HHS Public Access

Author manuscript

*Med Clin North Am*. Author manuscript; available in PMC 2018 November 01.

Published in final edited form as:

*Med Clin North Am*. 2017 November ; 101(6): 1053–1073. doi:10.1016/j.mcna.2017.06.003.

# Long Term and Latent Side Effects of Specific Cancer Types

**Nana Gegechkori, MD, PhD**[1], **Lindsay Haines, MD**[2], and **Jenny J. Lin, MD, MPH**[1]

[1]Division of General Internal Medicine, Icahn School of Medicine at Mount Sinai, New York, NY USA

[2]Department of Medicine, Icahn School of Medicine at Mount Sinai, New York, NY USA

## Synopsis

While many cancer survivors diagnosed with early-stage disease will outlive their cancer, they may continue to experience long-term and/or latent side effects due to cancer treatment. Many of these side effects are common and contribute to worse quality of life, morbidity and mortality for cancer survivors. We summarize the treatment side effects for several of the most prevalent cancers in the US.

### Keywords

cancer survivorship; side effects; cancer treatment; symptom management

## Introduction

There are currently over 15 million cancer survivors in the United States (US), and it is estimated that with improved treatment and early detection, the number of cancer survivors will increase to over 20 million by 2026.[1] Many of these survivors experience long-term and latent effects from cancer treatment. Long-term effects are side effects that arise during treatment and may persist over time, whereas latent effects may not appear until many years after treatment completion. This article summarizes the common long-term and latent treatment effects for several highly prevalent cancers.

## Breast Cancer

Breast cancer (BC) is the most common non-skin cancer among women, and there are currently >3.5 million BC survivors in the US, representing more than 40% of female cancer survivors.[1] Most women are diagnosed at early-stage, and 5-year survival rate is 89%. Risks

Corresponding author: Jenny J. Lin, MD, MPH, Division of General Internal Medicine, Icahn School of Medicine at Mount Sinai, One Gustave L. Levy Place, Box 1087, New York, NY 10029, USA; (212) 824-7537, jenny.lin@mssm.edu.
Authors' contact information: One Gustave L. Levy Place, Box 1087, New York, NY 10029 Nana. gegechkori@mountsinai.org: Lindsay.haines@mountsinai.org: Jenny.lin@mssm.edu



**Disclosures**: None of the authors have any conflicts of interest to disclose.

for developing long-term side effects after BC treatment are multifactorial and include age at the time of diagnosis, comorbidities and type, dose, and duration of treatment. Common side effects include lymphedema, cardiotoxicity, fatigue, neuropathy, cognitive dysfunction, endocrine disruptions, infertility, sexual health issues, body image concerns and mental health issues (Table 1).

## Lymphedema

Lymphedema is a common complication that occurs in approximately 20% of women following surgery or radiation.[2] Compared with isolated radiation to the breast or chest wall, regional lymph node radiation is associated with an increased risk of lymphedema (22% vs. 3%).[3] However, the severity of lymphedema varies, even among patients who receive similar treatment and can cause mild discomfort or pain to severe swelling and disfiguration and may increase risk for cellulitis.[4] Treatment of lymphedema includes lymphatic drainage massage and use of compression sleeves.

## Cardiotoxicity

Certain types of radiation and chemotherapy are associated with increased risk of developing cardiovascular complications, and some of these effects may not present until up to 20 years after cancer treatment.[5] Cardiovascular complications can include hypertension, arrhythmias, coronary artery disease, heart failure, valvular disease, thromboembolic disorders, peripheral vascular disease, stroke, pulmonary hypertension, and pericardial complications.[6] Anthracycline-induced dose-dependent cardiotoxicity has been observed in 9% of adult patients, with the highest incidence in the first year after chemotherapy completion.[7] However, there is significant variability among patients in their susceptibility to anthracyclines, and a recent study found an estimated cumulative incidence of 26% for doxorubicin-related heart failure.[8] Older age appears to be a significant risk factor for doxorubicin-related cardiotoxicity even with lower doses.[9] Furthermore, cisplatin can also increase the risk of cardiovascular events even decades after treatment completion.[10]

Studies have also shown cardiotoxicity in up to 30% of BC survivors who have received trastuzumab (for HER2+ BC).[11–15] Trastuzumab use in combination with doxorubicin leads to >7-fold increase risk of heart failure.[16] Recent studies suggest that cardiotoxicity associated with trastuzumab progressively increases during the 3–5 years after treatment completion and can persist many years.[12,17]

Radiation therapy (RT) is also associated with a variety of cardiovascular complications involving the pericardium, myocardium, valves, coronary arteries, and conduction system. Studies have identified regional perfusion defects in non-symptomatic BC survivors after RT, and the incidence and extent of perfusion defects are closely related to the volume of left ventricle included in the radiation field.[18] Incidence of radiation-induced cardiotoxicity is estimated to be 10–30% 5 to 10 years post-treatment.[19]

Lastly, BC survivors may be at higher risk for thrombus formation. A misbalance between release of von Willebrand factor and production of thrombomodulin and adenosine diphosphatase may lead to increased platelet adherence and thrombus formation in irradiated

capillaries and arteries. Adjuvant hormonal therapy (HT) with tamoxifen can also increase risk of venous thromboembolism.[20]

## Fatigue

Fatigue is the most common symptom experienced by BC survivors, with prevalence rates ranging from 15–30% to 70–99%.[21,22] Cancer-related fatigue may remain for years after treatment. Mechanisms for persistent fatigue among cancer survivors are not yet fully understood; several pathways, including chronic inflammation, autonomic imbalance, hypothalamic-pituitary-adrenal-axis dysfunction, and mitochondrial damage, may cause disruption of normal neuronal function and result in fatigue.[23] Physical activity has been shown to improve fatigue symptoms.[24]

## Neuropathy

About 58% of survivors develop chemotherapy-induced peripheral neuropathy (CIPN).[25] Docetaxel-related peripheral neuropathy can persist up to 1–3 years after treatment completion with significant impairment of quality of life.[26] At least one oncology-related neurological complication such as neuropathic pain, CIPN, phantom breast pain/syndrome and cognitive decline was found among 48% BC survivors.[27]

## Cognitive Dysfunction

Impairment of cognitive function such as problems with concentration, executive function, and memory are reported in up to 35% BC survivors after treatment completion.[28] Cognitive impairment is a multifactorial phenomenon and associated with chemotherapy, HT, and anesthesia during surgery. Age, comorbidities and genetic factors are significantly related to risk for cognitive dysfunction.[29]

## Bone Health and Musculoskeletal Issues

Almost 80% of BC survivors experience some degree of bone loss.[30] Long-term HT negatively influences bone mineral density and quality.[31,32] Treatment with aromatase inhibitors (AI) is associated with an almost 5-times higher fracture risk.[33] Current smoking, low body mass index, dementia, and corticosteroid use compound fracture risk associated with AIs.[34] Vertebral fractures unrelated to bone density have also been observed among BC survivors.[35]

BC survivors may report musculoskeletal issues after surgery, such as decreased shoulder range of motion, rotator cuff disease, adhesive capsulitis, or axillary web syndrome.[36] AIs are also associated with increased incidence of arthralgias and myalgias.[37] Treatment includes physical therapy and use of non-steroidal inflammatory agents.

## Premature Menopause and Infertility

Use of chemotherapeutic agents and adjuvant HT is linked with premature menopause and infertility.[38] Approximately 10% of BC survivors older than 45 experience chemotherapy-induced menopause, and tamoxifen use is associated with decreased fertility among premenopausal cancer survivors.[39,40] Menopausal symptoms such vasomotor hot flashes are

observed among 50–70% of tamoxifen users. Symptoms are often more severe in younger patients due to the abrupt change in hormonal status.[41]

### Sexual Dysfunction

Sexual issues such as decreased libido, arousal or lubrication, anorgasmia and dyspareunia are common complaints among BC survivors usually secondary to side effects from chemotherapy rather than RT or surgery.[42–44] Problems with sexual desire may also be related to complications of RT such as cardiac and respiratory dysfunction or skin fibrosis leading to decrease sensitivity.[45]

### Body Image Concerns

Body image changes caused by loss of a breast, lymphedema, hair loss, skin changes from RT, weight gain, or early menopause affect 31–67% of BC survivors and appear to be most relevant for younger women.[46] Sexually active survivors are more vulnerable to decreased selfesteem, poorer mental health, and difficulties in relationships with a partner due to body appearance concerns.[42]

### Mental Health Issues

Depression and anxiety symptoms affect up to a quarter of BC survivors.[47] Compared with the general female population, BC survivors have a 60% increased risk of developing depression, anxiety and stress-related disorders within 10 years after cancer diagnosis.[48] Fear of cancer recurrence affects over half of BC survivors and may increase risk for developing mental health problems.[49] Screening survivors for distress, depression and/or anxiety is important to allow clinicians to treat and/or refer survivors appropriately.

