

# Cancer Survivorship

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## 1. Introduction

Addressing the complications of living with cancer, both during and after completion of treatment, is increasingly recognized as an important aspect of providing care to the whole patient. Complications of cancer survivorship range from physical effects due to active therapy to tackling the psychological, sexual/fertility, and long-term risk of secondary malignancy that can persist or worsen after therapy ends. Awareness of the need to support cancer survivors was initially raised by the National Coalition for Cancer Survivorship, an advocacy group formed in 1986.<sup>1</sup> Further attention was raised when the Institute of Medicine released a report in 2005 defining the need for adult cancer survivors to receive coordinated monitoring and side effect management over time in the landmark report *From Cancer Patient to Cancer Survivor: Lost in Transition*.<sup>2</sup> As the number of cancer survivors grows each year, entities including the American Society of Clinical Oncology (ASCO), the American Cancer Society (ACS), and the American Urological Association (AUA) have emphasized the importance of addressing survivorship care.<sup>3-4</sup> Rather than focusing on the notion that cancer survivorship begins after cure, these organizations and others are increasingly describing **survivorship as a state that begins at the time of diagnosis and continues through the lifetime of the survivor**. In this article, we review the importance of addressing these survivorship needs, and provide a framework for comprehensive survivorship care.

## 2. Overview of Cancer Survivorship Plans



Figure 1. The cancer continuum from screening through end-of-life care, with survivorship care extending from the initiation of treatment through early end of life care.



Figure 2. Cancer survivorship programs must meet the multi-faceted needs of patients living with cancer, including an emphasis on the long-term/late effects of therapy, among others.

To standardize the approach to the care of cancer survivors, the American College of Surgeons' Commission on Cancer (CoC) developed guidelines for quality care delivery. In 2016 the CoC standard 3.3 described a suggested requirement for all patients treated with curative intent to receive a **survivorship care plan (SCP)** at the conclusion of therapy. These plans served as a **summary of prior cancer-directed treatment, suggested follow-up care plans including recommendations for surveillance for future malignancies, and supportive care recommendations**. Despite the mandate from the CoC, clinical teams seeking to meet the requirement to have all eligible patients receive a SCP by 2019 struggled to implement these effectively in practice.<sup>5</sup> The primary reasons underpinning low utilization included a lack of reimbursement, limited time during clinical visits, and competing responsibilities. Among patients with genitourinary malignancies specifically, the proportion of patients receiving SCPs increased after the CoC recommendation (27.2% vs 39.5% in 2012 vs 2017, respectively), but overall integration of SCPs has not approached the targets set by the CoC.<sup>6</sup>

More recently the CoC has updated its guidance and no longer recommends that all patients must receive a formally developed SCP, mandating instead that **clinical teams provide survivorship care programs that meet the needs of cancer patients, and patients must be aware of the services provided**. In contrast to a focus on patients treated with curative intent, the CoC has not defined the population to be included, enabling clinical teams to support cancer patients across the continuum of the cancer care, starting at diagnosis and including patients who are still receiving disease-directed treatment (Figure 1).<sup>7</sup> The updated guidance from the CoC is supported by ASCO, and a recently published editorial provides a comprehensive crosswalk comparing the prior standards with the new ones.<sup>8</sup> Importantly, rather than emphasizing delivery of SCPs, **CoC standard 4.8 is focused on the process of improving overall health of cancer survivors, identifying and addressing psychological complications, and screening for and preventing comorbid disease, including second cancers. Programs must make patients aware of supportive programs to meet the guidelines and offer at least three specialized services annually to cancer survivorship to meet the current CoC guidelines**. Delivery of a SCP can act as one of the three services.

There are a number of factors addressed by cancer survivorship plans (summarized in Figure 2). These include surveillance care to screen for second primary cancers and secondary malignancies related to prior therapy, surveillance for cancer recurrence, and dedicated systems that provide support and screening for long term physical and psychological effects from prior treatment.

Patients with genitourinary malignancies commonly experience tumor- and treatment-specific long-term effects from therapy, such as the late effects of profound hypogonadism associated with prostate cancer treatment, or the psychosexual effects experienced by patients who have undergone cystectomy or prostatectomy. Networks that integrate survivorship care across their existing framework, and incorporate policy, community, organizational, interpersonal and individual factors, serve as model systems in survivorship healthcare delivery.<sup>8</sup>

## 3. Mental Health

Cancer is a leading cause of mortality in the United States and is associated with significant morbidity, including psychiatric comorbidities. Given that more than 15% of North Americans endorse one or more of the following mental health concerns: a major depressive episode, bipolar disorder, generalized anxiety disorder, or substance abuse,<sup>9</sup> assessing the impact of these comorbidities among cancer patients is integral to cancer survivorship programs. Furthermore, approximately 70% of suicides occurring in patients >60 years of age are associated with medical illness, with higher rates among cancer patients.<sup>10-11-12</sup> The majority of the literature assessing mental health has focused on bladder, prostate and testicular cancer, which will be reviewed here.

### 3.1 Mental Health in Bladder Cancer

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Patients with **bladder cancer commonly have a greater number of comorbidities than other patients with genitourinary malignancies**,<sup>13</sup> as well as disproportionately higher rates of depression and suicidal death when compared to the general population. Vartolomei and colleagues<sup>14</sup> performed a systematic review assessing the prevalence of depression and anxiety among patients with bladder cancer, including 13 studies encompassing 1,659 patients. Six studies assessed depression prior to and at 1-, 6- and 12-months after treatment, whereas four studies investigated anxiety, and seven additional studies reported the prevalence of depression and anxiety among patients with bladder cancer at a specific time-point. Overall, pretreatment depression rates ranged from 5.7 to 23.1% and post-treatment from 4.7 to 78%, while post-treatment anxiety rates ranged from 12.5 to 71.3%. Zhang et al.<sup>15</sup> evaluated patient-reported anxiety, depression, and quality of life, as well as predictive factor for anxiety and depression exacerbation among 194 muscle-invasive bladder cancer patients receiving adjuvant chemotherapy after radical cystectomy. The Hospital Anxiety and Depression Scale (HADS) was used to evaluate anxiety and depression, and the EORTC QLQ-C30 Scale was used to assess quality of life. After adjuvant chemotherapy, this study found that HADS-Anxiety score ( $p = 0.042$ ), anxiety percentage ( $p = 0.036$ ), HADS-Depression score ( $p < 0.001$ ), depression percentage ( $p = 0.002$ ) and the EORTC QLQ-C30 Functional score ( $p = 0.002$ ) were increased compared with baseline, suggesting poorer self-reported mental health. Using multivariable analysis, increasing age ( $p < 0.001$ ), increasing BMI ( $p = 0.021$ ) and hypertension ( $p = 0.001$ ) were associated with worsening of the HADS-Anxiety score, while male gender ( $p < 0.001$ ) was associated with worsening of HADS-Depression score during adjuvant chemotherapy.

