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Review

Recommendations for Prostate Cancer Survivorship Care: An Update to the 2009 Michigan Cancer Consortium Guidelines for the Primary Care Management of Prostate Cancer Post-Treatment Sequelae

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Abstract

Background: Primary care providers inevitably care for prostate cancer survivors. However, few comprehensive resources exist to aid them in providing the most up-to-date and evidence-based care. To meet this clinical need, we examined and updated the Michigan Cancer Consortium prostate cancer survivorship guidelines.
Methods: Using an expert panel and focus groups comprised of prostate cancer stakeholders, we updated the Michigan Cancer Consortium's 2009 *Guidelines for the Primary Care Management of Prostate Cancer Post-Treatment Sequelae*.
Results: The guideline recommendations were modified to serve as a point-of-care resource and to facilitate care transitions between specialty and primary care. The modified recommendations were approved by the Michigan Cancer Consortium and now include the following elements: (1) patient-reported symptom assessment, (2) distinctions between medical and self-management strategies for prostate cancer treatment-related side effects, (3) recommendations for involving partners in survivorship care, and (4) care coordination strategies for primary and specialty care providers. Online guidance for medical therapy and self-management resources are also provided.
Conclusions: To remedy a persistent lack of guidance to direct prostate cancer survivorship care in the primary care setting, the updated Michigan Cancer Consortium prostate cancer survivorship tools convert a static guideline into a dynamic resource to improve outcomes and support coordination among primary care providers, cancer specialists, patients, and caregivers.

Introduction

There are over 2.5 million prostate cancer survivors in the United States.[1] Many live with burdensome side effects (e.g., urinary incontinence, sexual, bowel, and hormonal dysfunction) stemming from their prostate cancer treatment.[2] While primary care providers (PCPs) often care for these men, few comprehensive resources exist to guide their efforts in providing the most up-to-date and evidence-based care in partnership with specialists and patients.[3,4]

To help meet this need, the Michigan Cancer Consortium convened a multidisciplinary panel of experienced clinicians, public health experts, patients, and consumers from across the state to address issues among men treated for prostate cancer. Through partnership with the Centers for Disease Control and Prevention and the American Cancer Society, the panel sought to address the Institute of Medicine's calls for improving cancer survivorship care.[5] In 2009, the panel released clinical guidelines to assist PCPs in managing symptoms after prostate cancer treatment.[6]

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In 2011, a second expert working group was convened to examine and update the Michigan Cancer Consortium's 2009 prostate cancer survivorship guidelines to both reflect recent advances in prostate cancer care and to improve acceptance and use of the guidelines among the primary care community. This article reports the findings of the expert panel's recommendations to update the Michigan Cancer Consortium (MCC) guidelines and make them into an actionable resource to guide survivorship care across the life course. As part of this update the panel generated point-of-care, web-based algorithms to assist PCPs during clinical encounters and provided self-management resources to engage patients in their survivorship care.

Methods

Expert panel

The expert panel was comprised of a diverse set of prostate cancer stakeholders including five family practice and internal medicine PCPs (MJ, KR, JH, LA, JP), one urology nurse (VH), three urologic oncology nurse practitioners (NRG, DC, SM), one radiation oncology physician assistant (KO), three urologic oncologists (TS, DW, JM), one urologist (JW), one sexual health therapist (DW), two pelvic floor physical therapists (JS, KE), one health communications (MHR) and one behavioral medicine expert (LA), and two state-level public health professionals (PH, CG). All updates to the 2009 MCC guidelines that were based on expert panel input are specifically noted throughout the manuscript. References to existing guidelines or recommendations (e.g., National Comprehensive Cancer Network [NCCN]) were also included where appropriate.

Focus groups with clinical experts

To learn how to improve acceptance of the 2009 MCC guidelines among PCPs caring for prostate cancer survivors, we conducted three focus groups with a total of 10 PCPs at two university-based practices and 7 members of a university-based prostate cancer survivorship working group. The focus groups were conducted by one (TS) or more of the authors using the 2009 MCC guidelines and plain language prostate cancer survivorship fact sheets as templates to assess the acceptability and usability of the current guidelines as well as suggested modifications to facilitate use. For each topic area (e.g., urinary symptoms) and its corresponding Primary Care Management Option from the 2009 MCC guidelines, the moderator invited the participants to comment on feasibility, appropriateness, and barriers to implementing the recommendations in the primary care setting. Based on the importance of self-management approaches in chronic disease management, focus group participants were also asked to comment on their experiences with self-management of prostate cancer treatment sequelae according to the domains represented in the validated Expanded Prostate Cancer Index Composite (EPIC) instrument (urinary, sexual, bowel, and hormonal/vitality).[7] Notes from these focus groups were arranged by topic area to inform the guideline update.

Updating the 2009 MCC guidelines

Based on findings from focus groups, the expert panel modified the 2009 MCC guidelines using an iterative process until agreement among panel members was achieved on three components: (1) an updated two-page recommendation sheet, (2) online algorithms for medical and self-management resources, and (3) a manuscript for peer review. Disagreement regarding any of the components was resolved through further group correspondence and examination of the evidence base. The second and third components were thought necessary to improve the use and acceptance of the updated guidelines as a point-of-care resource among the primary care community. For this reason, each of the figures presented in this manuscript corresponds with an interactive MCC web page[6] where providers can be linked to more information regarding medical treatment and self-management of prostate cancer treatment-related side effects. All updates were presented to and approved by the Prostate Cancer Action Committee of the Michigan Cancer Consortium and its Board of Directors in September 2013.