## Colorectal Cancer

Colorectal cancer (CRC) is the third most common cancer diagnosed in the US and there are currently over 1.4 million CRC survivors.[1,50] Due to screening efforts, many patients are diagnosed at early stage and the overall 5-year survival rate is 65% (and 90% for those diagnosed at early-stage). The most common treatment is surgical resection, with additional systemic chemotherapy and/or RT used either in the neoadjuvant or adjuvant setting for more advanced-stage CRC. Long-term and latent side effects for CRC survivors include bowel, bladder or sexual dysfunction, complications related to an ostomy, peripheral neuropathy, and mental health issues (Table 2).[51]

### Bowel dysfunction

RT is linked to considerable bowel and anorectal side effects such as bowel frequency, urgency, fecal incontinence, radiation proctitis and perianal irritation. Approximately half of CRC survivors have chronic diarrhea, and RT remains an independent risk factor for long-term fecal incontinence.[52–54] Patients who undergo lower anterior resection, as well as those undergoing sphincter-saving surgery, are also more likely to experience bowel dysfunction.[55] Severe bowel dysfunction may also be associated with urinary dysfunction and negatively affects sexual function or satisfaction with sex life.[56]

### Bladder dysfunction

Bladder dysfunction may present as various complaints. Damage to the sacral splanchnic nerves can cause detrusor denervation leading to decreased sensitivity of the bladder. Preoperative RT is also associated with increased risk of difficulty with urinary voiding.[56] Primary symptoms are difficulties with bladder emptying, overflow incontinence, and loss of bladder fullness sensation. Long-term incontinence and/or difficulty in bladder emptying occur in approximately one-third of CRC survivors, although others have reported urinary urgency and urge- or stress-related incontinence in up to three-quarters of CRC survivors.[56,57]

### Sexual dysfunction

Treatment-related sexual dysfunction has been reported in over a third of CRC survivors.[57–60] Sacral plexus damage that can occur with surgery such as abdominal perineal resection (APR) is associated with erectile dysfunction and painful intercourse.[53,61] Sexual dysfunction is reported in up to two-thirds of CRC survivors and may be due to lack of libido, erectile dysfunction or ejaculatory problems in men, vaginal dryness in women, and dyspareunia.[56] Risk factors leading to sexual dysfunction include autonomic nerve damage, presence of a stoma, anastomotic leak, or preoperative radiation, the presence of a stoma, and perioperative blood loss.[59]

### Ostomy/stoma-related complications

Approximately 10% of patients undergoing sphincter-saving resections have a temporary ileostomy.[62] Complications associated with ostomies include peristomal skin irritation, leakage, odor, noise from the appliance, emotional and social distress. The presence of an ostomy may also impact CRC survivors' relationships and with sexual intimacy.[63]

### Neuropathy

CIPN is a potential long-term effect of oxaliplatin, which is often used to treat advanced CRC. Some studies report that about 77% cancer survivors experience oxaliplatin-induced grade 2 peripheral neuropathy.[64] Mostly large sensory nerves are affected leading to various types of paresthesias. Symptoms are partially reversible for the majority of patients, although less than 40% recover completely.[65]

### Cognitive dysfunction

Cognitive impairment has been found to range from from 36% to 52% among CRC survivors. The main cognitive domains affecting CRC survivors include processing speed, verbal memory, and attention/working memory.[66] Adjuvant chemotherapy may increase cognitive dysfunction in CRC survivors, although the majority will improve after treatment completion.[67]

### Other Treatment Effects

Up to a quarter of CRC survivors may experience chronic pain as a direct result of the cancer or treatment, thus dramatically influencing survivors' recovery and rehabilitation.[68] Radiotherapy may also increase fracture risk, particularly for pelvic fractures.[69] Lastly,

incidence of 5-fluorouracil (5FU)-associated cardiotoxicity can occur in up to 68% of CRC CRC survivors[70] and may include angina-like chest pain, myocardial infarction, arrhythmias, heart failure, cardiogenic shock and sudden death. A previous history of coronary artery disease and mediastinal radiotherapy are significantly associated with post-treatment cardiotoxicity.[71–73]

## Head and Neck Cancer

Head and neck cancer (HNC) survivors make up approximately 3% of the cancer survivor population.[1] Advances in ENT surgical techniques have improved survival in this population, and for those with early stage disease, it is estimated that about 80–90% will undergo full remission.[74] Many undergo multimodal treatments, including surgery, RT, and chemotherapy. Common side effects in HNC survivors include musculoskeletal and neuromuscular dysfunction, upper gastrointestinal (GI) dysfunction, lymphedema, sleep apnea, speech defects, oral health issues, as well as mental health issues (Table 3).

### Musculoskeletal and Neuromuscular Dysfunction

Development of nerve palsies after head and neck surgery is common, particularly spinal accessory nerve palsy after radical neck dissection.[75] This nerve palsy causes shoulder motion dysfunction by reducing innervation to the upper and middle trapezius. One study found that upper limb dysfunction was reported to some extent in 77% of patients.[76] Those with spinal accessory nerve palsy can undergo physical therapy to strengthen the affected shoulder to improve or maintain range of motion in the joint.

Patients may experience cervical dystonia when the cervical plexus and nerve roots are damaged during surgery or when progressive fibrosis to the nerve roots and plexus occur after radiation. Cervical dystonia tends to affect the sternocleidomastoid, scalene, and trapezius muscles and is characterized by repetitive flexion and rotation of the neck and elevation of the shoulder. The cervical dystonia found in HNC survivors is often progressive but is more responsive to treatment options aimed at strengthening and stabilizing the cervical musculature. Treatment for cervical dystonia includes neuromuscular and proprioceptive retraining, myofascial release, and restoration of ROM with physical therapy. Medications such as pregabalin, gabapentin, and duloxetine have also been found to help with neuropathic pain and spasm.[77] While botulinum toxin (botox) has been approved by the FDA for treatment of cervical dystonia, there is little evidence demonstrating the efficacy of botox in patients with radiation or surgically induced cervical dystonia. Small studies, however, have demonstrated that botox can be efficacious in alleviating both spasms and neuropathic pain in this population.[78–80]

Trismus—limited jaw range of motion–is common in HNC survivors and results in difficulty with eating, speaking and oral hygiene. Trismus is seen in 28% of patients one-year post treatment with highest rates after 6 months of treatment.[81] Physical therapy can be helpful but may be inadequate. Studies of HNC survivors who underwent RT and subsequently developed trismus found that a jaw motion appliance may slow progression of trismus.[82] Pregabalin, gabapentin, and duloxetine are also helpful in treating spasms and pain associated with trismus. Pentoxifylline may improve jaw opening, and botox may reduce

pain but does not have an effect on jaw opening.[83,84] A combination of therapies should be recommended to patients with trismus to attempt to maximize quality of life.

### Upper Gastrointestinal Symptoms

Upper GI side effects, particularly dysphagia, are especially common in those who have undergone RT, affects almost 50% of HNC survivors treated for locoregionally advanced-stage disease and 7% subsequently develop esophageal or pharyngeal strictures.[85,86] In extreme cases, dysphagia can lead to chronic aspiration and recurrent infections. While dysphagia cannot be completely reversed, swallowing exercises and biofeedback can help reduce dysphagia, while esophageal dilation can help alleviate stricture. Those with chronic dysphagia, aspiration episodes, post-prandial cough, weight loss, or recurrent pneumonia should be referred to a speech pathologist for swallowing assessments. Sudden onset dysphagia should be evaluated for new or recurrent disease.

### Lymphedema

Lymphedema is a common late effect of both surgery and radiation therapy, affecting up to three-quarters of survivors.[87] Lymphedema can cause decreased neck range of motion, hearing loss, decreased quality of life, while the cosmetic changes associated with lymphedema can also cause social anxiety and depression. Manual lymphatic drainage and compression garments are the standard of care for treatment.