Although the majority of the bladder cancer literature has been dedicated to optimizing oncological outcomes with a focus on physical prognostic criteria, emerging data has suggested that both **pre- and post-treatment mental health may play as important a role in patient outcomes as physical health**. In a systematic review assessing the prevalence and impact of mental health disorders in bladder cancer patients, Pham et al.<sup>16</sup> reported that mental health disorders, including depression and anxiety, often coexist with a diagnosis of bladder cancer and that those with a worse oncologic prognosis reported a greater psychological burden. Additionally, poor mental health was associated with adverse treatment outcomes, such as postsurgical complication rates and survival outcomes.

Accurate measurement of mental health disorders can be challenging. Utilization of psychiatric resources prior to a cancer diagnosis has been suggested as a more accurate assessment of mental health comorbidity burden at the population-level rather than use of specific ICD-9/ICD-10 codes for mental health illnesses. To assess this impact in a Canadian health care setting, Klaassen et al.<sup>17</sup> included all residents of Ontario diagnosed with one of the ten most prevalent malignancies, including bladder cancer, from 1997 to 2014. A psychiatric utilization grade (PUG) score in the five years prior to a cancer diagnosis was calculated as follows: 0 – none; 1 – outpatient psychiatric utilization; 2 – emergency department psychiatric utilization; and 3 – psychiatric specific hospital admission. Of 676,125 patients included, there were 359,465 (53.2%) with PUG score 0; 304,559 (45.0%) with PUG score 1; 7,901 (1.2%) with PUG score 2; and 4,200 (0.6%) with PUG score 3. **Increasing PUG score was independently associated with increased cancer-specific mortality**, with an effect gradient across the intensity of pre-diagnosis psychiatric utilization (vs PUG score 0): PUG score 1 HR 1.05 (95% CI 1.04-1.06), PUG score 2 HR 1.36 (95% CI 1.30-1.42), and PUG score 3 HR 1.73 (95% CI 1.63-1.84). In a subgroup analysis specific to anatomic site, patients with bladder cancer with pre-diagnosis psychiatric utilization of resources had worse cancer-specific morality with increasing PUG score.

Several studies of patients with bladder cancer have also assessed the impact of post-diagnosis mental health diagnosis on outcomes and survival. **Using the SEER-Medicare database from 2002 to 2011, Jazzar and colleagues<sup>18</sup> reported that half of all patients with cT2-4a bladder cancer were diagnosed with psychiatric disorders after treatment.** Patients who underwent radical cystectomy were identified as being at significantly greater risk of having a posttreatment psychiatric illness compared with those who received radiotherapy and/or chemotherapy (HR 1.19, 95% CI 1.07-1.31), and notably, diagnosis of a psychiatric disorder was independently associated with increased all-cause mortality (HR 2.80, 95% CI 2.47-3.17) and cancer-specific mortality (HR 2.39, 95% CI 2.05-2.78).

Over the last decade, there has been several studies demonstrating that **suicide rates among cancer patients, including patients with genitourinary malignancies**,<sup>11</sup> are higher than that of the general population.<sup>10</sup> Among cancer patients, individuals with bladder cancer have one of the highest rates of suicide. In the SEER database, over a 40-year time frame (1973-2013), 794 patients with bladder cancer (0.24%) died of suicide, 190,734 patients (57.2%) died from other causes, and 142,151 patients (42.6%) were alive.<sup>19</sup> Significant factors associated with suicide included being unmarried (vs married: HR 1.74, 95% CI 1.49-2.04), white race (vs black: HR 2.22, 95% CI 1.32-3.74), male (vs female: HR 6.91, 95% CI 5.04-9.47), having regional disease (vs. localized: HR 2.49: 2.05-3.03), living in the Southeast United States (vs. Northeast: HR 2.43, 95% CI 1.78-3.32), not undergoing a radical cystectomy (vs cystectomy: HR 1.42, 95% CI 1.03-1.94), and increasing age ( $\geq 80$  years vs 60-69 years HR 1.32, 95% CI 1.06-1.66).

Although there is a plethora of population-level studies demonstrating an increased risk of suicidal death among patients with cancer compared to the general population, none account for pre-diagnosis psychiatric care/psychiatric comorbidities, which may confound this relationship. In order to assess this discrepancy, Klaassen et al.<sup>20</sup> assessed the effect of a cancer diagnosis on the risk of suicide, accounting for pre-diagnosis psychiatric care utilization using population-level data from Ontario for the ten most prevalent cancer types. Among 676,470 patients with cancer and 2,152,682 matched non-cancer controls, the suicide rate was 8.2 and 11.4 per 1000 person-years of follow-up, respectively. Patients with cancer had an overall higher risk of suicidal death compared with matched patients without cancer (HR 1.34, 95% CI 1.22-1.48). This effect was most pronounced in the first 50 months following diagnosis with no increased risk of suicide thereafter.

Among individuals with a PUG score 0 or 1, those with cancer were significantly more likely to die of suicide compared with controls. There was no difference in suicide risk between patients with cancer or controls for those who had a PUG score of 2 or 3, suggesting that among patients with more severe psychiatric comorbidities, the impact of a cancer diagnosis was less associated with risk of suicide. When specifically assessing patients versus non-cancer controls, the risk of suicidal death (accounting for pre-diagnosis psychiatric utilization of resources) was significantly higher (HR 1.73, 95% CI 1.14-2.62), with only lung cancer (HR 2.49, 95% CI 1.98-3.13) and oral cancer (HR 2.55, 95% CI 1.59-4.12) having a higher risk of suicidal death.

### 3.2 Mental Health in Prostate Cancer

While many men with prostate cancer will be successfully treated and cured of their disease, the physical and psychological side effects of treatment have a significant negative effect for many. Approximately **60% of men with prostate cancer experience mental health distress**,<sup>20</sup> with 10-40% having clinically significant depression.<sup>21</sup> An analysis using the SEER-Medicare database demonstrated that the incidence of mental health illness at 10 years after diagnosis with localized prostate cancer was 29.7% for men on "watchful waiting", 29.0% for those undergoing radiation therapy, and 22.6% for those treated with radical prostatectomy.<sup>22</sup> A separate SEER-Medicare study including 78,552 men with localized prostate cancer found a significantly increased incidence of depression (7.1% vs 5.2%) in men treated with ADT compared to those not exposed to ADT, with higher rates of both inpatient and outpatient psychiatric treatment in men treated with ADT.<sup>23</sup>

Risk of suicide has also been assessed among patients with prostate cancer. A study using the SEER database demonstrated that men with prostate cancer are at increased risk for suicide even up to 15 years after diagnosis.<sup>11</sup> However, in the aforementioned study by Klaassen et al. among cancer patients from Ontario, Canada,<sup>12</sup> **patients with prostate cancer did not have an increased risk of suicid compared to non-cancer controls (HR 1.07, 95% CI 0.90-1.27) when accounting for pre-diagnosis mental health utilization.** A review of the risk factors for repeated suicide attempts by Beghi et al.<sup>24</sup> demonstrated an association between suicidal ideation and death, white ethnicity, older age, male gender, and living alone. Many prostate cancer patients fit aspects of this demographic profile (white, old age, and male), in addition to potentially having other treatment-related side effects, such as erectile dysfunction, incontinence, bowel dysfunction and depression, that may increase their risk of suicide and other mental health disorders.

