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ABSTRACT

Head and neck cancer will account for an estimated 59,340 (3%) new cancer cases in the United States in 2015.¹ Currently there are approximately 436,060 (3%) head and neck cancer survivors living in the US.² The American Cancer Society Head and Neck Cancer Survivorship Care Guidelines for Primary Care Providers were developed to assist with surveillance for head and neck cancer recurrence, screening for second primary cancers, long-term and late effects assessment and management, health promotion and care coordination.

INTRODUCTION

Head and neck cancer (HNC) will account for an estimated 59,340 (3%) new cancer cases in the United States (US) in 2015.¹ Currently there are approximately 436,060 (3%) HNC survivors living in the US.² Long-term survival is becoming more common.³ Nearly a decade ago, a landmark report from the Institute of Medicine, ‘From Cancer Patient to Cancer Survivor: Lost in Transition,’ highlighted the unique issues facing all cancer survivors as well as the growing need for guidance with respect to quality survivorship care.⁴ These
guidelines were developed in response to the need for guidance on how best to care for the growing number of HNC survivors.\textsuperscript{5}

**BACKGROUND**

In the US, there are nearly 60,000 people diagnosed with head and neck cancer (HNC) annually.\textsuperscript{1} Tobacco use accounts for approximately 85\% of HNC cases.\textsuperscript{6} In addition, the human papillomavirus (HPV) accounts for as many as 70\% or oral and oropharyngeal cancers.\textsuperscript{7} HPV-related HNC is a biologically and clinically distinct disease from tobacco-related HNC with now well-described differences in molecular alterations, clinical presentation, and prognosis.\textsuperscript{8, 9} Approximately, 20\% of the population is positive for exposure to HPV. Primary care clinicians (PCCs) are in a unique position to reduce the incidence of head and neck cancers by strongly recommending the HPV vaccination as indicated for pre-adolescent girls and boys.

Standard management of HNC is anatomic and TNM stage based. Early stage disease (stage I and II) is treated with a single modality – surgery or radiotherapy – depending primarily on tumor location, but also on tumor extent, anticipated cure rate, and functional and esthetic outcome. About 80-90\%, of early stage
patients will be cured. Advanced stage patients (stage III, IVa, and IVb) are treated with multi-modal therapy including surgery, radiotherapy, and chemotherapy. The sequencing and combination of therapies are based on stage, tumor location, expertise of treating physicians, and patient preference. Despite more aggressive treatment for advanced stage disease, cure rates remain low primarily due to locoregional recurrence. However, HPV-related HNC is associated with a significantly better prognosis even with stage IV disease, especially in never smokers. Cure rates for HPV-related HNC in some large studies approaches 90%.

Current research in HNC is focused on personalizing therapy based on molecular phenotypes, improving treatment efficacy, and reducing long-term morbidity. The latter is predominantly being studied in HPV-related HNC where reductions in radiation dose or volume are being studied with an aim to reduce acute and chronic toxicities.

**METHODS**

Methods used to develop this guideline were influenced by the American Cancer Society (ACS) screening\(^{10}\) and survivorship\(^{11}\)
guidelines. Where appropriate, this guideline builds upon the recently published American Society of Clinical Oncology (ASCO) symptom-based guidelines for adult cancer survivors.\textsuperscript{12, 13, 14}

\textit{Panel Formation}

A multidisciplinary expert workgroup was formed and tasked with drafting the ACS Head and Neck Cancer Survivorship Care Guidelines. Workgroup members had expertise in primary care, dentistry, surgical oncology, medical oncology, radiation oncology, speech language pathology, and nursing. In addition a cancer survivor was included to provide a patient perspective.

\textit{Literature Review}

The literature review began with an environmental scan of existing guidelines and guidance developed by other organizations [eg, NCCN\textsuperscript{\textregistered}15, 16; ASCO\textsuperscript{12, 13, 14}; specific medical centers (eg, The University of Texas MD Anderson Clinical Tools and Resources Head and Neck Cancer Survivorship algorithm), US Preventive Services Task Force\textsuperscript{17}, and those available from other countries (eg, Australian Cancer Survivorship Centre)].
Literature Search Strategy

A systematic review of the literature was conducted using PubMed for 2004 through April 2015. Studies on childhood cancers, qualitative studies, and non-English publications were excluded. Also excluded were studies that consisted of entirely non-North-American populations due to the fact that HNC prevalence is higher in some countries due to lifestyle causes and differing etiology. Search terms included: cancer survivor AND review OR meta-analysis OR systematic review OR guidelines; guidance AND head and neck cancer OR head and neck cancer survivor; head and neck cancer patient post-treatment AND symptom management OR late effects OR long-term effects OR psychosocial care OR palliative care OR health promotion OR surveillance OR screening for new cancers OR self-management OR guidelines OR guidance OR follow up OR follow-up OR side effects OR (chemotherapy AND side effects) OR (radiation AND side effects), OR surgery OR treatment complications OR genetic counseling and testing OR survivor or patient interventions OR provider interventions OR provider education OR barriers. Additional search attempts included head and neck cancer
OR head and neck cancer survivor OR head and neck cancer patient post-treatment AND (symptom-specific terms, such as swallowing, body image, neck dissection, etc.).