### Sleep Apnea

Obstructive Sleep Apnea (OSA) is a common among HNC survivors undergoing radiation and chemotherapy.[88] Both can cause tongue and laryngeal swelling that persists for years, and restricted neck motion from radiation can compromise airway positioning. Surgical reconstruction may also cause airway obstruction. OSA can lead to pulmonary hypertension, arrhythmias, and heart failure. Fatigue associated with OSA can worsen quality of life. Continuous positive airway pressure (CPAP) at night, behavioral therapy, weight loss may improve symptoms.

### Speech Alterations

Speech can be affected to varying degrees in HNC survivors, ranging from hoarseness to dysarthria.[89] Speech therapy can help improve speech. Those who have undergone a tracheostomy can use a valved voice prosthesis to improve intelligibility of speech. Those with palatal issues can have prosthetic obturators created to help improve speech.[90]

### Oral Health Issues

Oral health can often be compromised in HNC survivors. Disruption of salivary flow as well as damage to teeth from chemotherapy or emesis can put HNC survivors at increased risk of dental caries.[91] Furthermore, radiotherapy can remove the gingival attachment from teeth and increase risk of periodontitis, thus leading to tooth loss or infection. Severe cases of gingival attachment loss have resulted in osteonecrosis.[92] Xerostomia is also common due to loss of salivary gland tissue. Conscientious oral care and regular visits to the dentist can help prevent these symptoms.

### Mental Health Issues

Like all cancer survivors, HNC survivors are prone to increased risk of depression and anxiety. Unlike other cancer survivors, many HNC patients undergo surgical procedures that often dramatically change facial structure and appearance. These changes can cause avoidance of social situations, embarrassment, and shame, and providers should recognize and refer appropriate patients for counseling.

## Lung Cancer

Lung cancer (LC) is the second most common cancer diagnosed in the US, although LC survivors only comprise 3% of cancer survivors as a result of most patients being diagnosed at more advanced stage.[1] However, with increased screening for high-risk individuals, it is anticipated that there may be a stage shift so that the majority of LC will be diagnosed at early stage.[93] The 5-year survival rate for those diagnosed at early-stage is 55%. Most early-stage LC is treated with surgical resection and adjuvant chemotherapy +/− RT. Common long-term treatment side effects include impaired pulmonary function, fatigue, neuropathy, and mental health issues (Table 4).

### Impaired Pulmonary Function

Due to risk factors for LC such as heavy tobacco use, many LC survivors have decreased pulmonary function prior to diagnosis, and both surgery and RT can further reduce pulmonary function.[94] Approximately half of LC survivors have persistent dyspnea years after treatment completion.[95,96] In addition, many survivors report a chronic cough that may affect eating, sleeping and speaking.[97] Cough may also result from radiation pneumonitis in those who received RT.

### Fatigue

Fatigue is the most common side effect in LC survivors, affecting over 50% and up to 90% of survivors.[98,99] Mood disorders, comorbidities, poor functional status, sleep disturbances and decreased pulmonary function increase risk for fatigue. Moreover, fatigue symptoms often cluster with mood and sleep disorders, suggesting a possible common inflammatory pathway. While fatigue is hard to treat, physical activity and exercise may improve symptoms.[100–102] In addition, targeted therapy such as angiogenesis inhibitors or drugs for LC with *ALK* gene mutations may also cause fatigue but it is not yet known how long fatigue symptoms may persist given the very recent use of these drugs.

### Neuropathy

Treatment with platinum-based chemotherapy agents may cause CIPN in up to 50% of LC survivors and may persist for years after treatment completion.[103,104] Treatment is variably effective and may include tricyclic antidepressants, anticonvulsants (such as gabapentin or pregabalin) or topical agents. One study also found that duloxetine was effective in reducing pain in survivors with CIPN.[105]

### Mental Health Issues

Similar to other cancer survivors, LC survivors also experience higher rates of depression and anxiety, and both are associated with higher cancer-specific and overall mortality.[106–108] However, LC survivors also often cope with the stigma of LC being a “self-inflicted” illness due to its strong association with tobacco use; non-smokers in particular describe feeling stigmatized by LC diagnosis.[109–111]

### Other Treatment Effects

Targeted immunotherapy with angiogenesis inhibitors may cause hypertension, increased risk for bleeding or poor wound healing due to their effect on vascular growth. In addition, epidermal growth factor receptor (EGFR) inhibitors are often associated with an acneiform dermatitis that can range from a mild rash and itching to very severe dermatitis affecting most of the body, severe pruritis and increased risk for skin infections.[112,113]

## Prostate Cancer

Prostate cancer is the most common non-skin cancer among men in the US, and prostate cancer survivors comprise over 20% of all cancer survivors.[1] The 5-year survival rate is >95%, and most prostate cancer survivors die from non-cancer causes. The most common modes of treatment for patients with prostate cancer include surgery, RT, hormone therapy, and active surveillance, and each is associated with its own set of side effects. The most common side effects include urinary, sexual, or bowel dysfunction, and mental health issues (Table 5).

### Urinary Dysfunction

After surgery, many survivors experience stress incontinence. Urinary function for these patients generally improves gradually after surgery and reaches stability after one year.[114–116] RT can lead to mucositis and edema in the urinary tract which over time can lead to stricture, overactive bladder, fistulas, hematuria, decreased bladder capacity, weak urinary stream, and urinary retention. For those with post-prostatectomy incontinence–a form of stress incontinence–pelvic floor exercises may be beneficial but evidence of their efficacy is inconclusive.[117,118] Male urethral slings or artificial urinary sphincters can reduce or eliminate stress incontinence in this population.[119] For those with urge incontinence, often in post-radiation patients, anti-cholinergic medications can be helpful. However, given that many prostate cancer survivors are older, these medications should be given with caution. For those with difficulty emptying their bladder, alpha-blockers can be tried. In those with post-radiation cystitis, hyperbaric oxygen therapy can be useful.[120]

### Bowel Dysfunction

Bowel dysfunction is also common, especially in patients who underwent radiation. Acute side effects of RT include bowel irregularity, cramping, and diarrhea. Over time, patients may experience rectal bleeding due to thinning of the rectal mucosa. In severe cases, patients may develop ulcers and rectourethral fistulas. Patients may also develop sphincter dysfunction causing rectal urgency and frequency. Dietary changes and hyperbaric oxygen

therapy have been found to help these symptoms.[120] Fortunately, advances in radiation targeting and therapy have decreased the incidence of these issues.

## Sexual Dysfunction

Sexual dysfunction affects nearly all prostate cancer survivors at some point. Erectile dysfunction (ED) is common; those at highest risk for ED are older men and those with preexisting ED. Early penile rehabilitation after prostate cancer surgery can improve sexual function.[121] Penile rehabilitation includes early phosphodiesterase-5 (PDE-5) inhibitor administration to help preserve smooth muscle and improve erectile function through increased tissue perfusion. For those who fail or have contraindications to PDE-5 inhibitors, intraurethral prostaglandin, vacuum erection devices, and penile prosthesis can be tried. Furthermore, while many patients may initially have ED after surgery, some do recover up to 2–4 years after surgery.[122] In contrast to post-prostatectomy patients who often have rapid onset of ED with varying degrees of improvement over time, those undergoing RT often experience a delayed onset of symptoms, usually 6–36 months after treatment.[123] Those receiving androgen deprivation therapy (ADT) also suffer from ED, usually due to decreased libido.

While there are many physiological causes for sexual dysfunction after treatment, psychosocial issues also impact sexual functioning. Many prostate cancer survivors suffer from anxiety and depression after treatment, and these issues may affect sexual drive and function.[124–126] Furthermore, partners of prostate cancer survivors also have high rates of anxiety and depression which may compound a couple's difficulty achieving intimacy after treatment.[127–129] Concerns over physical changes such as lack of or changes in ejaculate, shortened penis size, or loss of male secondary sexual characteristics that can occur with certain treatments may also limit a patient's ability to seek sexual intimacy and may create a psychological barrier to attaining their prior sex life.

Tools such as the Sexual Health Inventory for Men can help clinicians screen for difficulties with sexual intimacy to determine who to refer for counseling as well as to initiate pharmacologic interventions. Besides ED itself, other side effects of treatment such as urinary and bowel dysfunction can interfere with sexual intimacy as well.

