et al. A walking intervention among men with prostate cancer: a pilot study. Clin Genitourin Cancer 2017;15: e1021–1028.
22. Lester-Coll NH, Goldhaber SZ, Sher DJ, D'Amico AV. Death from high-risk prostate cancer versus cardiovascular mortality with hormonal therapy. Cancer 2013;119:1808–1815.
23. Nanda A, Chen MH, Braccioforte MH, et al. Hormonal therapy use for prostate cancer and mortality in men with coronary artery disease–induced congestive heart failure or myocardial infarction. JAMA 2009; 302:866–873.
24. Meng F, Zhu S, Zhao J, et al. Stroke related to androgen deprivation therapy for prostate cancer: a meta-analysis and systematic review. BMC Cancer 2016;16:180.
25. Carneiro A, Sasse AD, Wagner AA, et al. Cardiovascular events associated with androgen deprivation therapy in patients with prostate cancer: a systematic review and meta-analysis. World J Urol 2015;33:1281–1289.
26. Lopes RD, Higano CS, Slovin SF, et al. Cardiovascular safety of degarelix versus leuprolide in patients with prostate cancer: the primary results of the PRONOUNCE randomized trial. Circulation 2021;144:1295–1307.
27. Schaeffer EM, Srinivas S, Adra N, et al. NCCN Clinical Practice Guidelines in Oncology: Prostate Cancer. Version 4.2024. Accessed August 30, 2024. To view the most recent version, visit https://www.nccn.org
28. Bhatia N, Santos M, Jones LW, et al. Cardiovascular effects of androgen deprivation therapy for the treatment of prostate cancer. Circulation 2016;133:537–541.
29. Basaria S, Bhasin S. Targeting the skeletal muscle–metabolism axis in prostate-cancer therapy. N Engl J Med 2012;367:965–967.
30. Kovač MB, Pavlin T, Čavka L, et al. The trajectory of sarcopenia following diagnosis of prostate cancer: a systematic review and meta-analysis. J Geriatr Oncol 2023;14:101594.
31. Shahinian VB, Kuo YF, Freeman JL, Goodwin JS. Risk of fracture after androgen deprivation for prostate cancer. N Engl J Med 2005;352: 154–164.
32. Suarez-Almazor ME, Pundole X, Cabanillas G, et al. Association of bone mineral density testing with risk of major osteoporotic fractures among older men receiving androgen deprivation therapy to treat localized or regional prostate cancer. JAMA Netw Open 2022;5:e225432.
33. Eastham JA. Bone health in men receiving androgen deprivation therapy for prostate cancer. J Urol 2007;177:17–24.
34. Houben LHP, Overkamp M, VAN Kraaij P, et al. Resistance exercise training increases muscle mass and strength in prostate cancer patients on androgen deprivation therapy. Med Sci Sports Exerc 2023;55:614–624.
35. Kenfield SA, Van Blarigan EL, Panchal N, et al. Feasibility, safety, and acceptability of a remotely monitored exercise pilot CHAMP: a clinical trial of high-intensity aerobic and resistance exercise for metastatic castrate-resistant prostate cancer. Cancer Med 2021;10:8058–8070.
36. Newton RU, Kenfield SA, Hart NH, et al. Intense exercise for survival among men with metastatic castrate-resistant prostate cancer (INTERVAL-GAP4): a multicentre, randomised, controlled phase III study protocol. BMJ Open 2018;8:e022899.
37. Shapiro CL, Van Poznak C, Lacchetti C, et al. Management of osteoporosis in survivors of adult cancers with nonmetastatic disease: ASCO clinical practice guideline. J Clin Oncol 2019;37:2916–2946.
38. Dalla Volta A, Mazziotti G, Maffezzoni F, et al. Bone mineral density and FRAX score may not predict fracture risk in patients with cancer undergoing hormone deprivation therapies. J Clin Oncol 2020;38:3363–3366.
39. Saylor PJ, Rumble RB, Tagawa S, et al. Bone health and bone-targeted therapies for prostate cancer: ASCO endorsement of a Cancer Care Ontario guideline. J Clin Oncol 2020;38:1736–1743.
40. Smith MR, Egerdie B, Toriz NH, et al. Denosumab in men receiving androgen-deprivation therapy for prostate cancer. N Engl J Med 2009;361: 745–755.
41. Serpa Neto A, Tobias-Machado M, Esteves MAP, et al. Bisphosphonate therapy in patients under androgen deprivation therapy for prostate cancer: a systematic review and meta-analysis. Prostate Cancer Prostatic Dis 2012;15:36–44.
42. Sølling AS, Harsløf T, Brockstedt HK, Langdahl B. Discontinuation of denosumab in men with prostate cancer. Osteoporos Int 2023;34: 291–297.
43. Gryzinski GM, Fustok J, Raheem OA, Bernie HL. Sexual function in men undergoing androgen deprivation therapy. Androg Clin Res Ther 2022;3: 149–158.
44. Donovan KA, Gonzalez BD, Nelson AM, et al. Effect of androgen deprivation therapy on sexual function and bother in men with prostate cancer: a controlled comparison. Psychooncology 2018;27:316–324.
45. Bolla M, Maingon P, Carrie C, et al. Short androgen suppression and radiation dose escalation for intermediate- and high-risk localized prostate cancer: results of EORTC trial 22991. J Clin Oncol 2016;34: 1748–1756.
46. Schover LR. Sexual healing in patients with prostate cancer on hormone therapy. Am Soc Clin Oncol Educ Book 2015:e562–566.
47. Fagerlund A, Cormio L, Palangi L, et al. Gynecomastia in patients with prostate cancer: a systematic review. Plos One 2015;10:e0136094.