Results and Recommendations for Prostate Cancer Survivorship Care

Prostate cancer treatment-related symptom assessment

Straightforward and easy to use measurement of patient-reported symptoms after prostate cancer treatment was deemed critical to understanding patients' side effect burden, the impact of different management approaches, and to track patients' quality of life over time. Focus groups and the expert panel recommended the addition of patient-reported outcomes to be included in the updated guidelines.

Recommendation: Primary care providers should assess the severity of symptoms due to prostate cancer and its treatments during routine clinical care. Instruments include the Expanded Prostate Cancer Index Composite (EPIC) – Short Form,[7] its abridged Clinical Practice (EPIC-CP),[8] version and others. The EPIC instruments measure a prostate cancer survivor's quality of life with respect to four domains—urinary, sexual, bowel, and hormonal/vitality—regardless of their prostate cancer treatment or recurrence status. The EPIC-CP survey can be completed by the patient in less than 10 minutes at the time of the visit, and its itemized responses examined and documented to guide the clinical encounter with respect to the symptom domains and longitudinal symptom management.[8] Providers should consider these assessments at diagnosis to help inform treatment decisions, at 3-month intervals during the first year after treatment, and at least annually thereafter to follow patient symptom burden over time. (Supplementary Fig. S1, Supplementary Data are available online at www.liebertpub.com/jomh). The panel felt that bothersome symptoms should first be managed using the algorithms provided below with specialist referral for refractory symptoms.

Identifying prostate cancer recurrence and progression: Different PSA thresholds after surgery and radiation therapy

The NCCN guideline recommendations for prostate cancer surveillance with prostate-specific antigen (PSA) testing and digital rectal examination indicate that intervals from 3 to 12 months are appropriate depending on disease risk and time from treatment as described below.[9] Due to the absence

of clinical trials to establish superiority of one practice pattern over another, the evidence base is poor and surveillance is typically driven by provider preference, treatment sequelae, and likelihood of recurrence.

As illustrated in Supplementary Fig. S2, different PSA thresholds may indicate treatment failure after surgery versus radiation. According to an American Urological Association 2007 statement, ''following radical prostatectomy, the Panel recommends defining biochemical recurrence as an initial serum prostate specific antigen of $>$ or $=0.2$ ng/mL, with a second confirmatory level of prostate specific antigen of >0.2 ng/mL.''[10,11] Therefore, any detectable PSA after surgery or PSA that increases on two or more determinations is an indication for referral back to the specialist. Based on a variety of factors—including time to PSA failure, PSA doubling time, and pathology—patients may be observed, referred for salvage radiation treatment, or placed on androgen deprivation therapy (ADT) at the specialist's discretion.

This is in contrast to treatment failure for patients following radiation therapy, where nadir PSA level plus 2 ng/mL is applied.[12,13] The panel updated this definition of biochemical recurrence after radiation therapy as the prior guidelines used an outdated definition. For patients receiving radiation therapy, the time to reach nadir is typically 6 to 24 months.[14] These patients, especially those treated with brachytherapy, may have a ''PSA bounce'' (a benign PSA elevation) which can occur within first 4 years of treatment.[11] In this case, repeating the PSA in 3 months is warranted.

Recommendation: The updated recommendations are consistent with recommendations from the American Urological Association[12] and NCCN[9] and include PSA testing every 6 to 12 months following treatment for 5 years, then annually. Digital rectal examination should be performed annually, may be omitted in cases of undetectable PSA, and coordinated between primary and specialty care providers. Because androgen deprivation is typically administered in 3-month depot injections, PSA testing every 3 months is recommended for these individuals; however, in the setting of an undetectable PSA (<0.1 ng/mL) during androgen deprivation, PSA testing every 6 months may be considered. Rising PSA levels while on ADT and active surveillance may indicate disease progression.[9] For patients treated with ADT, checking testosterone levels to ensure they are at appropriately reduced (i.e., castrate) levels should be considered prior to specialist referral or inquiry for rising PSA.[9,15] Prostate cancer specialists should designate responsibility for serial PSA monitoring after initial treatment in their treatment summary. In cases where there is no established PCP, the specialist is responsible for ongoing PSA surveillance.

In cases where PSA levels are detectable and rising on two or more occasions after surgery or radiation therapy, referral should be made.[9,13] Specifically after surgery, confirmed detectable PSA levels >0.2 ng/mL warrant referral. Radiation oncologists should indicate in their treatment summaries each patient's nadir PSA level and the $+2$ ng/mL threshold defining biochemical recurrence in order for PCPs to properly follow recommendations. Referral for rising PSA after radiation therapy can be made sooner if there is a persistent slow rise that does not meet the nadir $+2$ ng/mL threshold.[11] Rising PSA levels during ADT should always be referred for specialist evaluation.[9,11,12] In general, contacting the treating specialist whenever there is uncertainty in interpreting PSA trends or levels is recommended.