## Mental Health Issues

Like other survivors, prostate cancer survivors experience greater levels of anxiety and depression. Up to 30% of those with prostate cancer experience general distress, 25% have increased anxiety, and 10% have clinically significant depression.[124–126] While the bulk of studies assessing mental health examined patients within the first year after treatment, over time the level of distress that prostate cancer survivors experience appears to decrease.[130] Routine distress screening is effective and can also help relieve the distress felt by these survivors.[131]

## Other Treatment Effects

ADT can increase risk for obesity and diabetes due to its effect on fat and lipid metabolism, as well as possibly increase risk for cardiovascular disease.[132–134] In addition, ADT use has

been associated with increased bone loss and higher incidence of osteoporosis and fractures. Men who have received ADT also may experience vasomotor symptoms such as hot flashes and night sweats. Periodic screening for diabetes, lipid profiles and bone density are recommended for prostate cancer survivors who have received ADT.

A summary of treatment side effects associated with each of the cancers described is presented in Table 6.

## Future Considerations/Summary

With improved screening and treatment, the number of cancer survivors in the US is expected increase by another 5 million in the next decade. While many cancer survivors, especially those diagnosed at early-stage, will outlive their cancer and die of other comorbidities, their cancer treatments may lead to long-term and/or latent side effects. These side effects often have significant impact on survivors' quality of life, morbidity and overall mortality. Clinicians—both in primary care and oncology—should be aware of these issues so that they can routinely and actively screen for and treat these side effects in cancer survivors.

## References

1. Miller KD, Siegel RL, Lin CC, et al. Cancer treatment and survivorship statistics, 2016. CA Cancer J Clin. Jul; 2016 66(4):271–289. [PubMed: 27253694]
2. DiSipio T, Rye S, Newman B, Hayes S. Incidence of unilateral arm lymphoedema after breast cancer: a systematic review and meta-analysis. Lancet Oncol. May; 2013 14(6):500–515. [PubMed: 23540561]
3. Warren LE, Miller CL, Horick N, et al. The impact of radiation therapy on the risk of lymphedema after treatment for breast cancer: a prospective cohort study. Int J Radiat Oncol Biol Phys. Mar 01; 2014 88(3):565–571. [PubMed: 24411624]
4. The diagnosis and treatment of peripheral lymphedema: 2013 Consensus Document of the International Society of Lymphology. Lymphology. Mar; 2013 46(1):1–11. [PubMed: 23930436]
5. Okwuosa TM, Anzevino S, Rao R. Cardiovascular disease in cancer survivors. Postgraduate medical journal. Feb; 2017 93(1096):82–90. [PubMed: 28123076]
6. Zamorano JL, Lancellotti P, Rodriguez Munoz D, et al. 2016 ESC Position Paper on cancer treatments and cardiovascular toxicity developed under the auspices of the ESC Committee for Practice Guidelines: The Task Force for cancer treatments and cardiovascular toxicity of the European Society of Cardiology (ESC). European heart journal. Sep 21; 2016 37(36):2768–2801. [PubMed: 27567406]
7. Cardinale D, Colombo A, Bacchiani G, et al. Early detection of anthracycline cardiotoxicity and improvement with heart failure therapy. Circulation. Jun 02; 2015 131(22):1981–1988. [PubMed: 25948538]
8. Bristow MR, Thompson PD, Martin RP, Mason JW, Billingham ME, Harrison DC. Early anthracycline cardiotoxicity. The American journal of medicine. 1978; 65(5):823–832. [PubMed: 707541]
9. Swain SM, Whaley FS, Ewer MS. Congestive heart failure in patients treated with doxorubicin: a retrospective analysis of three trials. Cancer. Jun 01; 2003 97(11):2869–2879. [PubMed: 12767102]
10. Brouwers EE, Huitema AD, Beijnen JH, Schellens JH. Long-term platinum retention after treatment with cisplatin and oxaliplatin. BMC clinical pharmacology. Sep 17.2008 8:7. [PubMed: 18796166]

11. Piccart-Gebhart MJ, Procter M, Leyland-Jones B, et al. Trastuzumab after Adjuvant Chemotherapy in HER2-Positive Breast Cancer. New England Journal of Medicine. 2005; 353(16):1659–1672. [PubMed: 16236737]
12. Ewer SM, Ewer MS. Cardiotoxicity profile of trastuzumab. Drug safety. 2008; 31(6):459–467. [PubMed: 18484781]
13. Joensuu H, Kellokumpu-Lehtinen P-L, Bono P, et al. Adjuvant Docetaxel or Vinorelbine with or without Trastuzumab for Breast Cancer. New England Journal of Medicine. 2006; 354(8):809–820. [PubMed: 16495393]
14. Smith I, Procter M, Gelber RD, et al. 2-year follow-up of trastuzumab after adjuvant chemotherapy in HER2-positive breast cancer: a randomised controlled trial. The Lancet. 369(9555):29–36.
15. Slamon DJ, Leyland-Jones B, Shak S, et al. Use of Chemotherapy plus a Monoclonal Antibody against HER2 for Metastatic Breast Cancer That Overexpresses HER2. New England Journal of Medicine. 2001; 344(11):783–792. [PubMed: 11248153]
16. Pearson EJ, Nair A, Daoud Y, Blum JL. The incidence of cardiomyopathy in BRCA1 and BRCA2 mutation carriers after anthracycline-based adjuvant chemotherapy. Breast Cancer Res Treat. Feb; 2017 162(1):59–67. [PubMed: 28066861]
17. Riccio G, Coppola C, Piscopo G, et al. Trastuzumab and target-therapy side effects: Is still valid to differentiate anthracycline Type I from Type II cardiomyopathies? Human vaccines & immunotherapeutics. May 03; 2016 12(5):1124–1131. [PubMed: 26836985]
18. Stewart FA, Hoving S, Russell NS. Vascular damage as an underlying mechanism of cardiac and cerebral toxicity in irradiated cancer patients. Radiation research. Dec; 2010 174(6):865–869. [PubMed: 21128810]
19. Hong RA, Iimura T, Sumida KN, Eager RM. Cardio-oncology/onco-cardiology. Clinical cardiology. Dec; 2010 33(12):733–737. [PubMed: 21184556]
20. Decensi A, Maisonneuve P, Rotmensz N, et al. Effect of tamoxifen on venous thromboembolic events in a breast cancer prevention trial. Circulation. Feb 08; 2005 111(5):650–656. [PubMed: 15699284]
21. Andrykowski MA, Donovan KA, Laronga C, Jacobsen PB. Prevalence, predictors, and characteristics of off-treatment fatigue in breast cancer survivors. Cancer. Dec 15; 2010 116(24): 5740–5748. [PubMed: 20734399]
22. Curt GA, Breitbart W, Cella D, et al. Impact of cancer-related fatigue on the lives of patients: new findings from the Fatigue Coalition. Oncologist. 2000; 5(5):353–360. [PubMed: 11040270]
23. Berger AM, Mooney K, Alvarez-Perez A, et al. Cancer-Related Fatigue, Version 2.2015. Journal of the National Comprehensive Cancer Network: JNCCN. Aug; 2015 13(8):1012–1039. [PubMed: 26285247]
24. Canario AC, Cabral PU, de Paiva LC, Florencio GL, Spyrides MH, Goncalves AK. Physical activity, fatigue and quality of life in breast cancer patients. Revista da Associacao Medica Brasileira (1992). Jan-Feb;2016 62(1):38–44. [PubMed: 27008491]
25. Bao T, Basal C, Seluzicki C, Li SQ, Seidman AD, Mao JJ. Long-term chemotherapy-induced peripheral neuropathy among breast cancer survivors: prevalence, risk factors, and fall risk. Breast cancer research and treatment. Sep; 2016 159(2):327–333. [PubMed: 27510185]
26. Eckhoff L, Knoop A, Jensen MB, Ewertz M. Persistence of docetaxel-induced neuropathy and impact on quality of life among breast cancer survivors. European journal of cancer (Oxford, England: 1990). Feb; 2015 51(3):292–300.
27. Pereira S, Fontes F, Sonin T, et al. Neurological complications of breast cancer: A prospective cohort study. Breast (Edinburgh, Scotland). Oct; 2015 24(5):582–587.
28. Von Ah D, Habermann B, Carpenter JS, Schneider BL. Impact of perceived cognitive impairment in breast cancer survivors. European journal of oncology nursing: the official journal of European Oncology Nursing Society. Apr; 2013 17(2):236–241. [PubMed: 22901546]
29. Fernandez-de-las-Penas C, Fernandez-Lao C, Cantarero-Villanueva I, et al. Catechol-O-methyltransferase genotype (Val158met) modulates cancer-related fatigue and pain sensitivity in breast cancer survivors. Breast Cancer Res Treat. Jun; 2012 133(2):405–412. [PubMed: 21898113]
30. Chen Z, Maricic M, Pettinger M, et al. Osteoporosis and rate of bone loss among postmenopausal survivors of breast cancer. Cancer. Oct 01; 2005 104(7):1520–1530. [PubMed: 16110508]