### 3.3 Mental Health in Testicular Cancer

In addition to concern for long-term treatment toxicity, infertility, secondary malignancy, and increased risk of cardiovascular disease, testicular cancer survivors are also at increased risk of mental health issues, which has only recently been adequately brought to light in national guidelines.<sup>25</sup> A recent population-level study evaluated the impact of a testicular cancer diagnosis and treatment on subsequent mental illness and utilization of mental illness healthcare resources.<sup>26</sup> This study included all incident cases of testicular cancer treated with orchietomy in Ontario, Canada from 2000 to 2010, identified using the Ontario Cancer Registry. Cases were matched to controls in a 1:5 ratio based on age and geography. After matching 2,619 men with testicular cancer to 13,095 controls, there was no baseline difference in the rate of mental health service use. Patients with testicular cancer were significantly more likely than controls to have an outpatient visit for a mental health concern in the peri-treatment (adjusted rate ratio [aRR] 2.45, 95% CI 2.06 to 2.92) and post-treatment periods (adjusted RR 1.30, 95% CI 1.12 to 1.52). The difference in mental health service use persisted over a median follow-up of 12 years.

In the post-orchietomy period, cases with baseline mental health service use were those most likely to use mental health services (aRR 5.64, 95% CI 4.64 to 6.85). Furthermore, in the pre-treatment period, cases and controls had comparable use of mental health services for anxiety (61% v 51%) and depression (11% v 7%).<sup>26</sup>

Zaorsky et al.<sup>27</sup> assessed the impact of testicular cancer diagnosis on suicidal death in a SEER dataset pooling data from 1973 to 2014. For testicular cancer patients, the standardized mortality ratio (SMR) for suicide compared to the general population was 6 when assessing follow-up  $<1$  year after diagnosis. Notably, with increasing follow-up, unlike the majority of other cancers in this study, the SMR increased for testicular cancer patients with the SMR rising from 12 in the 1-5 years after diagnosis to 17 after  $>5$  years of follow-up. In a study using the Cancer Registry of Norway dataset that included individuals diagnosed with cancer before the age of 25 matched to cancer-free individuals, Gunnes et al.<sup>28</sup> found a significantly increased risk of suicidal death for testicular cancer patients (HR 2.9, 95% CI 1.3-6.4). Taken together, **testicular cancer patients at the population-level appear to be at increased risk of suicide for years after their initial diagnosis.**

### 3.4 Considerations for Addressing Mental Health Care

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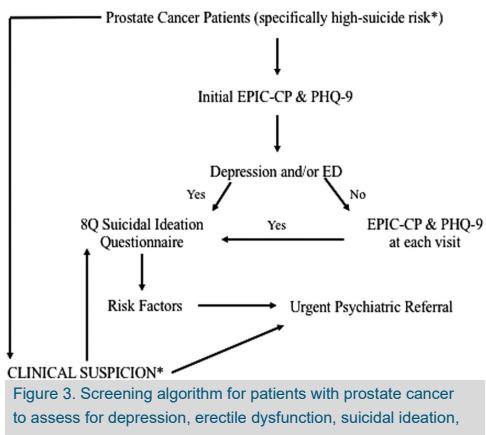
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**Figure 3. Screening algorithm for patients with prostate cancer to assess for depression, erectile dysfunction, suicidal ideation, and need for psychiatric evaluation.**

There are several ways that members of the healthcare team can screen/assess for mental health illness, as well as potentially decrease rates of suicidal death among cancer patients. **All cancer patient should be routinely screened for distress, depression, and suicidal ideation and appropriately referred for urgent psychologic/psychiatric evaluation as necessary.** The NCCN offers distress guidelines and provides a **distress thermometer tool** to identify at-risk patients.<sup>29</sup>

Among patients with prostate cancer (who are susceptible to developing long-term depression),<sup>22</sup> screening for depression, in addition to suicidal ideation has also been recommended (**Figure 3**).<sup>30</sup>

Patients with known risk factors (e.g. white ethnicity, older age, male gender, and living alone) should be offered counseling or psychiatric referral regardless of suicidal ideation, in addition to smoking cessation assistance, when necessary. **Patients with suicidal ideation should maintain a close alliance with their oncology team while also undergoing a complete psychiatric evaluation with trained mental health professionals.** Patients with advanced cancer who maintain a strong therapeutic alliance with their oncologist have better protection against suicidal ideation than those treated with other mental health interventions, including psychotropic medications.<sup>31</sup> Additionally, there is a benefit to ancillary services, such as lymphedema and stoma clinics, in assisting patients who are coping with changes in body image and psychological distress following treatment. Ultimately, prospective trials evaluating the value of suicide prevention interventions in high-risk individuals will help to further delineate the management of these patients.

#### 4. Financial Toxicity

**Financial toxicity**, defined by the National Cancer Institute as **the issues a cancer patient faces related to the cost of treatment**, may contribute to lasting effects on a patient's quality of life due to both the direct and indirect effects, potentially resulting in bankruptcy in severe cases.<sup>32</sup> In the United States, as many as 2 out of 5 cancer patients report financial hardship as a result of the costs incurred due to cancer treatment.<sup>33</sup> In spite of this, the **financial effects of cancer care are under-appreciated by physicians and often not included in patient counselling and shared decision-making process regarding treatment selection.**

**Cancer-related financial toxicity arises due to the costs borne by a patient as a result of their cancer diagnosis.** These include **direct out-of-pocket health care costs** from inpatient or outpatient facility fees, physician fees, prescription medications, laboratory or radiologic testing, as well as **indirect costs**, including loss of income due to travel or illness, parking costs, physical limitations resulting in productivity loss, need for caregiver assistance, early retirement, psychosocial costs, and others. In the context of the American health system, direct health care related out-of-pocket costs include the following categories:

1. **Copayments**: the amount that an insured patient pays for each healthcare service;
2. **Coinsurance**: the proportion of insured healthcare costs that a patient must pay once reaching their deductible; and
3. **Deductibles**: the amount that an insured patient must pay for health care services before coverage from a health insurance plan begins.

Cancer is one of the most expensive medical conditions to treat in the United States due to the use of multiple treatment modalities, prolonged treatment and observation periods, and frequent need for hospitalization.<sup>34-35</sup> Additionally, as treatment approaches have advanced, newer treatments are almost inevitably more expensive than those they replace, resulting in a worsening of financial toxicity over time.<sup>36</sup> In the United States, patients are increasingly bearing the cost of care through high deductible insurance plans, copayments and premiums, and co-insurance fees.<sup>6</sup> Indeed, patient-borne out-of-pocket costs, totaling  $\geq \$300$  billion annually, comprise approximately 10-20% of total healthcare costs in the United States.<sup>37-38</sup>

Furthermore, the financial burden of cancer therapy may impact the entirety of a patient's financial life.<sup>39</sup> Among individuals in Washington State, cancer patients were 2.65 times more likely to declare bankruptcy than people without cancer,<sup>39</sup> with higher rates among younger cancer patients (up to 2 to 5 times higher). In addition to the immediate financial implications of the costs of healthcare, time off work for cancer treatment may adversely affect patient's career advancement, an effect which disproportionately harms younger cancer patients. Additionally, due to the profound financial challenges related to cancer diagnosis and treatment, patients may face very difficult decisions including choosing between paying for healthcare costs or essentials of daily living, including rent, groceries, and other necessities, which increases the risk of **medical nonadherence**,<sup>33-40</sup> when patients allocate their limited funds to priorities other than their cancer care. Young adults diagnosed with cancer may be at particularly elevated risk of financial toxicity.<sup>39</sup> Indeed, one survey of young adults reported that 13.5% of patients reported forgoing care as a result of finances,<sup>32</sup> and this is believed to be an underestimate underscoring the importance for urologists to consider the financial effects of therapy in patients with germ cell tumors.