Managing urinary control problems after prostate cancer treatment

Urinary symptoms during and after treatment for prostate cancer are common and usually the worst during the first 3 months after treatment.[2,16] Both urinary symptoms and bother can be evaluated with the EPIC instrument. The management recommendations for urinary symptoms after prostate cancer treatment include assessment of symptom burden, pharmacologic therapy, self-management techniques, device use, and referral for specialized care. The panel recommended separating the side effects according to treatment type (e.g., surgery, radiation) to make guideline recommendations easier to understand and use. In addition, the updated MCC recommendations provide self-management recommendations for urinary problems using hyperlinks to patient and provider support materials.

Urinary symptoms and treatment after radiation therapy. The typical short-term side effects of external beam radiation therapy consist of urinary urgency, frequency, dysuria, and in a minority of patients, incontinence.[17] For most patients, dysuria, frequency, and urgency are resolved after several weeks.[18] While some may have some degree of urinary bother that persists, incontinence tends to be minimal for most patients.[2] Providers should also be aware that radiation therapy patients, like surgery patients, may develop urethral stricture disease leading to overflow incontinence; such patients should be referred to urology for assessment.[18] Radiation cystitis may also occur after radiation therapy leading to urinary symptoms and hematuria. Urinary symptoms after brachytherapy tend to occur shortly after the procedure due to trauma followed by irritative and obstructive symptoms generally peaking at 1 month.[17] These symptoms usually resolve over a 1-year period and may be more prominent in men with larger prostate size.[19]

Urinary incontinence after surgery: Post-prostatectomy incontinence. Nearly all radical prostatectomy patients experience some degree of stress urinary incontinence after surgery (i.e., post-prostatectomy incontinence).[20] Fortunately, over 80% of men recover their urinary control by 12 months after surgery.[21] Incontinence following an observation period of at least 12 months may warrant surgical intervention (possibly less in the setting of severe incontinence); however, self-management and medical therapy typically precede invasive procedures.

Recommendation: As illustrated in Supplementary Fig. S3, men experiencing urinary bother may benefit from pyridium, alpha-adrenergic blockers (e.g., tamsulosin), and anticholinergic therapy (e.g., oxybutynin).[17] Because behavioral therapy (i.e., pelvic floor physical therapy) has been shown to decrease post-prostatectomy incontinence,[22] the panel recommends the PCP make a referral to a local physical therapist to explore pelvic floor rehabilitation options. As illustrated in Supplementary Fig. S4, post-prostatectomy incontinence may also be treated with medical therapy such as anticholinergic agents and imipramine.[23] Anticholinergic medications

include oxybutynin, tolterodine, trospium, solifenacin, and darifenacin. Imipramine is unique in that it exerts its effects through an anticholinergic relaxation of the bladder and a sympathetic activation of the bladder neck to improve urinary control.[24] Because of variable success in post-prostatectomy incontinence, the use of other medical therapy has been limited. In some cases, a soft penile clamp (i.e., Cunningham clamp) may be used to control urinary leakage (Supplementary Appendix S1). In addition, the leakage of urine during sexual intercourse, (i.e., climacturia), can be distressing for men and partners. Condom use and bladder emptying prior to sexual activity may help.[25] Approaches to surgical management include injection of bulking agents into the bladder neck, periurethral balloon compression devices, urethral slings and artificial urinary sphincters.[23] Referral to a urologist for consideration of these procedures is warranted in the setting of persistent incontinence 12 or more months after surgery.

The burden of sexual side effects from prostate cancer treatment

The sexual side effects of prostate cancer treatment are well documented.[2,16] Men develop erectile dysfunction immediately after surgery, fairly quickly after hormonal treatment, and over a period of 2 years after radiation therapy. Recovery of erectile function after surgery may take up to 2 years and often requires medical assistance.[26] Several factors including older age, ADT, non-nerve-sparing surgery and comorbidities may all contribute to worsened sexual function after prostate cancer treatment. For men previously treated with ADT and struggling with libido, testosterone levels may be slow to recover to physiologic levels.[15,27,28] Sexual function and bother are both evaluated in the EPIC instrument although other measures are available such as the Sexual Health Inventory for Men[29] and the University of California Los Angeles Prostate Cancer Index.[30]

Most interventions in sexual health for prostate cancer survivors have focused on the recovery of erectile function. Despite the fact that the pro-erectile aids are fairly effective and available, there is evidence that some men who could benefit from these interventions are reluctant to try them, or they do not sustain their use even after trying.[26] A review of the literature suggests that biopsychosocial interventions that couple erectile aids with education and counseling may be needed to promote and sustain their use.[31] In its publication devoted to the psychosocial needs of cancer survivors, the Institute of Medicine recognized that a multidisciplinary approach is not only relevant, but also critical to the care for the whole person.[32]

After treatment, many men experience sadness about loss of sexual function and resultant lack of confidence in their sexual relationships.[33–35] Moreover, female partners of men with prostate cancer are often postmenopausal, potentially adding to couples' sexual difficulties. Couples' may also have difficulty communicating about sexual problems, or they may report chronic dissatisfaction with their sexual relationship or a decline in mental health.[36–39]