31. Hong AR, Kim JH, Lee KH, et al. Long-term effect of aromatase inhibitors on bone microarchitecture and macroarchitecture in non-osteoporotic postmenopausal women with breast cancer. Osteoporosis international: a journal established as result of cooperation between the European Foundation for Osteoporosis and the National Osteoporosis Foundation of the USA. Jan 12.2017
32. Wright LE, Harhash AA, Kozlow WM, et al. Aromatase inhibitor-induced bone loss increases the progression of estrogen receptor-negative breast cancer in bone and exacerbates muscle weakness in vivo. Oncotarget. Jan 31; 2017 8(5):8406–8419. [PubMed: 28039445]
33. Villa P, Lassandro AP, Amar ID, et al. Impact of aromatase inhibitor treatment on vertebral morphology and bone mineral density in postmenopausal women with breast cancer. Menopause (New York, NY). Jan; 2016 23(1):33–39.
34. Schimdt N, Jacob L, Coleman R, Kostev K, Hadji P. The impact of treatment compliance on fracture risk in women with breast cancer treated with aromatase inhibitors in the United Kingdom. Breast Cancer Res Treat. Jan; 2016 155(1):151–157. [PubMed: 26687384]
35. Pedersini R, Monteverdi S, Mazziotti G, et al. Morphometric vertebral fractures in breast cancer patients treated with adjuvant aromatase inhibitor therapy: A cross-sectional study. Bone. Jan 16.2017 97:147–152. [PubMed: 28104509]
36. Stubblefield MD, Keole N. Upper body pain and functional disorders in patients with breast cancer. PM & R: the journal of injury, function, and rehabilitation. Feb; 2014 6(2):170–183.
37. Barron TI, Cahir C, Sharp L, Bennett K. A nested case-control study of adjuvant hormonal therapy persistence and compliance, and early breast cancer recurrence in women with stage I–III breast cancer. Br J Cancer. Sep 17; 2013 109(6):1513–1521. [PubMed: 24002590]
38. Lambertini M, Cinquini M, Moschetti I, et al. Temporary ovarian suppression during chemotherapy to preserve ovarian function and fertility in breast cancer patients: A GRADE approach for evidence evaluation and recommendations by the Italian Association of Medical Oncology. Eur J Cancer. Jan.2017 71:25–33. [PubMed: 27940355]
39. Shandley LM, Spencer JB, Fothergill A, et al. Impact of tamoxifen therapy on fertility in breast cancer survivors. Fertility and sterility. Jan; 2017 107(1):243–252.e245. [PubMed: 27887709]
40. Dohou J, Mouret-Reynier MA, Kwiatkowski F, et al. A Retrospective Study on the Onset of Menopause after Chemotherapy: Analysis of Data Extracted from the Jean Perrin Comprehensive Cancer Center Database Concerning 345 Young Breast Cancer Patients Diagnosed between 1994 and 2012. Oncology. Feb 08.2017
41. Stan D, Loprinzi CL, Ruddy KJ. Breast cancer survivorship issues. Hematology/oncology clinics of North America. Aug; 2013 27(4):805–827. ix. [PubMed: 23915746]
42. Fobair P, Spiegel D. Concerns about sexuality after breast cancer. Cancer J. Jan-Feb;2009 15(1): 19–26. [PubMed: 19197169]
43. Gilbert E, Ussher JM, Perz J. Sexuality after breast cancer: a review. Maturitas. Aug; 2010 66(4): 397–407. [PubMed: 20439140]
44. Ussher JM, Perz J, Gilbert E. Changes to sexual well-being and intimacy after breast cancer. Cancer Nurs. Nov-Dec;2012 35(6):456–465. [PubMed: 22222680]
45. Berkey FJ. Managing the adverse effects of radiation therapy. American family physician. Aug 15; 2010 82(4):381–388, 394. [PubMed: 20704169]
46. Falk Dahl CA, Reinertsen KV, Nesvold IL, Fossa SD, Dahl AA. A study of body image in long-term breast cancer survivors. Cancer. Aug 01; 2010 116(15):3549–3557. [PubMed: 20564138]
47. Zainal NZ, Nik-Jaafar NR, Baharudin A, Sabki ZA, Ng CG. Prevalence of depression in breast cancer survivors: a systematic review of observational studies. Asian Pac J Cancer Prev. 2013; 14(4):2649–2656. [PubMed: 23725190]
48. Yang H, Brand JS, Fang F, et al. Time-dependent risk of depression, anxiety, and stress-related disorders in patients with invasive and in situ breast cancer. Int J Cancer. Feb 15; 2017 140(4): 841–852. [PubMed: 27859142]
49. Ellegaard MB, Grau C, Zachariae R, Bonde Jensen A. Fear of cancer recurrence and unmet needs among breast cancer survivors in the first five years. A cross-sectional study. Acta oncologica (Stockholm, Sweden). Jan 17.2017 :1–7.

50. Howlader, N., Noone, A., Krapcho, M., et al. Based on November 2011 SEER data submission, posted to the SEER web site April 2012. Vol. 22. Bethesda, MD: National Cancer Institute; SEER cancer statistics review, 1975–2009 (vintage 2009 populations). seer.cancer.gov/csr/1975_2009_pops09/ Accessed April. 2012
51. Rim SH, Seeff L, Ahmed F, King JB, Coughlin SS. Colorectal cancer incidence in the United States, 1999–2004: an updated analysis of data from the National Program of Cancer Registries and the Surveillance, Epidemiology, and End Results Program. Cancer. May 01; 2009 115(9): 1967–1976. [PubMed: 19235249]
52. Bruheim K, Guren MG, Skovlund E, et al. Late side effects and quality of life after radiotherapy for rectal cancer. Int J Radiat Oncol Biol Phys. Mar 15; 2010 76(4):1005–1011. [PubMed: 19540058]
53. Marijnen CA, van de Velde CJ, Putter H, et al. Impact of short-term preoperative radiotherapy on health-related quality of life and sexual functioning in primary rectal cancer: report of a multicenter randomized trial. J Clin Oncol. Mar 20; 2005 23(9):1847–1858. [PubMed: 15774778]
54. Lange MM, Martz JE, Ramdeen B, et al. Long-term results of rectal cancer surgery with a systematical operative approach. Annals of surgical oncology. Jun; 2013 20(6):1806–1815. [PubMed: 23536052]
55. Bregendahl S, Emmertsen KJ, Lous J, Laurberg S. Bowel dysfunction after low anterior resection with and without neoadjuvant therapy for rectal cancer: a population-based cross-sectional study. Colorectal disease: the official journal of the Association of Coloproctology of Great Britain and Ireland. Sep; 2013 15(9):1130–1139. [PubMed: 23581977]
56. Bregendahl S, Emmertsen KJ, Lindegaard JC, Laurberg S. Urinary and sexual dysfunction in women after resection with and without preoperative radiotherapy for rectal cancer: a population-based cross-sectional study. Colorectal disease: the official journal of the Association of Coloproctology of Great Britain and Ireland. Jan; 2015 17(1):26–37. [PubMed: 25156386]
57. Lange MM, Maas CP, Marijnen CA, et al. Urinary dysfunction after rectal cancer treatment is mainly caused by surgery. Br J Surg. Aug; 2008 95(8):1020–1028. [PubMed: 18563786]
58. Peeters KC, van de Velde CJ, Leer JW, et al. Late side effects of short-course preoperative radiotherapy combined with total mesorectal excision for rectal cancer: increased bowel dysfunction in irradiated patients–a Dutch colorectal cancer group study. J Clin Oncol. Sep 01; 2005 23(25):6199–6206. [PubMed: 16135487]
59. Lange MM, Marijnen CA, Maas CP, et al. Risk factors for sexual dysfunction after rectal cancer treatment. Eur J Cancer. Jun; 2009 45(9):1578–1588. [PubMed: 19147343]
60. Pollack J, Holm T, Cedermark B, et al. Late adverse effects of short-course preoperative radiotherapy in rectal cancer. Br J Surg. Dec; 2006 93(12):1519–1525. [PubMed: 17054311]
61. Havenga K, Maas CP, DeRuiter MC, Welvaart K, Trimbos JB. Avoiding long-term disturbance to bladder and sexual function in pelvic surgery, particularly with rectal cancer. Seminars in surgical oncology. Apr-May;2000 18(3):235–243. [PubMed: 10757889]
62. Kim MJ, Kim YS, Park SC, et al. Risk factors for permanent stoma after rectal cancer surgery with temporary ileostomy. Surgery. Mar; 2016 159(3):721–727. [PubMed: 26490725]
63. Dabirian A, Yaghmaei F, Rassouli M, Tafreshi MZ. Quality of life in ostomy patients: a qualitative study. Patient Prefer Adherence. Dec 21.2010 5:1–5. [PubMed: 21311696]
64. Dault R, Rousseau MP, Beaudoin A, Frenette MA, Lemay F, Beauchesne MF. Impact of oxaliplatin-induced neuropathy in patients with colorectal cancer: a prospective evaluation at a single institution. Current oncology (Toronto, Ont). Feb; 2016 23(1):e65–69.
65. Beijers AJ, Mols F, Vreugdenhil G. A systematic review on chronic oxaliplatin-induced peripheral neuropathy and the relation with oxaliplatin administration. Support Care Cancer. Jul; 2014 22(7): 1999–2007. [PubMed: 24728618]
66. Vardy J, Dhillon H, Pond G, et al. Cognitive function and fatigue after diagnosis of colorectal cancer. Annals of oncology. 2014; 25(12):2404–2412. [PubMed: 25214544]
67. Cruzado JA, López-Santiago S, Martínez-Marín V, José-Moreno G, Custodio AB, Feliu J. Longitudinal study of cognitive dysfunctions induced by adjuvant chemotherapy in colon cancer patients. Supportive Care in Cancer. 2014; 22(7):1815–1823. [PubMed: 24535240]