**Financial toxicity is associated with worse cancer-related symptoms, emotional and psychological distress, quality of life, and even overall survival.**<sup>41-42-43-44-45-46-47-48-49-50</sup> Nearly two-thirds of cancer patients report a desire to have cost-related discussions of care plans with their physicians; however, only one-third report engaging in these discussions.<sup>51</sup> Thus, it is critical that physicians engage their patients and clinical teams in considering the financial implications of cancer treatment for their patients. Financial toxicity may be mitigated through integrating financial advisors and social workers to help with disability paperwork, applications for financial aid, and informing patients of advocacy groups and foundational funding opportunities.

#### 5. Fear of Recurrence

As survival outcomes for patients with genitourinary malignancies improve, fear of cancer recurrence is becoming a more prevalent clinical problem. **Fear of cancer recurrence is defined as "fear, worry, or concern relating to the possibility that cancer will come back or progress."**<sup>52</sup> This is a concern for both patients with treated with curative intent who are at risk of disease recurrence and those with advanced or metastatic disease who are at risk of disease progression. While normal levels of fear of cancer recurrence are associated with adherence to recommended surveillance protocols, high levels of fear of cancer recurrence can negatively affect quality of life, function, and may be associated with reduced adherence to surveillance recommendations. Fear of cancer recurrence is described in prostate cancer, renal cell carcinoma, and testicular cancer patients. For example, in a large study of prostate cancer survivors, approximately one-third of patients displayed high fear of cancer recurrence.<sup>53</sup>

Additionally, this was a common problem among survivors with localized renal cell carcinoma with over 50% of patients experiencing moderate to severe distress and fear of cancer recurrence.<sup>54</sup>

Awareness of fear of cancer recurrence as a clinical dilemma is important in developing strategies to proactively manage this condition. Clinicians, advanced practice providers, social workers and other members of the multidisciplinary team can play an important role in recognizing severe fear of cancer recurrence and implementing effective intervention strategies to improve outcomes for patients.

**Providing adequate information about prognosis, signs and symptoms of recurrence, recommended behaviors to reduce risk, and monitoring schedules are effective methods to dispel misinformation about recurrence. Additionally, normalizing feelings, encouraging patients to disclose concerns, and making appropriate referrals when needed are additional approaches to lower the risk of developing chronic, severe, fear of cancer recurrence.**

#### 6. Health Related Quality of Life and Patient Reported Outcome Measures (PROMs)

Patient reported outcomes (PROs) are data collected directly from patients at a particular point in time without modification by clinicians or researchers.<sup>55</sup> They are often utilized to assess health-related quality of life, functional status, cognitive function, pain, fatigue, depression, anxiety, satisfaction, medication adherence, and other parameters. Direct reporting of the patient experience is important in optimizing treatment strategies given variability in clinician and patient assessment of symptoms and quality of life.<sup>56</sup>

While efforts to standardize the use of PROs in clinical trials are underway, there remains considerable variability in the collection and reporting of PRO data. Various consortia and guidelines panels including PROTEUS (PRO tools: engaging users and stakeholders), SPIRIT (Standard Protocol Items: Recommendations for Interventional Trials), and CONSORT (Consolidated Standards of Reporting

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Trials) PRO have been developed to provide guidance for integrating PROs in clinical trials. A systematic review of 33 phase 2-3 clinical trials of immune checkpoint inhibitors in predominately melanoma, lung, and renal cell carcinoma, reported considerable heterogeneity in the quality of reporting of PROs<sup>7</sup>

Multiple tools, termed **Patient Reported Outcome Measures (PROMs)** are currently used to assess overall health-related quality of life (HRQOL) for patients with genitourinary malignancies. ([Table 1](#)).

**Table 1. PROMs assessing health-related quality of life in clinical trials of genitourinary malignancies.**

Instrument	Items	Focus
General Cancer		
Functional Assessment of Cancer Therapy—General (FACT-G)	27	Assess four domains of HRQOL in cancer patients: Physical, social, emotional, and functional well-being
European Organization for Research and Treatment of Cancer (EORTC) Quality of Life Questionnaire—Core 30 (QLQ-C30)	30	Assess physical, psychological and social functions
Prostate Cancer		
Functional Assessment of Cancer Therapy—Prostate (FACT-P)	39	For all patients with prostate cancer
European Organization for Research and Treatment of Cancer (EORTC) Quality of Life Questionnaire (QLQ)-PR25	25	For all patients with prostate cancer
Prostate Cancer Specific Quality of Life Instrument (PROSQOLI)	9	For patients with advanced prostate cancer
Quality of life module for advanced prostate cancer (QLM-P14)	14	For patients with advanced prostate cancer
Expanded Prostate Cancer Index Composite (EPIC)/EPIC-26	32/26	For patients with localized prostate cancer (urinary, bowel, and sexual symptoms)
University of California Los Angeles—Prostate Cancer Index (UCLA-PCI)	20	For patient with localized prostate cancer (urinary, bowel, and sexual symptoms)
Patient-Oriented Prostate Utility Scale (PORPUS)	10	For patient with localized prostate cancer (urinary, bowel, and sexual symptoms)
Prostate Cancer Quality of Life Instrument (PC-QoL)	11	For patient with localized prostate cancer (urinary, bowel, and sexual symptoms)
Bladder Cancer		
European Organization for Research and Treatment of Cancer Quality of Life Core Questionnaire—Bladder Cancer Superficial (EORTC-QLQ-NMIBC24)	24	For patients with non-muscle invasive bladder cancer
European Organization for Research and Treatment of Cancer Quality of Life Core Questionnaire—Bladder Cancer Muscle Invasive (EORTC-QLQ-BLM30)	30	For patients with muscle invasive bladder cancer
Functional Assessment of Cancer Therapy—Bladder Cystectomy (FACT-BI-Cys)	44	For patients undergoing radical cystectomy and urinary diversion
Functional Assessment of Cancer Therapy—Bladder (FACT-BI)	39	All stages of bladder cancer
Bladder Cancer Index (BCI)	34	All stages of bladder cancer
Kidney Cancer		
Functional Assessment of Cancer Therapy—Kidney Symptom Index (FKSI)	Varies	For metastatic disease; Assess physician and emotional disease-related symptoms, treatment side effects, function
Renal Cell Carcinoma—Symptom Index (RCC-SI)	30	For localized and metastatic disease
Testicular Cancer		
European Organization for Research and Treatment of Cancer Quality of Life Core Questionnaire—Testicular Cancer (EORTC QLQ-TC26)	26	Testicular cancer with or without relapse
Cancer Assessment for Young Adults—Testicular (CAYA-T)	90	Any testicular cancer diagnosis

Additionally, the PRO-Common Terminology Criteria for Adverse Events (CTCAE) is a PRO measurement system developed to evaluate symptomatic toxicity in patients on clinical trials. This tool was designed as a companion to standard clinician reporting of adverse events. While the National Cancer Institute recommends EPIC-26 for NCI-sponsored clinical trials for localized prostate cancer,<sup>58-59</sup> consensus guidelines on choice of instrument across other prostate cancer disease states and genitourinary malignancies are lacking.