The highest priority was given to articles that met the following criteria: peer reviewed publication in English since 2004 unless a seminal article published before that date still carried the most weight, including randomized controlled trials (RCTs), prospective cohort studies, and population-based, case-control studies; studies of more than 50 cancer cases analyzed and with high-quality assessment of covariates, and analytic methods; and analyses controlled for important confounders (eg, preexisting comorbid conditions).

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A total of 182 articles (list is available as a supplement to this manuscript) met inclusion criteria and 136 were included as references. Recommendations provided in this guideline are based on current evidence in the literature, but most evidence is not sufficient to warrant a strong recommendation. Rather, recommendations should be viewed as consensus-based management strategies given the limited evidence base.

Workgroup members were also asked to consider the specific level of evidence criteria along with consistency across studies and study designs; dose-response when presenting treatment impacts; race / ethnicity differences; and second primary cancers (SPC) for which survivors are at high risk due to treatment and behavioral considerations. After finalization by the workgroup, the guideline manuscript was sent to additional internal and external experts for review and comment prior to submission for publication. The manuscript summarizes literature with the highest level of evidence. A comprehensive list of evidence is available in the Appendix. The
guideline will be updated every 5 years or as new evidence becomes available to support revision.

GUIDELINES FOR THE PRIMARY CARE MANAGEMENT OF HEAD AND NECK CANCER SURVIVORS

SURVEILLANCE FOR HEAD AND NECK CANCER RECURRENCE
(Table 1: Guidelines for Surveillance for Head and Neck Cancer Recurrence)

*History and Physical*

Recommendation 1.1: It is recommended that primary care clinicians (a) Should individualize clinical follow-up care provided to HNC survivors based on age, specific diagnosis and treatment protocol. (LOE=2A); (b) Should review patient medical history, conduct a head and neck physical exam, and assess for long-term and late effects and information needs every 1-3 months for the first year after primary treatment, every 2-6 months in the second year, every 4-8 months in years 3-5, and annually after 5 years. (LOE = 2A)

Surveillance, regardless of stage of disease from the primary tumor includes history and physical examination with assessment for long-term or late effects of treatment, to include xerostomia,
swallowing and speech difficulties, voice deficits, pharyngoesophageal strictures, oral and dental health deterioration, and hypothyroidism. Surveillance for HNC recurrence (locally, regionally in the neck, or distant metastasis), and second primary HNC, as well as SPC in other high risk sites (lung, esophagus) are essential components of evaluation.¹⁸

Outcome for recurrent HNC is very poor, with notable exception of those whose HNC was early stage, and for those with local only recurrence. Hence salvage therapy for recurrent disease may preferentially benefit this subset.¹⁹ No physical exam of the head and neck is complete without the complete (direct) nasopharyngolaryngoscopy of the entire upper-aerodigestive tract to include the oral cavity, oropharynx, hypopharynx, and larynx. Complete head and neck physical examination includes nasopharyngolaryngoscopy of the oral cavity, oropharynx, hypopharynx, and larynx and palpation of the neck.

The literature is not definitive on the optimal frequency of surveillance, and it is unclear whether surveillance provides any survival advantage.²⁰ However, NCCN® guidelines provide a schedule for follow-up evaluation every 1-3 months during year 1 posttreatment, every 2-6 months during year 2 posttreatment, every
4-8 months during years 3-5, and yearly after 5 years. [LOE 2A] (See Table 1: Guidelines for Surveillance for Head and Neck Cancer Recurrence) Primary care clinician monitoring is important, since one large study showed diminishing frequency of follow-up by oncologists over time.²⁰

**Surveillance Education**

Recommendation 1.2: It is recommended that primary care clinicians should educate and counsel all patients about the signs and symptoms of local recurrence (LOE=0).

Physicians should educate and counsel patients about the signs and symptoms of recurrence including swelling or sore that does not heal; red or white patch in the mouth; lumps, bumps or masses; persistent sore throat; foul mouth odor independent of hygiene practices; persistent nasal obstruction or congestion; frequent nose bleeds; unusual discharge from the nose; difficulty breathing; double vision; numbness/weakness; ear or jaw pain; difficulty chewing, swallowing or moving the jaw or tongue; blood in saliva or phlegm; loose teeth; ill-fitting dentures; unexplained weight loss and/or fatigue. (http://www.cancer.net/cancer-types/head-and-neck-cancer/symptoms-and-signs) Evaluation of patient-reported
symptoms is essential in detecting a recurrence as early as possible which may impact survival.