68. Brown MR, Ramirez JD, Farquhar-Smith P. Pain in cancer survivors. British journal of pain. Nov; 2014 8(4):139–153. [PubMed: 26516548]
69. Baxter NN, Habermann EB, Tepper JE, Durham SB, Virnig BA. Risk of pelvic fractures in older women following pelvic irradiation. Jama. Nov 23; 2005 294(20):2587–2593. [PubMed: 16304072]
70. Rezkalla S, Kloner RA, Ensley J, et al. Continuous ambulatory ECG monitoring during fluorouracil therapy: a prospective study. Journal of clinical oncology: official journal of the American Society of Clinical Oncology. Apr; 1989 7(4):509–514. [PubMed: 2466960]
71. Yeh ETH, Bickford CL. Cardiovascular Complications of Cancer Therapy: Incidence, Pathogenesis, Diagnosis, and Management. Journal of the American College of Cardiology. Jun 16; 2009 53(24):2231–2247. [PubMed: 19520246]
72. Jones RL, Ewer MS. Cardiac and cardiovascular toxicity of nonanthracycline anticancer drugs. Expert review of anticancer therapy. Sep; 2006 6(9):1249–1269. [PubMed: 17020459]
73. Saif MW, Shah MM, Shah AR. Fluoropyrimidine-associated cardiotoxicity: revisited. Expert opinion on drug safety. Mar; 2009 8(2):191–202. [PubMed: 19309247]
74. Cohen EE, LaMonte SJ, Erb NL, et al. American Cancer Society Head and Neck Cancer Survivorship Care Guideline. CA Cancer J Clin. May; 2016 66(3):203–239. [PubMed: 27002678]
75. Erisen L, Basel B, Irdesel J, et al. Shoulder function after accessory nerve-sparing neck dissections. Head Neck. Nov; 2004 26(11):967–971. [PubMed: 15459926]
76. Carr SD, Bowyer D, Cox G. Upper limb dysfunction following selective neck dissection: a retrospective questionnaire study. Head Neck. Jun; 2009 31(6):789–792. [PubMed: 19260131]
77. Moore RA, Wiffen PJ, Derry S, Toelle T, Rice AS. Gabapentin for chronic neuropathic pain and fibromyalgia in adults. Cochrane Database Syst Rev. Apr 27.2014 (4):CD007938. [PubMed: 24771480]
78. Stubblefield MD, Levine A, Custodio CM, Fitzpatrick T. The role of botulinum toxin type A in the radiation fibrosis syndrome: a preliminary report. Arch Phys Med Rehabil. Mar; 2008 89(3):417–421. [PubMed: 18295617]
79. Stubblefield MD, Manfield L, Riedel ER. A preliminary report on the efficacy of a dynamic jaw opening device (dynasplint trismus system) as part of the multimodal treatment of trismus in patients with head and neck cancer. Arch Phys Med Rehabil. Aug; 2010 91(8):1278–1282. [PubMed: 20684911]
80. Bach CA, Wagner I, Lachiver X, Baujat B, Chabolle F. Botulinum toxin in the treatment of post-radiosurgical neck contracture in head and neck cancer: a novel approach. Eur Ann Otorhinolaryngol Head Neck Dis. Feb; 2012 129(1):6–10. [PubMed: 22104582]
81. Pauli N, Johnson J, Finizia C, Andrell P. The incidence of trismus and long-term impact on health-related quality of life in patients with head and neck cancer. Acta oncologica (Stockholm, Sweden). Aug; 2013 52(6):1137–1145.
82. Tang Y, Shen Q, Wang Y, Lu K, Peng Y. A randomized prospective study of rehabilitation therapy in the treatment of radiation-induced dysphagia and trismus. Strahlenther Onkol. Jan; 2011 187(1): 39–44. [PubMed: 21136031]
83. Chua DT, Lo C, Yuen J, Foo YC. A pilot study of pentoxifylline in the treatment of radiation-induced trismus. Am J Clin Oncol. Aug; 2001 24(4):366–369. [PubMed: 11474263]
84. Hartl DM, Cohen M, Julieron M, Marandas P, Janot F, Bourhis J. Botulinum toxin for radiation-induced facial pain and trismus. Otolaryngol Head Neck Surg. Apr; 2008 138(4):459–463. [PubMed: 18359354]
85. Francis DO, Weymuller EA Jr, Parvathaneni U, Merati AL, Yueh B. Dysphagia, stricture, and pneumonia in head and neck cancer patients: does treatment modality matter? Ann Otol Rhinol Laryngol. Jun; 2010 119(6):391–397. [PubMed: 20583737]
86. Wang JJ, Goldsmith TA, Holman AS, Cianchetti M, Chan AW. Pharyngoesophageal stricture after treatment for head and neck cancer. Head Neck. Jul; 2012 34(7):967–973. [PubMed: 21953721]
87. Deng J, Ridner SH, Dietrich MS, et al. Prevalence of secondary lymphedema in patients with head and neck cancer. J Pain Symptom Manage. Feb; 2012 43(2):244–252. [PubMed: 21802897]
88. Zhou J, Jolly S. Obstructive sleep apnea and fatigue in head and neck cancer patients. Am J Clin Oncol. Aug; 2015 38(4):411–414. [PubMed: 24762708]

89. van der Molen L, van Rossum MA, Jacobi I, et al. Pre- and posttreatment voice and speech outcomes in patients with advanced head and neck cancer treated with chemoradiotherapy: expert listeners' and patient's perception. J Voice. Sep; 2012 26(5):664 e625–633.