Innovative strategies to enhance PRO integration, reporting, and analysis are critically important as the resultant data provides key information that can inform counseling patients regarding treatment decisions. This is particularly helpful for shared decision-making in settings where multiple treatments are available with comparable efficacy. A model clinical trial incorporating PROs is the IRONMAN registry (NCT03151629), an international, prospective, population-based study that collects disease related and QOL data of patients receiving standard of care therapies for metastatic prostate cancer.<sup>60</sup> In addition to collecting clinical outcomes, epidemiological data, and biospecimens, the study is collecting PROs with a focus on inclusion of minority populations to bridge the disparities gap in prostate cancer care.

## 7. Nutrition and Cancer Survivorship

Malnutrition is common among cancer survivors, resulting from the impact of the tumor itself (e.g. obstruction causing early satiety, paraneoplastic syndromes resulting in anorexia or cancer cachexia), as well as due to effects from surgical and medical treatments. The severity of malnutrition can range from minor, sub-clinical manifestations to severe, with an estimated 10 to 20% of cancer patients dying as a result of malnutrition itself. However, unfortunately, cancer-related malnutrition remains largely underestimated and unrecognized in clinical practice.

Since 2017, the European Society for Clinical Nutrition and Metabolism (ESPEN) guidelines on nutrition in cancer patients<sup>61</sup> have provided the foremost guidance on nutrition among cancer survivors. These guidelines note that it is important to detect nutritional disturbances at an early stage and to regularly evaluate nutritional intake, weight change, and body mass index, beginning with the cancer diagnosis, and repeated depending on the clinical situation. Specific to genitourinary malignancies and their general treatment modalities, clinicians should be aware of recommendations for patients undergoing surgery, radiotherapy, and systemic therapy under the care of medical oncology.<sup>62</sup>

Given the importance of malnutrition among cancer survivors, and the relative paucity of awareness among patients with genitourinary malignancies, particularly those undergoing radical cystectomy or systemic therapy, the ESPEN recommendations should provide a basis for incorporating this important aspect of survivorship into clinical practice.

## 8. Genitourinary Cancer Site Specific Survivorship Considerations

While there are general survivorship principles that may apply to all patients with genitourinary cancers, as described above, there are unique issues resulting from both the cancer itself and the consequences of treatment for each tumor site. These will be outlined in the following sections.

### 8.1 Prostate

#### 8.1.1 Localized Prostate Cancer and Treatment Toxicities

Definitive therapies for localized prostate cancer can impact sexual, urinary, and bowel function, with significant implications for survivorship. This is especially relevant for localized prostate cancer given the high probability of long-term survival following treatment.<sup>63-64</sup> For these reasons, a thorough and balanced discussion of the risks of surgical and radiation-based interventions is an important component of shared decision-making around treatment—especially for men who are healthy enough to undergo all of the available therapies. Several high-quality studies have been conducted that have assessed patient reported outcomes around the treatment of localized prostate cancer, which include CEASAR, the ProtecT trial, and the PROS-QA study.<sup>65-66-67</sup> We will focus on these three studies recognizing that there are other randomized control trials and cohort studies that confirm the findings of these studies.

Also see: AUA Core Curriculum **Prostate Cancer Localized and Locally Advanced Treatment**.

##### 8.1.1.1 Urinary function:

Men may experience a variety of urinary symptoms following definitive treatment for localized prostate cancer, including urinary incontinence, irritative urinary symptoms, and obstructive urinary symptoms. These side effects vary based on treatment modality and timing from the intervention. For instance, urinary incontinence is commonly experienced by men immediately following surgery, with the most severe effects within the first 6-months after surgery. Conversely, men undergoing radiation therapy more commonly report experiencing irritative urinary symptoms during the course of radiation therapy with improvement following treatment completion, followed by a risk of subsequent long-term bladder outlet obstruction or incontinence.

The percentage of men reporting significant urinary incontinence following radiation therapy ranges from 2% to 7% at 2-3 years following treatment.<sup>66-67-68</sup> Roughly 10% of men treated by primary brachytherapy reported leaking more than once a day at 3-years following treatment in PROS-QA.<sup>67</sup> Irritative urinary symptoms such as bladder overactivity characterized by urgency or frequency are much more common with radiation therapy, with 34-45% men reporting urinary frequency 2 months following radiation treatments.<sup>67</sup> Among men undergoing brachytherapy, 24% reported dysuria 2-months following treatment.<sup>67</sup> These urinary symptoms improve at 12 months and approach baseline function.<sup>67</sup> Obstructive urinary symptoms (i.e., weak stream) were reported in 23% and 40% of external beam radiation and brachytherapy patients, respectively, at 2-months after treatment, but decreased to roughly 10% in both treatment groups at 24-months.<sup>67</sup>

Irritative urinary symptoms were less frequent among surgical patients, with dysuria being reported in 7% and 1% of men at 2- and 12-months following treatment.<sup>67</sup> However urinary incontinence is much more common following surgery with 67%<sup>67</sup> and 34-46%<sup>66-67</sup> of men requiring at least 1 pad per day for urinary leakage at 2- and 6-months, respectively. Incontinence generally improves over time, but up to 10-21% of surgical reports suggest bothersome urinary incontinence 2 or more years following surgery.<sup>65-66-67</sup> The risk of incontinence varies by surgical approach (i.e., nerve-sparing) and disease risk group.<sup>65</sup>

Additional urinary symptoms associated with radiation therapy to the prostate include **hemorrhagic cystitis**, which can occur early or late following treatment.<sup>69</sup> There is also a small absolute increased risk (2-4%) of **secondary malignancies** including bladder and colorectal cancer following radiation treatment for prostate cancer.<sup>70</sup> Finally, men may experience **climacteria—urinary incontinence with orgasm**—which may additionally impact quality of life following treatment.<sup>69</sup>

##### 8.1.1.2 Sexual function:

**Erectile dysfunction is a common side effect of localized treatment for prostate cancer.** Studies demonstrate that over half of men undergoing radiation therapy develop worsening erectile dysfunction, with several studies demonstrating that **61-66% of men are unable to achieve erections firm enough for sexual activity 2-years following radiation therapy**.<sup>66</sup> Immediately following radical prostatectomy, 90% of men report erectile function that is not satisfactory for penetrative sexual intercourse.<sup>67</sup> With longer follow-up, roughly 60-80% of men report some form of erectile dysfunction following surgery. These rates are dependent on baseline erectile function and nerve-sparing at the time of prostatectomy—with nerve-sparing reducing the reported rates of erectile dysfunction decreases to roughly 50% with longer-term follow-up.<sup>65</sup> Erectile dysfunction following localized treatment is common and is a function of baseline erectile function, competing comorbid conditions, psychologic health, and technical considerations at the time of treatment.