Recommendation: The panel recommends documenting the sexual health burden of patients and their partners upon prostate cancer diagnosis, every 3 months during the first year and at least annually thereafter. Addressing sexual function and relationships early in the diagnosis and treatment process is important as it can legitimize and normalize patients' and partners' concerns. Using EPIC to understand pre- and postoperative function provides an objective measure of sexual recovery. As illustrated in Supplementary Fig. S5, approaches to sexual health recovery include pharmacologic therapy, self-management techniques, device use, and referral for specialized care. Penile rehabilitation should be considered as an early intervention. For men who do not recover erections sufficiently for penetrative sex, erectogenic aids—such as vacuum erectile devices (see Supplementary Appendix S2 for generic prescription), penile injections, or transurethral suppositories—may be an appropriate option.[40–42] Urologist referral for these erectogenic aids are appropriate for men who do not recover erections sufficiently for penetrative sex after a trial of phosphodiesterase type 5 inhibitors (e.g., sildenafil) if no contraindications are present. Providing the patient with both medical and psychosocial support for sexual recovery enhances prostate cancer patients' ability to recover sexual intimacy and improve their quality of life. The National Cancer Institute website on sexuality and cancer[43] and referral to sexual health therapists through the American Association of Sex Educators, Counselors, and Therapists website[44] are excellent resources.

Managing bowel symptoms after radiation therapy

Because of its fixed position in the pelvis, the rectum is the most common site of bowel injury from radiation therapy. Radiation exposure to the rectal wall may cause microvascular injury, leading to ischemia and neovascularization that can promote rectal bleeding years after treatment completion.[45,46] Endoscopic examination of the rectum in such cases demonstrates pallor with telangectasias and friability. Radiation can also cause connective tissue fibrosis and smooth muscle hypertrophy leading to internal and external sphincter dysfunction and decreased rectal capacity.[45,47]

Acute proctitis can occur during and for several months after treatment and is due to direct damage to the mucosa. Symptoms include increased stool frequency, urgency, inflammation of internal hemorrhoids, soft stools, and/or diarrhea. These symptoms are generally managed by the radiation oncology staff with dietary modifications and antidiarrheals and rarely can take 1–2 years to resolve. Long-term gastrointestinal (GI) toxicity most commonly presents as intermittent rectal bleeding but can also involve increased stool frequency, urgency, and fecal incontinence. Late rectal toxicity can present more than 9 months after completion of treatment with median time to late rectal toxicity of approximately 12–30 months.[48] Symptoms rarely present more than 5 years posttreatment, although emerging data suggests that fecal incontinence may become apparent during this time.

Reported rates of grade 2 or greater late GI toxicity range from 5% to 26%, and as radiation techniques have become more precise, toxicity has decreased.[49] Intensity-modulated radiation therapy (IMRT), one such technique, is now the standard treatment for localized prostate cancer and has nearly replaced three-dimensional (3D) conformal therapy.[50] One large study showed an actuarial likelihood of grade 2 or greater GI toxicity to be 5% in patients treated with IMRT compared with 13% in patients treated with

3D-conformal therapy, with the risk of grade 3 toxicity at < 1% for IMRT patients.[49] Studies also show that rectal dose is a strong predictor of late toxicity.[51] Standard guidelines for dose to the rectum, bowel, bladder and femoral heads are now a part of radiation therapy planning; this is expected to decrease GI toxicity in the future. Rectal dose is decreased further with image guidance (e.g., gold fiducial markers, Calypso beacons) which allow for narrower margins in the radiation field.

In addition to radiation techniques, there are other established risk factors for late GI complications. Patients with severe acute GI side effects have an increased likelihood of developing late GI toxicity.[49] The use of anticoagulants is also associated with a significant increase in the risk of rectal bleeding.[46] Other risk factors for late GI toxicity include diabetes,[52] age,[53] prior abdominal surgery (cholecystectomy and appendectomy),[54,55] baseline GI disease (inflammatory bowel disease and hemorrhoids)[56,57] and other medical comorbidities such as cardiac disease.[58]

Fecal incontinence can occur after radiation therapy due to injury of the anal musculature, decreased storage capacity, and thickening of the external anal sphincter.[59,60] It is likely under reported in the literature due to the fact that most toxicity forms capture bleeding and bowel frequency but not urgency or incontinence. In addition, some patients note a loss of sensation of rectal filling after radiation. Pelvic floor physical therapy and biofeedback can often assist with fecal urgency and incontinence. Treatment with bulking agents and antidiarrheals can help when patients have liquid stool triggering urgency and leakage. Loperamide increases internal anal sphincter tone and improves compliance; anticholinergics may also provide relief.

Recommendation: As illustrated in Supplementary Fig. S6, frequent and/or loose stools are often effectively treated with antidiarrheals such as loperamide and Imodium, which can also decrease urgency. Fiber supplements can help patients who have either loose stools or constipation. Rectal pain, itching, and hemorrhoidal flares can be treated with TUCKS, Preparation H, or Anusol suppositories. Although rectal bleeding after radiation therapy may be due to telangiectasias and the friability of the rectal wall, clinicians should ensure that patients with rectal bleeding have regular colonoscopies to rule out other causes of bleeding. Bleeding associated with radiation therapy is usually moderate, intermittent, related to straining, hard or large stools, and self-limited. Bleeding may be reduced with fiber supplements, stool softeners, and dietary modifications to avoid constipation. Topical steroids, topical sucralfate, and 5- aminosalicylic acid enemas can also decrease bleeding. For patients with persistent, significant bleeding that does not respond to conservative measures, referral back to the radiation oncologist and an experienced gastroenterologist for consideration of colonoscopy with argon plasma coagulation (APC), i.e., non-contact coagulation using high frequency electrosurgically ionized argon gas, is warranted. This approach treats superficial vessels and can be repeated at 1–2 week intervals as needed with a success rate of almost 98%.[61] While rectal fistulae are rare, biopsy and/or coagulation in the irradiated field may provoke their formation. Rare cases of bleeding refractory to treatment with APC may respond to hyperbaric oxygen treatment, though this is a time intensive course of treatment.