90. Marunick M, Tselios N. The efficacy of palatal augmentation prostheses for speech and swallowing in patients undergoing glossectomy: a review of the literature. J Prosthet Dent. Jan; 2004 91(1):67–74. [PubMed: 14739896]

91. Epstein JB, Thariat J, Bensadoun RJ, et al. Oral complications of cancer and cancer therapy: from cancer treatment to survivorship. CA Cancer J Clin. Nov-Dec;2012 62(6):400–422. [PubMed: 22972543]

92. Marques MA, Dib LL. Periodontal changes in patients undergoing radiotherapy. J Periodontol. Sep; 2004 75(9):1178–1187. [PubMed: 15515331]

93. Heuvelmans MA, Groen HJ, Oudkerk M. Early lung cancer detection by low-dose CT screening: therapeutic implications. Expert Rev Respir Med. Feb; 2017 11(2):89–100. [PubMed: 28005439]

94. Poghosyan H, Sheldon LK, Leveille SG, Cooley ME. Health-related quality of life after surgical treatment in patients with non-small cell lung cancer: a systematic review. Lung Cancer. Jul; 2013 81(1):11–26. [PubMed: 23562675]

95. Kenny PM, King MT, Viney RC, et al. Quality of life and survival in the 2 years after surgery for non small-cell lung cancer. J Clin Oncol. Jan 10; 2008 26(2):233–241. [PubMed: 18086802]

96. Ozturk A, Sarihan S, Ercan I, Karadag M. Evaluating quality of life and pulmonary function of long-term survivors of non-small cell lung cancer treated with radical or postoperative radiotherapy. Am J Clin Oncol. Feb; 2009 32(1):65–72. [PubMed: 19194128]

97. Harle AS, Blackhall FH, Smith JA, Molassiotis A. Understanding cough and its management in lung cancer. Curr Opin Support Palliat Care. Jun; 2012 6(2):153–162. [PubMed: 22469666]

98. Huang X, Zhou W, Zhang Y. Features of fatigue in patients with early-stage non-small cell lung cancer. J Res Med Sci. Mar; 2015 20(3):268–272. [PubMed: 26109974]

99. Hung R, Krebs P, Coups EJ, et al. Fatigue and functional impairment in early-stage non-small cell lung cancer survivors. J Pain Symptom Manage. Feb; 2011 41(2):426–435. [PubMed: 21216563]

100. Paramanandam VS, Dunn V. Exercise for the management of cancer-related fatigue in lung cancer: a systematic review. Eur J Cancer Care (Engl). 2015; 24(1):4–14. [PubMed: 24720528]

101. Lin YY, Rau KM, Lin CC. Longitudinal study on the impact of physical activity on the symptoms of lung cancer survivors. Support Care Cancer. Dec; 2015 23(12):3545–3553. [PubMed: 25855040]

102. Crandall K, Maguire R, Campbell A, Kearney N. Exercise intervention for patients surgically treated for Non-Small Cell Lung Cancer (NSCLC): a systematic review. Surg Oncol. Mar; 2014 23(1):17–30. [PubMed: 24529937]

103. Winton T, Livingston R, Johnson D, et al. Vinorelbine plus cisplatin vs. observation in resected non-small-cell lung cancer. N Engl J Med. Jun 23; 2005 352(25):2589–2597. [PubMed: 15972865]

104. Bezjak A, Lee CW, Ding K, et al. Quality-of-life outcomes for adjuvant chemotherapy in early-stage non-small-cell lung cancer: results from a randomized trial, JBR.10. J Clin Oncol. Nov 01; 2008 26(31):5052–5059. [PubMed: 18809617]

105. Smith EM, Pang H, Cirrincione C, et al. Effect of duloxetine on pain, function, and quality of life among patients with chemotherapy-induced painful peripheral neuropathy: a randomized clinical trial. Jama. Apr 03; 2013 309(13):1359–1367. [PubMed: 23549581]

106. Hopwood P, Stephens RJ. Depression in patients with lung cancer: prevalence and risk factors derived from quality-of-life data. J Clin Oncol. Feb; 2000 18(4):893–903. [PubMed: 10673533]

107. Vodermaier A, Lucas S, Linden W, Olson R. Anxiety after diagnosis predicts lung-cancer specific and overall survival in patients with stage III non-small cell lung cancer. A population-based cohort study. J Pain Symptom Manage. Jan 04.2017

108. Sullivan DR, Forsberg CW, Ganzini L, et al. Longitudinal Changes in Depression Symptoms and Survival Among Patients With Lung Cancer: A National Cohort Assessment. J Clin Oncol. Nov 20; 2016 34(33):3984–3991. [PubMed: 27996350]

109. Chambers SK, Dunn J, Occhipinti S, et al. A systematic review of the impact of stigma and nihilism on lung cancer outcomes. BMC Cancer. May 20.2012 12:184. [PubMed: 22607085]

110. Chapple A, Ziebland S, McPherson A. Stigma, shame, and blame experienced by patients with lung cancer: qualitative study. Bmj. Jun 19.2004 328(7454):1470. [PubMed: 15194599]
111. Cataldo JK, Jahan TM, Pongquan VL. Lung cancer stigma, depression, and quality of life among ever and never smokers. European journal of oncology nursing: the official journal of European Oncology Nursing Society. Jul; 2012 16(3):264–269. [PubMed: 21803653]
112. Becker A, van Wijk A, Smit EF, Postmus PE. Side-effects of long-term administration of erlotinib in patients with non-small cell lung cancer. J Thorac Oncol. Sep; 2010 5(9):1477–1480. [PubMed: 20736807]
113. Bachet JB, Peuvrel L, Bachmeyer C, et al. Folliculitis induced by EGFR inhibitors, preventive and curative efficacy of tetracyclines in the management and incidence rates according to the type of EGFR inhibitor administered: a systematic literature review. Oncologist. 2012; 17(4):555–568. [PubMed: 22426526]
114. Sandhu JS, Eastham JA. Factors predicting early return of continence after radical prostatectomy. Curr Urol Rep. May; 2010 11(3):191–197. [PubMed: 20425626]
115. Skolarus TA, Weizer AZ, Hedgepeth RC, He C, Wood DP Jr, Hollenbeck BK. Understanding early functional recovery after robotic prostatectomy. Surg Innov. Mar; 2012 19(1):5–10. [PubMed: 21521701]
116. Srivastava A, Peyser A, Gruschow S, Harneja N, Jiskrova K, Tewari AK. Surgical strategies to promote early continence recovery after robotic radical prostatectomy. Arch Esp Urol. Jun; 2012 65(5):529–541. [PubMed: 22732779]
117. Campbell SE, Glazener CM, Hunter KF, Cody JD, Moore KN. Conservative management for postprostatectomy urinary incontinence. Cochrane Database Syst Rev. Jan 18.2012 1:CD001843. [PubMed: 22258946]
118. Goode PS, Burgio KL, Johnson TM 2nd, et al. Behavioral therapy with or without biofeedback and pelvic floor electrical stimulation for persistent postprostatectomy incontinence: a randomized controlled trial. Jama. Jan 12; 2011 305(2):151–159. [PubMed: 21224456]
119. Herschorn S. Update on management of post-prostatectomy incontinence in 2013. Can Urol Assoc J. Sep; 2013 7(9–10 Suppl 4):S189–191. [PubMed: 24523842]
120. Hampson NB, Holm JR, Wreford-Brown CE, Feldmeier J. Prospective assessment of outcomes in 411 patients treated with hyperbaric oxygen for chronic radiation tissue injury. Cancer. Aug 01; 2012 118(15):3860–3868. [PubMed: 22139864]
121. Brewer ME, Kim ED. Penile rehabilitation therapy with PDE-V inhibitors following radical prostatectomy: proceed with caution. Adv Urol. 2009; 852437
122. McCullough AR. Rehabilitation of erectile function following radical prostatectomy. Asian J Androl. Jan; 2008 10(1):61–74. [PubMed: 18087645]
123. Skolarus TA, Wolf AM, Erb NL, et al. American Cancer Society prostate cancer survivorship care guidelines. CA Cancer J Clin. Jul-Aug;2014 64(4):225–249. [PubMed: 24916760]
124. Jayadevappa R, Malkowicz SB, Chhatre S, Johnson JC, Gallo JJ. The burden of depression in prostate cancer. Psychooncology. Dec; 2012 21(12):1338–1345. [PubMed: 21837637]
125. Korfage IJ, Essink-Bot ML, Janssens AC, Schroder FH, de Koning HJ. Anxiety and depression after prostate cancer diagnosis and treatment: 5-year follow-up. Br J Cancer. Apr 24; 2006 94(8): 1093–1098. [PubMed: 16622434]
126. Punnen S, Cowan JE, Dunn LB, Shumay DM, Carroll PR, Cooperberg MR. A longitudinal study of anxiety, depression and distress as predictors of sexual and urinary quality of life in men with prostate cancer. BJU Int. Jul; 2013 112(2):E67–75. [PubMed: 23795800]
127. Tanner T, Galbraith M, Hays L. From a woman's perspective: life as a partner of a prostate cancer survivor. J Midwifery Womens Health. Mar-Apr;2011 56(2):154–160. [PubMed: 21429081]
128. Couper J, Bloch S, Love A, Macvean M, Duchesne GM, Kissane D. Psychosocial adjustment of female partners of men with prostate cancer: a review of the literature. Psychooncology. Nov; 2006 15(11):937–953. [PubMed: 16521081]
129. Heins M, Schellevis F, Rijken M, Donker G, van der Hoek L, Korevaar J. Partners of cancer patients consult their GPs significantly more often with both somatic and psychosocial problems. Scand J Prim Health Care. Dec; 2013 31(4):203–208. [PubMed: 24299045]

130. Carlson LE, Angen M, Cullum J, et al. High levels of untreated distress and fatigue in cancer patients. Br J Cancer. Jun 14; 2004 90(12):2297–2304. [PubMed: 15162149]

131. Norris L, Pratt-Chapman M, Noblick JA, Cowens-Alvarado R. Distress, Demoralization, and Depression in Cancer Survivorship. Psychiatric Annals. 2011; 41(9):433–438.