##### 8.1.1.3 Bowel function:

Radiation treatment is associated with bowel toxicities such as diarrhea and fecal urgency. These side effects are reported in 10-15% of men who undergo radiation treatment. Innovations in radiation therapy (i.e., intensity-modulated radiotherapy)<sup>71</sup> and technologies such as the SpaceOAR hydrogel,<sup>72</sup> have significantly reduced radiation toxicity to the bowel. Bowel function may be affected in the short-term following radical prostatectomy, but longer-term side effects of the bowel are less common.

When compared to definitive therapy, a strategy of **active surveillance is associated with superior urinary, sexual, and bowel functional outcomes**.<sup>66-68</sup> These data demonstrate the importance of considering surveillance in appropriately identified men with favorable risk disease due to a low risk of adverse oncologic outcomes and the benefit of avoiding the short-, intermediate-, and long-term side effects of definitive treatment.

#### 8.1.2 Androgen Deprivation and Common Side Effects

Although it is associated with improving oncologic outcomes in specific settings, treatment with ADT also induces a constellation of side effects that can negatively impact patient quality of life, increasing morbidity and mortality related to non-cancer medical complications. **The most commonly patient-reported side effects include hot flashes, sexual dysfunction, gynecomastia, breast tenderness, fatigue, depression and other mood effects, cognitive decline, and changes in body habitus (i.e., weight gain).** Medical complications include the loss of bone mineral density and increased risk of osteoporosis and fracture, acceleration of muscle loss/development of sarcopenia, hyperlipidemia and cardiovascular disease, insulin insensitivity and diabetes, and anemia.

ADT causes a decline in bone mineral density, with prolonged exposure inducing ongoing loss that can result in osteopenia or osteoporosis. Due to this, ADT exposure is associated with an increased risk of fractures. The risk of developing osteoporosis or fracture increases with duration of treatment, with as little as 6-12 months inducing measurable bone loss and longer durations significantly increasing the risk of fracture.<sup>73-74-75</sup> Managing this risk requires frequent DXA scan and supplementation with Calcium and vitamin D.

Vasomotor symptoms or “hot flashes” are reported in 50-80% of men receiving ADT, although many men choose to defer pharmacologic treatment unless they cause significant bother.<sup>76</sup>

Sexual dysfunction is also common with over 80% and 95% of men on ADT noting erectile dysfunction and loss of libido, respectively.<sup>77</sup> Androgen deprivation is also associated with weight gain, muscle loss, and increased adiposity, with a 2-4% weight gain following one year of treatment.<sup>78</sup> These complications may contribute to the development of cardiovascular complications, insulin insensitivity, and diabetes.

See the AUA Core Curriculum **Prostate Cancer: Advanced and Metastatic Disease**.

### 8.1.3 Causes of Death Among Prostate Cancer Survivors

Given the >3 million prostate cancer survivors, it is important to understand causes of mortality among these patients in order to focus on specific points relevant to a survivorship care plan in this population. Among 752,092 men with prostate cancer diagnosed between 2000-2016, Weiner et al<sup>89</sup> reported that 200,302 (27%) died. Overall, 29,048 men with local/regional disease (17%) died of prostate cancer, whereas 83% died of other causes, most commonly cardiovascular-related causes of mortality (23%; SMR 0.76, 95% CI 0.75-0.77). Among men with metastatic prostate cancer, the majority of deaths were secondary to prostate cancer (74%), however cardiac-related death (SMR 1.48, 95% CI 1.41-1.54) and suicide (SMR 2.32, 95% CI 1.78-2.96) were the most common causes of non-cancer related death.

## 8.2 Bladder Cancer Survivorship Considerations

See **Treatment of Non-Metastatic Muscle-Invasive Bladder Cancer: AUA/ASCO/ASTRO/SUO Guideline (2020)** and AUA Core Curriculum **Bladder Neoplasms: Muscle Invasive Bladder Cancer**.

### 8.2.1 Body Image

Patients undergoing radical cystectomy with an ileal conduit urinary diversion not only face a potentially long recovery after surgery with significant risk of complications, readmission, and death, but also must adapt to a new body image. Qualitative studies have suggested that patients and care-givers adapting to a stoma after surgery often have poor psychological preparation for surgery, with limited preoperative hands-on training on stoma care and utility of stomal appliance<sup>90</sup>.

In appropriately selected patients, a continent urinary diversion (ie. neobladder) obviates the need for a stoma and potentially may improve quality of life. In a study from the University of Michigan, Hedgepeth et al<sup>91</sup> assessed urinary, bowel, and sexual outcomes using the Bladder Cancer Index, and body image was evaluated using the EORTC Body Image Scale at baseline, 1 month, 6 months, and 1, 2, 4, 6, and 8 years after treatment. The study compared 112 patients who underwent cystoscopy to 139 patients who underwent a neobladder and 85 patients who received an ileal conduit. This study found that **after cystectomy, both conduit and neobladder groups had worse body image scores that improved over time, but did not return to baseline in either urinary diversion group**. In a systematic review of 29 studies (3,754 patients), Yang et al<sup>92</sup> assessed quality of life aspects of continent and incontinent urinary diversion. Qualitative analysis suggested that patients undergoing a neobladder had superior emotional function and body image compared to cutaneous diversion. Interestingly, in a European study of patients undergoing radical cystectomy, family, relationships, health, and finance, were the most important determinants of quality of life, whereas body image was not mentioned by any patients<sup>93</sup>.

**Appropriate ostomy teaching pre- and post-operatively is important to patient recovery and decreasing patient anxiety in the immediate recovery period. Outpatient and inpatient ostomy nursing**, if available, can alleviate anxiety related to a patient's new body image as well as reduce frustrations with stoma fitting, urinary leakage, skin breakdown; which represent important aspect that we see in our clinical practices but which are poorly described in the literature. In addition to added patient stress, ostomy complications can be a source of considerable distress to patient care givers and may increase health care utilization for patients (e.g. clinic and emergency room visits).