48. Serretta V, Altieri V, Morgia G, et al. A randomized trial comparing tamoxifen therapy vs. tamoxifen prophylaxis in bicalutamide-induced gynecomastia. Clin Genitourin Cancer 2012;10:174–179.
49. Di LG, Perdon ÀS, De PS, et al. Gynecomastia and breast pain induced by adjuvant therapy with bicalutamide after radical prostatectomy in patients with prostate cancer: the role of tamoxifen and radiotherapy. J Urol 2005;174:2197–2203.
50. Sentana-Lledo D, Dodge LE, Chang P, Einstein DJ. Prevalence and morbidity of local treatment-related side effects in metastatic prostate cancer patients. Urol Oncol 2023;41:204.e1–6.
51. Michalski JM, Yan Y, Watkins-Bruner D, et al. Preliminary toxicity analysis of 3DCRT versus IMRT on the high dose arm of the RTOG 0126 prostate cancer trial. Int J Radiat Oncol Biol Phys 2013;87:932–938.
52. Hamstra DA, Mariados N, Sylvester J, et al. Continued benefit to rectal separation for prostate radiation therapy: final results of a phase III trial. Int J Radiat Oncol Biol Phys 2017;97:976–985.
53. Langston B, Armes J, Levy A, et al. The prevalence and severity of fatigue in men with prostate cancer: a systematic review of the literature. Support Care Cancer 2013;21:1761–1771.
54. Grossmann M, Zajac JD. Hematological changes during androgen deprivation therapy. Asian J Androl 2012;14:187–192.
55. Tsou PH, Lan TC, Tam KW, Huang TW. Essential of immediate exercises on cancer-related fatigue in patients with prostate cancer receiving androgen deprivation therapy: a meta-analysis of randomized controlled trials. Semin Oncol Nurs 2023;39:151368.
56. Nelson CJ, Lee JS, Gamboa MC, Roth AJ. Cognitive effects of hormone therapy in men with prostate cancer. Cancer 2008;113:1097–1106.
57. Gonzalez BD, Jim HSL, Booth-Jones M, et al. Course and predictors of cognitive function in patients with prostate cancer receiving androgen-deprivation therapy: a controlled comparison. J Clin Oncol 2015;33: 2021–2027.
58. Nead KT, Gaskin G, Chester C, et al. Association between androgen deprivation therapy and risk of dementia. JAMA Oncol 2017;3:49–55.
59. Khosrow-Khavar F, Rej S, Yin H, et al. Androgen deprivation therapy and the risk of dementia in patients with prostate cancer. J Clin Oncol 2017; 35:201–207.
60. Morote J, Tabernero ÁJ, Ossorio JLÁ, et al. Cognitive function in patients with prostate cancer receiving luteinizing hormone-releasing hormone analogues: a prospective, observational, multicenter study. Int J Radiat Oncol Biol Phys 2017;98:590–594.
61. Guo Z, Gan S, Li Y, et al. Incidence and risk factors of suicide after a prostate cancer diagnosis: a meta-analysis of observational studies. Prostate Cancer Prostatic Dis 2018;21:499–508.
62. Nead KT, Sinha S, Yang DD, Nguyen PL. Association of androgen deprivation therapy and depression in the treatment of prostate cancer: a systematic review and meta-analysis. Urol Oncol 2017;35:664.e1–9.
63. Jayadevappa R, Malkowicz SB, Chhatre S, et al. The burden of depression in prostate cancer. Psychooncology 2012;21:1338–1345.
64. Sharpley CF, Christie DRH, Bitsika V. Depression and prostate cancer: implications for urologists and oncologists. Nat Rev Urol 2020;17:571–585.
65. Tsao PA, Ross RD, Bohnert ASB, et al. Depression, anxiety, and patterns of mental health care among men with prostate cancer receiving androgen deprivation therapy. Oncologist 2022;27:314–322.
66. Irani J, Salomon L, Oba R, et al. Efficacy of venlafaxine, medroxyprogesterone acetate, and cyproterone acetate for the treatment of vasomotor hot flushes in men taking gonadotropin-releasing hormone analogues for prostate cancer: a double-blind, randomised trial. Lancet Oncol 2010;11: 147–154.
67. Harding C, Harris A, Chadwick D. Auricular acupuncture: a novel treatment for vasomotor symptoms associated with luteinizing-hormone releasing hormone agonist treatment for prostate cancer. BJU Int 2009;103: 186–190.
68. James C, Brunckhorst O, Eymech O, et al. Fear of cancer recurrence and PSA anxiety in patients with prostate cancer: a systematic review. Support Care Cancer 2022;30:5577–5589.

69. Volz Y, Troost J, Eismann L, et al. The burden of fear of cancer recurrence in genitourinary cancers: a prospective study (NCT04535921). Oncol Res Treat 2022;45:744–751.
70. Kazer MW, Bailey DE Jr, Chipman J, et al. Uncertainty and perception of danger among patients undergoing treatment for prostate cancer. BJU Int 2013;111:E84–91.
71. Kang DW, Fairey AS, Boulé NG, et al. A randomized trial of the effects of exercise on anxiety, fear of cancer progression and quality of life in prostate cancer patients on active surveillance. J Urol 2022;207:814–822.
72. Lin J, Zhan X, Chen R, et al. Increased burden of second bladder cancer and rectal cancer in prostate cancer treated with radiotherapy: results from Surveillance, Epidemiology, and End Results. Cancer Control J Control 2023;30:10732748231177544.
73. Choi Y, Smith KC, Shukla A, et al. What are survivorship care plans failing to tell men after prostate cancer treatment? Prostate 2021;81:398–406.