132. Taylor LG, Canfield SE, Du XL. Review of major adverse effects of androgendeprivation therapy in men with prostate cancer. Cancer. Jun 01; 2009 115(11):2388–2399. [PubMed: 19399748]

133. Saylor PJ, Smith MR. Metabolic complications of androgen deprivation therapy for prostate cancer. J Urol. Jan; 2013 189(1 Suppl):S34–42. discussion S43–34. [PubMed: 23234628]

134. Nguyen PL, Je Y, Schutz FA, et al. Association of androgen deprivation therapy with cardiovascular death in patients with prostate cancer: a meta-analysis of randomized trials. Jama. Dec 07; 2011 306(21):2359–2366. [PubMed: 22147380]

**Key Points**

1. Most cancer survivors experience some long-term or latent side effects as a result of cancer treatment.
2. Fatigue and mental health issues are very common long-term side effects associated with treatment for many different cancers.
3. Clinicians should be aware of these long-term and latent side effects so that they can routinely screen for and treat cancer survivors appropriately.

**Table 1**

Long term and latent effects of breast cancer treatment

| Side effect | Treatment type | | | | |
|---|---|---|---|---|---|
| | Chemo | HT | IM | RT | Surgery |
| General | | | | | |
| Fatigue | X | | | X | |
| Pain | | | | X | X |
| Weakness | X | | | X | X |
| Cardiac | | | | | |
| Cardiomyopathy | X | | X | X | |
| Thromboembolism | | X | | | |
| Endocrine | | | | | |
| Bone loss | | X | | | |
| Infertility | X | X | | | |
| Premature menopause | X | X | | | |
| Vasomotor symptoms | X | X | | | |
| Musculoskeletal | | | | | |
| Arthralgia/myalgias | | X | | | |
| Lymphedema | | | | X | X |
| Rotator cuff disease | | | | | X |
| Neurologic | | | | | |
| Cognitive dysfunction | X | X | | | X |
| Neuropathy | X | | | | |
| Psychosocial (anxiety, body image concerns, depression) | | X | | X | X |
| Pulmonary (pneumonitis) | | | | X | |
| Sexual dysfunction (decreased libido, vaginal dryness, dyspareunia) | X | | | | |

Chemo: chemotherapy; HT: hormonal therapy; IM: immune modulators (trastuzumab); RT: radiation therapy

## Table 2

Long term and latent effects of colorectal cancer treatment

| Side effect | Treatment type | | |
|---|---|---|---|
| | Chemotherapy | Radiation | Surgery |
| General | | | |
| Fatigue | X | X | |
| Pain | | X | X |
| Weakness | | | |
| Cardiotoxicity | X | | |
| Gastrointestinal | | | |
| Bowel urgency | | X | X |
| Chronic diarrhea | | X | X |
| Fecal incontinence | | X | |
| Ostomy complications | | | X |
| Genitourinary (difficulty voiding or incontinence) | | X | X |
| Neurologic | | | |
| Cognitive dysfunction | X | | |
| Neuropathy | X | | |
| Psychosocial (anxiety, distress, depression) | | X | X |
| Sexual dysfunction (decreased libido, erectile dysfunction, vaginal dryness, dyspareunia) | | X | X |

## Table 3

Long term and latent effects of head and neck cancer treatment

| Side effect | Treatment type | | |
|---|---|---|---|
| | Chemotherapy | Radiation | Surgery |
| General | | | |
| Fatigue | X | X | |
| Pain | | | X |
| Weakness | X | X | |
| Musculoskeletal | | | |
| Cervical dystonia | | X | X |
| Lymphedema | | X | X |
| Shoulder dysfunction | | X | X |
| Neurologic | | | |
| Cognitive dysfunction | X | | |
| Cervical radiculopathy | X | X | X |
| Neuropathy | X | | X |
| Oropharyngeal | | | |
| Dental caries | | X | |
| Dysarthria | | X | X |
| Dysphagia/esophageal stricture | | X | X |
| Reflux disease | | X | |
| Taste disturbance | | X | |
| Trismus | | X | X |
| Xerostomia | | X | X |
| Psychosocial (anxiety, distress, depression) | X | X | X |
| Pulmonary (pulmonary fibrosis) | X | X | |

## Table 4

Long term and latent effects of lung cancer treatment

| Side effect | Treatment type | | | |
|---|---|---|---|---|
| | Chemo | RT | Surgery | Targeted |
| General | | | | |
| Fatigue | X | X | | X |
| Pain | | | X | |
| Weakness | X | X | | |
| Dermatitis | | | | X |
| Hypertension | | | | X |
| Neurologic | | | | |
| Cognitive dysfunction | X | | | |
| Neuropathy | X | | | |
| Psychosocial (anxiety, distress, depression) | X | X | X | |
| Pulmonary | | | | |
| Chronic cough | | X | | |
| Dyspnea | | X | X | |
| Pneumonitis | | X | | |

Chemo: chemotherapy; RT: radiation therapy

Targeted refers to immunotherapy drugs that target specific gene mutations (e.g. *ALK*), angiogenesis inhibitors or EGFR inhibitors

## Table 5

Long term and latent effects of prostate cancer treatment

| Side effect | Treatment type | | |
|---|---|---|---|
| | Hormonal (ADT) | Radiation | Surgery |
| General | | | |
| Fatigue | X | X | |
| Pain | | X | X |
| Weakness | X | X | X |
| Bowel dysfunction | | | |
| Fecal urgency/incontinence | | X | |
| Proctitis | | X | |
| Cardiovascular disease | X | | |
| Endocrine | | | |
| Bone loss | X | | |
| Metabolic syndrome/diabetes | X | | |
| Vasomotor symptoms | X | | |
| Weight gain/obesity | X | | |
| Psychosocial (anxiety, body image concerns, depression) | X | X | X |
| Sexual dysfunction (decreased libido, erectile dysfunction) | X | X | X |
| Urinary dysfunction | | | |
| Incontinence | | X | X |
| Urethral stricture | | X | X |
| Urgency/frequency | | X | X |

ADT: androgen deprivation therapy

**Table 6**

Common long-term and latent treatment side effects by cancer type

| | Cancer Type | | | | |
|---|---|---|---|---|---|
| **Side effect** | **Breast** | **CRC** | **HNC** | **Lung** | **Prostate** |
| Bone loss | X | | | | X |
| Bowel dysfunction | | X | | | X |
| Cardiovascular disease | X | X | | X | X |
| Cognitive dysfunction | X | X | | X | |
| Dermatitis | | | | X | |
| Dysphagia/GERD | | | X | | |
| Endocrine disruptions (infertility, metabolic syndrome, vasomotor symptoms) | X | | | | X |
| Fatigue | X | X | X | X | X |
| Lymphedema | X | | X | | |
| Mental health issues (anxiety, depression, body image concerns) | X | X | X | X | X |
| Musculoskeletal pain | X | | X | | |
| Neuropathy | | X | X | X | |
| Oral health issues | | | X | | |
| Pulmonary dysfunction | X | | X | X | |
| Sexual dysfunction | X | X | | | X |
| Sleep apnea | | | X | | |
| Urinary dysfunction | | X | | | X |

CRC: colorectal; HNC: head and neck

*Med Clin North Am*. Author manuscript; available in PMC 2018 November 01.