### 8.2.2 Nutrition

Patients undergoing radical cystectomy have a high burden of comorbidity in addition to being at risk of malnutrition given the often advanced age and medical complexity of patients undergoing this procedure. The **prevalence of malnutrition among cystectomy patients is estimated to be 16-22%**, with a consistent association demonstrated between malnourishment and adverse post-operative outcomes.<sup>84</sup> Recent work has also assessed the interaction of obesity and malnutrition among patients undergoing radical cystectomy. Arora et al<sup>85</sup> used the American College of Surgeons National Surgical Quality Improvement Program database to identify 2,055 patients who underwent radical cystectomy to assess the association between hypoalbuminemia (<3.5 g/dL), >10% preoperative weight loss, obesity (as characterized by BMI class I: 30-34.9, II: 35-39.9, III: ≥40 kg/m<sup>2</sup>), and 30-day complications and mortality. Hypoalbuminemia and >10% weight loss was present in 16.7% and 3.5%, respectively, and among obese patients 13.4% had hypoalbuminemia. On multivariable analysis, class I-III obesity (OR 1.43 to 2.32) and hypoalbuminemia (OR 1.47, p = 0.02) were significantly associated with 30-day complications. Furthermore, class III obesity (OR 2.96, p = 0.02) and hypoalbuminemia (OR 2.33, p = 0.03) were independently associated with 30-day mortality. It is important to note that obese patients, particularly those with recent weight loss, are at risk for concomitant malnutrition. **All patients should be assessed for malnutrition and be counseled about nutritional optimization prior to radical cystectomy**.

**Preoperative immunonutritional supplementation** has recently been reported in literature and has potential to improve nutritional status and post-radical cystectomy outcomes. Khaleel et al.<sup>86</sup> retrospectively assessed 204 patients undergoing radical cystectomy, of which 104 (51%) received preoperative immunonutritional supplementation with an oral L-arginine-based supplement. Patients who received preoperative immunonutritional supplementation had significantly lower odds of requiring postoperative total parenteral nutrition (17.3% vs 35.6%; p=0.015) and developing postoperative infection (25% vs 45%; p=0.003) but no significant difference in the rates of other outcomes. Preoperative immunonutritional supplementation has been extensively investigated in the gastrointestinal oncologic literature, which suggests that a 5-7 day supplementation regimen is optimal<sup>87</sup>. An ongoing large double-blinded Phase III Cooperative Group Trial (SWOG 1600) seeks to evaluate the impact of a perioperative immune nutrition supplement (5-days before and after radical cystectomy) on 30- and 90-day postoperative complications and infections, patient-reported health-related quality of life, body composition, oncologic outcomes and performance status up to 3-years following surgery.

## 8.3 Renal Cell Carcinoma Survivorship Considerations

See **AUA Guideline Renal Mass and Localized Renal Cancer** and AUA Core Curriculum **Renal Neoplasms**.

### 8.3.1 Considerations for localized disease

Nephrectomy is the gold standard treatment for localized renal cell carcinoma. Radical nephrectomy is the preferred surgical approach for stage 2 and greater renal tumors, with partial nephrectomy generally favored for patients with pre-existing renal conditions, a solitary kidney, or bilateral renal tumors and preferred for cT1 tumors if feasible.<sup>88</sup> The management of small, localized renal masses has evolved substantially over time. Over the last several decades, the negative impact of radical nephrectomy for small renal masses has come to light given that 1) a subset of renal tumors are benign or indolent in nature, 2) numerous retrospective and observational studies demonstrate that oncologic outcomes of partial nephrectomy are comparable to radical nephrectomy, and 3) partial nephrectomy has prevented or delayed the onset of chronic kidney disease and cardiovascular morbidity.<sup>89</sup> To this point, in 2009, the American Urologic Association published guidelines recommending partial nephrectomy as a standard of care option for T1a renal cell carcinoma and a viable option for T1b tumors.<sup>90</sup>

Risk factors for development of de novo chronic kidney disease or acceleration of existing chronic kidney disease after nephrectomy for renal cell carcinoma are delineated in **Table 2**.<sup>91</sup>

**Table 2. Risk factors for chronic kidney disease development after nephrectomy for renal cell carcinoma.**

Risk Category	Risk Factor
Nephron loss	Solitary kidney Radical nephrectomy
Surgical conditions	Perioperative events Surgical technique
Demographics	Age Ethnicity
Environmental factors	Smoking Diet (high protein, high salt)
Genetic factors	<i>APOL1</i> gene mutation
Comorbid conditions	Obesity Metabolic syndrome Diabetes mellitus Hypertension Cardiovascular disease
Pre-existing renal conditions	Microalbuminuria Proteinuria Low glomerular filtration rate Glomerular and interstitial renal disease Pre-renal states Obstruction conditions History of acute kidney injury
Other factors	Nonmalignant tissue histology

**Risk stratification prior to nephrectomy is critical to ensuring patients achieve optimal functional renal outcomes.** Several models have been developed to aid in risk stratification and prediction of chronic kidney disease following nephrectomy. The Screening for Occult Renal Disease (SCORED) tool uses factors including age, gender, presence of anemia, proteinuria, and cardiovascular disease to predict risk of chronic kidney disease development.<sup>92</sup> Additionally, Sorbellini and colleagues developed a nomogram which incorporates change in kidney volume to predict the risk of renal insufficiency following partial or radical nephrectomy.<sup>93</sup>

Strategies to preserve renal function post nephrectomy are multifactorial. **Monitoring renal function via assessment of creatinine and glomerular filtration rate, proteinuria, and blood pressure is important for survivors' following nephrectomy.** Dietary and lifestyle modifications are the foundation of kidney preserving care. This includes a plant-based diet, low sodium intake, routine physical activity, weight loss, and smoking cessation.<sup>94</sup> Additionally, for patients with chronic kidney disease, pharmacologic agents can be used to slow disease progression, such as renin-angiotensin-aldosterone system blockade, and reduce cardiovascular risk, such as lipid-lowering, blood pressure-lowering, and glucose-lowering treatments.<sup>94</sup> Prevention of acute kidney injury and infection are also important. Ultimately, optimized survivorship care necessitates awareness of the potential renal and cardiovascular risk post nephrectomy and developing strategies to prevent and minimize risk is critical to improving long-term outcomes for patients.

Additionally, now there are significant complexities regarding the use of adjuvant immunotherapy post-resection. Data are still maturing but adjuvant Pembrolizumab has demonstrated prolonged disease-free survival<sup>95</sup> in patients with localized high risk clear cell renal cell carcinoma. Thus, patients now must weigh the options of continued surveillance versus further treatment with the attendant risks associated with immunotherapy following surgery. This adds additional layer of psychosocial complexities in caring for patients with localized disease.

### 8.3.2 Considerations of advanced/metastatic disease

Treatment options for patients with advanced or metastatic renal cell carcinoma have rapidly expanded over the past several years. While vascular endothelial growth factor (VEGF) tyrosine kinase inhibitors were historically the frontline standard treatment for patients, immunotherapy combinations have emerged as the new standard for patients with newly diagnosed metastatic disease. Combination of nivolumab + ipilimumab (CheckMate-214)<sup>96</sup> pembrolizumab + axitinib (Keynote-426),<sup>97</sup> nivolumab + cabozantinib (CheckMate-9ER),<sup>98</sup> and pembrolizumab + lenvatinib (CLEAR)<sup>99</sup> have all improved objective response rate, progression-free survival, and overall survival for patients with clear cell renal cell carcinoma. Given the numerous frontline options, all with established efficacy, it is becoming increasingly difficult to select the optimal regimen for a given patient. The impact of these regimens on safety, tolerability, and quality of life is becoming more important in treatment selection. All these studies embedded prospective quality of life evaluation, however the instruments utilized and time points assessed were variable across the studies. While cross-trial comparisons are not possible, in aggregate, health-related quality of life was comparable between the intervention and control arms in the Keynote-426 and Clear<sup>100</sup> trials and improved between the intervention and control arms in the CheckMate-214<sup>101</sup> and CheckMate-9ER trials<sup>98</sup> (**Table 3**).