Managing the side effects of androgen deprivation therapy

Androgen deprivation therapy (ADT) is used in men with advanced prostate cancer to reduce levels of testosterone and dihydrotestosterone to prevent these androgens from stimulating prostate cancer cells. ADT is also used when patients cannot undergo radiation or surgery, in conjunction with other types of treatment, or in men with recurrence of prostate cancer after surgery or radiation therapy. The most common form of ADT uses gonadotropin releasing hormone (GnRH) agonists, given by injection or subcutaneous implant. Antiandrogen medications are also used, either as monotherapy or together with GnRH agonists (i.e., combined androgen blockade), and many new forms of androgen deprivation are becoming available for use in advanced disease.[62] Orchiectomy is the simplest and least expensive form of ADT, but it is not reversible and is psychologically unacceptable to most men.

Androgen deprivation has a variety of adverse effects.[63] Patients and their physicians should discuss these potential risks prior to treatment, and caregivers should be informed and offered guidance on dealing with side effects of treatment. Metabolic side effects can include weight gain, insulin resistance, and changes in lipid profile, potentially increasing patients' risk of both diabetes and cardiovascular disease.[64–66] The endocrine side effects may include decreased libido, hot flashes, gynecomastia, and nipple tenderness.[67,68] Primary care providers should have a heightened awareness for diabetes mellitus and dyslipidemia in this population, and help these men reduce their risk of cardiovascular disease using standard approaches (i.e., smoking cessation, diet, exercise).

Skeletal effects of ADT

Skeletal effects of ADT include osteopenia, osteoporosis, and a greater incidence of clinical fractures.[69–71] ADT accelerates loss of bone mineral density (BMD), particularly in the first couple of years of treatment.[72] When men choose ADT as an option for prostate cancer treatment, the risks of osteoporosis and treatment-related fractures should be discussed with careful attention toward prevention. A study of over 50,000 men at least 5 years after their prostate cancer diagnosis found that 19.4% of men who received ADT had a fracture, compared with 12.6% who did not receive ADT.[73] Skeletal morbidity is a significant risk for men with metastatic prostate cancer, causing severe pain as well as increased risk of fracture and structural complications.

Osteoporosis treatment for men on ADT

Bisphosphonates are an established component of care for patients with bone metastasis, yet their ability to delay the progression of visceral and skeletal metastasis has not yet been determined. A randomized trial of 643 castration-resistant men with bone metastases found a significant decrease in skeletal-related events (33.2% vs. 44.2%) when zoledronic acid was used, making it the standard of care for this population.[74,75] The treatment is administered by means of an intravenous infusion every 3–4 weeks. In contrast to bisphosphonates, denosumab is a human monoclonal immunoglobulin G2 antibody that binds and inactivates receptor activator of nuclear factor κ-B ligand (RANKL), a critical

mediator of osteoclast differentiation, activation, and survival. Denosumab subcutaneous injection therapy is associated with significant increases in BMD at the hip, femoral neck, and distal radius, and a decreased incidence of vertebral fractures at 36 months (1.5% compared with 3.9% in placebo group; relative risk = 0.38, 95% confidence interval = 0.19–0.78).[76,77]

Endocrine and other effects of androgen deprivation

ADT can also cause fatigue, depression, low libido, and erectile dysfunction, as well as endocrine effects such as hot flashes, gynecomastia, and nipple tenderness.[68] Hot flashes are common in men on ADT, occurring after the first few months of treatment in up to 70% of men treated with GnRH agonists.[78] They generally resolve over time but can persist for up to 2 years after ADT. Gynecomastia and nipple tenderness occur in up to 16% of men treated with GnRH agonists or orchiectomy, but the incidence is much higher (up to 79%) with antiandrogen monotherapy, due to peripheral aromatization of excess testosterone to estrogen.[79]

Recommendation: For prostate cancer survivors treated with ADT, it is important to remember that they may be at increased risk for cardiovascular disease, diabetes, metabolic syndrome, and osteoporosis (Supplementary Fig. S7). Primary care providers are likely best positioned to deal with these serious side effects. Prevention of side effects includes promoting healthy behaviors (exercise, reducing caloric intake, smoking cessation, and caffeine and alcohol reduction) and addressing bone health. Adequate intake of calcium and vitamin D is an important way for men to reduce their risk of osteoporosis. The panel supported the NCCN recommendations to follow the National Osteoporosis Foundation (NOF) guidelines on bone health such as bone mineral density (BMD) testing for all men 70 years or older, as well as for men aged 50 to 69 years based on their risk factor profiles.[9] The NOF guidelines also recommend men aged 19 to 70 should intake 1000 mg of calcium and 600 IU of vitamin D3 daily, and men aged 71 and older should intake 1200 mg of calcium and 800 IU of vitamin D daily. The men most likely to benefit from osteoporosis screening are those with calculated 10-year risks for osteoporotic fracture greater than or equal to those of 65-year-old Caucasian women who have no additional risk factors (i.e., when the 10-year probability of hip fracture is 3% or the 10-year probability of a major osteoporosis-related fracture is 20%).[9] Fracture risk can be assessed using the FRAX® algorithm from the World Health Organization.[80] Use of ADT can be considered ''secondary osteoporosis'' when applying the FRAX® algorithm.

The panel agreed with the NCCN recommendation to consider a BMD scan 2 years after ADT initiation or earlier for patients at increased risk of osteoporosis. Biphosphonates (i.e., Fosamax, Boniva, Zometa) may be indicated in the setting of prolonged ADT. Current evidence supports the use of weekly or monthly bisphosphonates as the mainstay of therapy for men with bone-metastatic castration-resistant prostate cancer.[72] Antidepressants such as venlafaxine, fluoxetine, and paroxetine may be used for hot flashes and can be especially helpful in men with depression. Megestrol or gabapentin may also relieve hot flashes. Alternative treatments such as acupuncture, black cohosh, ginseng, licorice, and vitamin E are also used, although definite evidence of benefit is lacking. Referral to specialists for consideration of pretreatment breast irradiation or tamoxifen, surgical breast reduction, or to manage the metabolic aspects of ADT (endocrinology) may be warranted.

Provider collaboration and care coordination of prostate cancer survivors

The panel believed that care coordination among primary and specialty care providers is essential to optimizing prostate cancer survivorship care. However, this topic was lacking in the 2009 MCC guidelines. Therefore, care coordination in prostate cancer survivorship care is reviewed and recommendations follow.

Collaboration between PCPs and cancer specialists is critical for efficient, patient-centered survivorship care. The World Health Organization defines collaborative practice as ''multiple health workers from different professional backgrounds work[ing] together with patients, families, carers, and communities to deliver the highest quality of care.'' One potential barrier to more collaborative survivorship practice in the United States stems from the projected shortage of both prostate cancer specialists and PCPs with expertise in caring for cancer survivors.[81–83] Another barrier is that the tools to support PCPs in the provision of prostate cancer survivorship care remain underdeveloped.[84] Last, there remains a lack of clarity in who is responsible for side effect management.

Poor communication between the cancer specialist team and PCPs can make the transitions of care difficult.[85] Moreover, cancer survivors themselves have concerns regarding their PCP's ability to provide care that is specific to their needs.[82] While PCPs provide comprehensive preventive services, including other cancer screening tests, some fall short when it comes to adequate cancer-specific care such as surveillance for recurrence.[86–88] Likewise, cancer specialists may provide excellent cancer-specific care but are likely to perform less well in providing general preventative services.[86–88] When PCPs and cancer specialists coordinate care, both the adequacy of cancer-specific service and of other preventive services improve.[89,90]

Prostate cancer treatment summary and survivorship care plan

The Institute of Medicine's report *From Cancer Patient to Cancer Survivor: Lost in Transition*[5] highlighted a need for better survivorship care plans and enhanced care coordination to improve the quality of cancer care. The report notes that survivorship care plans should have a summary of the critical information needed for the survivor's long-term care: the treatment received; short- and long-term treatment consequences; pharmacologic therapy; medical, surgical and self-management techniques for side effect management; specific information regarding the timing of PSA testing, office visits, and follow up imaging (including who is responsible for each service); and instruments to monitor treatment-related symptoms. Creating such a survivorship care plan may be resource intensive, but the increasing adoption of electronic health records and demand by cancer advocacy groups and survivors supports such efforts.

Recommendation: The panel supported clear delineation of responsibility across the primary and specialty care

Table 1. Michigan Cancer Consortium Recommendations for Prostate Cancer Survivorship Care