**Table 3. Health-related quality of life assessments in frontline line immunotherapy combination studies in advanced or metastatic clear cell renal cell carcinoma. Upward arrow indicates relative improvement over control; downward error indicates relative decline over control; equal sign indicates similarity to control.**

It is worth highlighting the subset of patients with bone metastases, which comprises 30% of individuals with advanced disease. Patients with bone metastases are particularly susceptible to disease-related increased morbidity and at risk of symptomatic skeletal events including pain to the bone requiring radiation, symptomatic pathologic fracture, symptomatic bone metastases requiring surgical intervention, and symptomatic spinal cord compression. Additionally, multiple series have demonstrated that the presence of bone metastases is associated with inferior survival outcomes compared to patients without bone metastases.<sup>102-103</sup> Management of bone metastases requires multidisciplinary care between medical oncology, radiation oncology, orthopedics, palliative care, and other disciplines to improve symptoms and quality of life for patients. Use of osteoclast targeted therapies including zoledronic acid<sup>104</sup> and denosumab<sup>105</sup> can help decrease the frequency of symptomatic skeletal events. Additionally, novel therapies are being investigated to improve outcomes for these patients. The Radical trial (Alliance A031801; NCT04071223 is a phase II randomized, open-label, multicenter study investigating the cabozantinib with or without radium-223 dichloride in patients with renal cell carcinoma and bone metastases.<sup>106</sup> The primary endpoint is symptomatic skeletal event-free survival and the trial is currently accruing patients. Additional strategies are warranted to improve quality of life outcomes for this susceptible patient population.

### 8.3.3 Causes of death during renal cell carcinoma survivorship

Similar to the aforementioned causes of death among prostate cancer survivors, it is important to understand causes of mortality among survivors of renal cell carcinoma. Among 106,118 patients with RCC, Yu et al<sup>107</sup> observed that 39,630 (27%) patients died. For patients with stage I/II disease, 23.1% died of RCC, while 20.1% of patients died of heart disease. Among stage IV patients, most patients (95%) died within 5 years of diagnosis. While RCC was the leading cause of death (85.7%) in this subgroup, these patients also had a higher risk of noncancer death compared to the general population (SMR 2.24, 95% CI 2.11-2.38).

## 8.4 Testis Cancer Survivorship Considerations

Survivorship in testicular cancer presents unique considerations given the age of disease onset (age 20-30 years) and the high rate of treatment success—even in the advanced setting. Consequently, treatment toxicities and quality of life are important considerations for young men diagnosed with testicular cancers. Exposure to treatment toxicities is a function of the disease stage at presentation and the need for adjuvant/salvage therapies.

### 8.4.1 Long-Term Toxicities of Treatment

The most significant long-term toxicities of treatment are related to chemotherapy, and notably include cardiac toxicity, ototoxicity, peripheral neuropathy, Raynaud phenomenon, pulmonary and renal impairment, and secondary cancers. The relative risk of cardiovascular disease in testis cancer patients who have received chemotherapy ranges from 1.4 to 7-fold higher than the general public or patient who did not receive chemotherapy.<sup>108-109</sup> This correlates with increased risk of coronary artery disease, hypertension, and diabetes.<sup>25</sup> Nearly 20% of testis cancer patients receiving chemotherapy report severe hearing loss<sup>110</sup> and 20-30% of patients report peripheral neuropathy.<sup>111-112</sup> The risk of developing hematologic malignancies and other solid organ malignancies is increased in testis cancer patients, and is correlated with receipt of both chemotherapy and radiation therapy.<sup>25</sup>

### 8.4.2 Fertility and Testis Cancer Treatment

Men with stage 1 disease are at risk for hypo- or infertility related to impaired spermatogenesis, orchectomy, adjuvant chemotherapy or radiotherapy, or salvage chemotherapy in the setting of recurrence.<sup>25</sup> At diagnosis, and prior to the initiation of any therapies, men should be counseled on the importance of sperm banking and semen analysis. This can be a means of preserving fertility for men undergoing testis cancer treatment and is important to proactively offer as a combination of young age and oncologic concern may lead these young men to neglect considerations regarding future fertility. Furthermore, surgical management of retroperitoneal metastasis can result in ejaculatory dysfunction due to injury to the hypogastric plexus.

Cisplatin chemotherapy is also associated with infertility.<sup>112</sup> Successful paternity following chemotherapy has been shown to decrease with the number of treatment cycles;<sup>113</sup> however, the 15-year cumulative incidence of successful paternity was approximately 50% and 60% for men receiving a total cisplatin dose > 850mg and < 850 mg, respectively.<sup>114</sup>

### 8.4.3 Hypogonadism Following Therapy

It is estimated that roughly 40% of men treated for testicular cancer experience hypogonadism.<sup>25</sup> Hypogonadism is associated with increased risk of metabolic syndrome, cardiovascular disease, depression, cognitive dysfunction, poor bone health, sexual dysfunction, muscle loss, and infertility. The factors driving hypogonadism likely include orchectomy, radiation therapy, chemotherapy, and testicular dysgenesis, and is likely worsened by the intensity of treatment needed.<sup>25</sup> Testosterone levels should be assessed on a symptomatic basis, with testosterone replacement commenced and managed as per the [AUA Testosterone Deficiency Guidelines](#).

## 9. Summary

Cancer survivorship plans should be established for all genitourinary cancer survivors and specified to their post-treatment recovery needs.

- Mental health is a critical aspect of cancer survivorship plans and is particularly important among bladder cancer and testicular cancer patients (highlighting the necessity for long-term surveillance).
- Financial toxicity, even among insured patients, has a detrimental impact on a cancer patient's quality of life, and should be screened for and addressed by oncology providers. Additionally, fear of recurrence has an impact on a cancer survivor's quality of life, and should be evaluated for and addressed by clinicians throughout survivorship.
- To assist clinicians with assessing for needs during cancer follow-up, there are many PROMs to evaluate patient QoL, many of which are disease-specific.

Finally, there are many disease-specific considerations that must be contemplated. Prostate cancer patients with localized disease treated with curative intent often have side effects of treatment, such as sexual, urinary, and bowel side effects, whereas those with more advanced disease treated with ADT must deal with many cumbersome side effects and potential long-term medical complications. Bladder cancer patients undergoing cystectomy must adapt to a new body image, particularly those undergoing urinary diversion with an ileal conduit. Treatment of localized RCC must take into account risk of renal impairment, particularly among patients with comorbid conditions, baseline renal dysfunction, and those with solitary kidneys. Finally, testicular cancer patients have several unique survivorship challenges, including long-term toxicity of treatment, fertility, and hypogonadism.

## 10. Podcasts

[AUAUniversity Podcast Series: Episode No. 173](#)

## Presentations

[Cancer Survivorship Presentation I](#)

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