Problem	*Onset*	*Primary care management options*	
Recurrence	Lifelong	Confirm that PSA testing and digital rectal examinations are being done at appropriate intervals: PSA every 3–12 months after prostatectomy or radiation therapy; PSA every 3–6 months during androgen deprivation therapy. Any confirmed PSA >0.2 ng/mL or two consecutive rises after surgery are indications for referral to specialist. Referral to radiation therapist is indicated for PSA levels greater than nadir (i.e., lowest level) after radiation, plus 2 ng/mL. Digital rectal examination may be performed annually and coordinated between providers.	
Symptom assessment	Lifelong	Assess the severity of symptoms due to prostate cancer and its treatments. Shared decision making may help ensure that symptom management is aligned with patient preferences and values. The Expanded Prostate Cancer Index Composite for Clinical Practice (EPIC-CP) is a 1-page, 16-item questionnaire that takes <10 minutes for patients to fill out. It is easy to interpret and measures urinary incontinence, urinary irritation, and the bowel, sexual, and hormonal health-related quality of life domains for prostate cancer survivors.	
Communication	Lifelong	Prostate cancer treatment summary and survivorship plans may facilitate transitions between specialty and primary care. Highlighted in such documents would be an information summary needed for the survivor's care beginning immediately after treatment and continuing over time. For example, the treatment received; shor-t and longer-term treatment consequences; pharmacologic therapy; and medical, surgical, and self-management techniques for side effect management are important. Specific information regarding the timing of PSA testing, office visits and imaging (including who is responsible for each service), and instruments to monitor treatment-related symptoms support shared decision making to ensure optimal care coordination and adherence with the survivorship plan.	
Urine control (Leaked urine; increased frequency; dysuria; weak stream)	Variable: Leaked urine more common after surgery than radiation; symptoms caused by urethral irritation after radiation may occur in the short term, but generally resolve with minimal intervention. Checking post-void residual will diagnose urinary retention due to urethral stricture or other causes.	**After surgery** **Pharmacologic**[94, 95 (LOE=0,III)] For urgency, frequency Oxybutynin (Ditropan) Tolterodine (Detrol) Imipramine (Tofranil) **Self-management strategies** Limit fluid intake[96 (LOE=0)] Avoid bladder irritants (coffee, acidic juices) [96 (LOE=0)] Weight loss[96 (LOE=0)] Increase physical activity[96 (LOE=0)] Smoking cessation[96 (LOE=0)] **Pelvic floor physical therapy** Pelvic floor exercises (stress incontinence)[95, 97 (LOE=I)] Biofeedback **Devices** Incontinence pads/undergarments External penile clamp[98 (LOE=I),] Condom catheter **For profound problems, refer to urologist to consider further surgery** (bulking agents, urethral sling, urinary sphincter).[96, 99–104 (LOE=II, 0, III, III, III, III,III)]	**After radiation therapy** **Pharmacologic**[94, 95 (LOE=0,III)] For urgency, frequency Oxybutynin (Ditropan) Tolterodine (Detrol) Tamsulosin (Flomax) For dysuria Phenazopyridine **Self-management strategies** Limit fluid intake[96 (LOE=0),] Keep a urinal next to the bed for nighttime problems Avoid bladder irritants (coffee, acidic juices) [96 (LOE=0)] **Pelvic floor physical therapy** Pelvic floor exercises (urge incontinence) [95, 97 (LOE=I)] Biofeedback **Devices** Incontinence pads/undergarments/bed liners External penile clamp[98 (LOE=I),] Condom catheter **If persistent incontinence or hematuria, refer to urologist for possible urodynamic evaluation and cystoscopy.**

(*continued*)

TABLE 1. (CONTINUED)

Problem	*Onset*	*Primary care management options*
Sexual dysfunction (including ED) (Erections not firm enough; erections not reliable; poor erections; poor orgasm; libido decreased or nonexistent)	Variable onset depending on type of treatment—can be immediate (surgery, androgen deprivation) or delayed (radiation).	Assess pretreatment function Evaluate for medications (eg, antidepressants, beta-blockers) and treatable medical conditions (eg, poorly controlled diabetes, depression, smoking) that may be interfering with erectile function Assess status of marital/primary relationship to identify psychological issues that may contribute to ED.[b] **Pharmacologic** Sildenafil[105,106 (LOE = III, 0) (Viagra, Revatio)] Tadalafil[106(LOE = 0) (Cialis)] Vardenafil[106 (LOE = 0) (Levitra)] If one is ineffective or side effects are not well tolerated then change to another Prostaglandin E1[107 (LOE = I)]; Alprostadil (Caverject intracavernosal injection) (Muse intraurethral pellet) **Self-management strategies** Minimize alcohol and tobacco use, schedule intimacy for when you are well rested and with an empty bladder, stay close to partner through hugging, kissing, and cuddling **Medical/surgical interventions** Vacuum erection device[108,109 (LOE = 0,0)] Surgery to place penile prosthesis[110 (LOE = 0)] Counseling/therapy (general and/or sexual) at the American Association of Sex Educators, Counselors, and Therapists website[44]
Bowel problems (Fecal incontinence, increased urgency to defecate, increased frequency, pain, hematochezia)	Occur after radiation; urgency, frequency of defecation may begin to improve soon after completion of therapy though can last for 1–2 years as well as present as late effects.	Dietary changes, evaluate for hemorrhoids and rectal fissure For blood in stool, referral to radiation oncology and GI for colonoscopy to rule out colon cancer, especially if they have not had a screening colonoscopy, biopsy and/or coagulation may provoke rectal fistulae, may check hemoglobin if there has been persistent blood loss **Pharmacologic** For loose stools: consider short course of Immodium or Lomotil—titrate to effect For rectal pain/itching: Preparation H, Tucks, Anusol suppositories **Self-management strategies** Stay well hydrated for constipation and diarrhea, keep stool soft and avoid straining, fiber for constipation **Other Strategies**[111 (LOE=0)] Assess for contributing comorbidities (eg, IBD); Biofeedback, pelvic floor exercise **For intractable symptoms, refer to prostate cancer or gastrointestinal specialist.**
Hot flashes[a]	After androgen suppression/ deprivation therapy (ADT); may persist for up to 2 years even with less than 1 year of ADT	**Pharmacologic** Consider antidepressant therapy, especially if there are elements of depression present [e.g., venlafaxine [Effexor], fluoxetine [Prozac], paroxetine [Paxil])[112 (LOE = 0)] Gabapentin[113 (LOE = I)] (Neurontin); Megace (megesterol acetate) **Self-management strategies** Wear layered clothing, use cooling fan **Other strategies** Alternative therapies (acupuncture, black cohash, ginseng, licorice, vitamin E)[114, 115 (LOE = 0, III)] **Check for possible interactions between alternative therapies and medications; avoid DHEA supplements.**

Levels of evidence (LOE) indicated if research available: LOE I = randomized controlled trial; LOE II = non-randomized controlled trial; LOE III = case series; LOE O = opinion, observation, literature review, pilot study.

[a]For prostate cancer survivors treated with ADT, it is important to remember that they may be at increased risk for cardiovascular disease, diabetes, metabolic syndrome and osteoporosis. Prevention includes promoting healthy behaviors (exercise, smoking cessation, caffeine and alcohol reduction)[116 (LOE = 0)] and supplementation of calcium and vitamin D[9,117(LOE = 1)]. Consider bone density scan 2 years after ADT or earlier for patients at increased risk of osteoporosis.[116 (LOE = 0)] Bisphosphonates[118 (LOE = III)] (i.e., Fosamax, Boniva, Zometa) may be indicated in the setting of prolonged ADT. Men undergoing ADT are also at risk for gynecomastia and nipple tenderness. Refer to specialists for consideration of pre-treatment radiation or Tamoxifen, surgical reduction, or to manage the metabolic aspects of ADT (endocrinology).

[b]Cancer survivors may be particularly prone to relationship issues and fear of the unknown. Consider appropriate medications to treat underlying depression/anxiety after appropriate evaluation. Healthy coping strategies should be encouraged. Support groups and counseling resources are also available. Local sexual therapy providers can be found at the American Association of Sex Educators, Counselors, and Therapists website.[44] The National Cancer Institute website on sexuality and cancer is also a good resource.[43] For more information, go to the Michigan Cancer Consortium Making the Choice website.[6]

ED, erectile disfunction; GI, gastroenterology; PSA, prostate specific antigen.

interface to facilitate prostate cancer survivorship care transitions. While the evidence supporting care plans and treatment summaries remains unclear, these approaches can relay the critical information needed for the survivor's long-term care and care coordination recommendations. Adhering to the updated Primary Care Management Options herein may also support care coordination efforts.

Discussion

Future research in prostate cancer survivorship care

The panel highlighted five prostate cancer survivorship topics that would help inform future guideline updates and advance quality of care: (1) Further research is needed to understand the intensity and value of PSA testing during survivorship, especially among patients without disease recurrence 10 years following surgery due their low risk of recurrence.[91] (2) Transitioning of PSA testing and side effect management to PCPs needs to be better understood in terms of timing, responsibility and communication of results among primary and specialty care providers. Consideration of primary care workload, workforce, expertise and interest in caring for prostate cancer-related issues, as well as specialist availability through telemedicine, electronic and in-person consultation, may help avoid an in-person referral when it is not necessary and prevent misinterpretation of initial signs of serious problems (e.g., hematuria, rising PSA). (3) How best to support men's and their partners' sexual recovery after prostate cancer treatment is unknown but increasingly relevant given our increased awareness of partner roles in survivorship. Biopsychosocial models of sexual recovery are needed to inform interventions that focus on patients and partners. (4) Comparative effectiveness research investigating the optimal survivorship care delivery models for prostate cancer patients is needed. (5) Development of technology-based, scalable tools that (a) allow patients to enter information at their convenience, (b) receive prompt personalized feedback regarding self-management and medical treatments for their side effects, and (c) allow providers to track progress or deterioration at the point-of-care would be an extraordinary advancement in cancer survivorship care.[92,93]

Conclusions

There is increasing recognition that PCPs need help taking over management of survivorship care from specialists. Due to a persistent lack of guidance to direct prostate cancer survivorship care, the updated Michigan Cancer Consortium prostate cancer survivorship guidelines and corresponding online algorithms offer an innovative resource to support PCPs and cancer specialists caring for men with prostate cancer. Using multidisciplinary input, these open-access guidelines are designed to make that transition easier and can help answer PCP questions regarding when to refer patients back to specialty care. As shown in Table 1,[9,45,46,94–118] these guidelines suggest expert- and evidence-based strategies for addressing common issues facing prostate cancer survivors including identification of cancer recurrence and managing specific treatment-related symptoms: sexual dysfunction, urinary incontinence, bowel problems, hot flashes, bone health, and metabolic syndrome. The expert panel addressed essential topics so that PCPs can be confident they are meeting the standards set by specialists. Moreover, these recommendations lend themselves to tailoring to specific patient needs to guide survivorship care across the primary and specialty care interface. Future research should develop and test strategies for implementation in clinical practice.

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In the spring of 2010 the Michigan Department of Community Health (MDCH) and the Blue Cross Blue Shield of Michigan (BCBSM) Foundation solidified their public–private partnership and issued a request for proposals to better understand how the MDCH prostate cancer survivorship guidelines might be received among primary care providers in the state. Funding for the proposal was supported by *Act No. 135, Michigan Public Acts of 2007*, which created the Prostate Cancer Research Fund, which consists of contributions made through State of Michigan income tax forms. The funds collected from the income tax check-off option during 2008 were matched by the BCBSM Foundation in an effort to maximize the benefit for Michigan men with a history of prostate cancer and their families. This guideline update is supported by this public–private venture.

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