SCREENING FOR SECOND PRIMARY CANCERS
(Table 2: Guidelines for Screening and Early Detection of Second Primary Cancers)

Recommendation 2.1: It is recommended that primary care clinicians (a) Should screen patients for other cancers as they would in the general population by adhering to the ACS Early Detection Recommendations (cancer.org/professionals). (LOE = 0) (b) Should screen patients for lung cancer according to NCCN® recommendations for annual lung cancer screening with low-dose CT for high-risk patients (all HNC survivors, particularly HPV-negative survivors). (LOE = 2A) (c) Should screen patients for another head and neck and esophageal cancer as they would for patients of increased risk. (LOE = 0)

Approximately 23% of HNC survivors will develop one or multiple SPCs. The organs at highest risk are head and neck, lung, and esophagus,21 [LOE IIA] accounting for 89% of SPC. Approximately 20% will develop one, 3% will develop 2, and less
than 1% will develop 3 SPC. The risk of SPC has increased since 1975 for all sub-sites of the primary HNC with notable exception of oropharyngeal cancer.\textsuperscript{22} Since 1991 there has been a decline in SPC risk for patients with index oropharyngeal cancers.\textsuperscript{22} As more HPV-associated oropharyngeal cancer has been prevalent since 1990. Patients with the index HNC of hypopharynx and larynx are more likely to develop a SPC in the lung, while those with index HNC in oral cavity or oropharynx are more likely to get a SPC in other head and neck sites.\textsuperscript{22, 23} \textsuperscript{[LOE IIA]} HNC survivors with a SPC have a very poor prognosis with median survival of 12 months following diagnosis of SPC.\textsuperscript{24} Early detection and aggressive treatment are strategies that might be employed for improving survival.\textsuperscript{23}

Among long-term survivors of HNC beyond 3 years, 15% die within 5 years and 41% die within 10 years. The leading causes of death in this group are late recurrence or second primary HNC (29%), non-head and neck SPC (23%), cardiovascular (21%), and other causes (23%).

Head and neck sites are the second most common site of SPC among HNC survivors accounting for 23% of SPCs.\textsuperscript{21} Head and neck SPCs are associated more with oral cavity and non-HPV-related oropharyngeal cancer.\textsuperscript{23} When the primary care clinician is
concerned about potential recurrence or second head and neck primary cancer, a referral to the specialist should be initiated.

**Lung Cancer**

Lung is the most common site of SPC among HNC survivors (33% of all SPC).²¹ 5% of survivors of HNC will go on to develop a new primary lung cancer.²⁵ This is three times higher than the rate of second primary lung cancers for survivors of lung cancer.²⁵ Survival in this group is worse than in the overall population of patients with lung cancer. [LOE IIA] Patients with hypopharyngeal and laryngeal cancer are at higher risk of developing second primary lung cancer compared to other head and neck sites. [LOE IIA]

Currently guidelines for lung cancer screening recommend low dose non-contrast chest computed tomography (LDCT) for individuals aged 55 to 74 years who have a history of smoking 30-packs/year, and have quit smoking within the last 15 years, or who have a history of smoking 20-packs/year and one additional risk such as prior HNC. Currently, the NCCN® guidelines recommend chest imaging for surveillance of HNC survivors as clinically indicated.
Esophageal Cancer

The esophagus is the third most common site of SPC\textsuperscript{19, 21} and is most commonly associated with oral cavity, oropharyngeal, and hypopharyngeal cancer. The risk of SPC in the esophagus is declining in HNC survivors. Routine surveillance imaging for second primary esophageal cancer among HNC survivors is not recommended. [LOE 0] In patients who have new onset of esophageal dysphagia symptoms following completion of HNC treatment, esophageal evaluation with transnasal esophagoscopy (TNE) under local anesthesia should be performed by a head and neck surgeon or gastroenterologist [LOE II-A]. Findings on esophagoscopy include 4\% rate of esophageal carcinoma in addition to peptic esophagitis (63\%), stricture (23\%), candidiasis (9\%), Barrett -esophagitis (8\%), and gastritis (4\%).\textsuperscript{26}

ASSESSMENT & MANAGEMENT OF PHYSICAL AND PSYCHOSOCIAL EFFECTS OF HEAD AND NECK CANCER AND TREATMENT

(Table 3: Summary of Potential Long-Term and Late Effects of Head and Neck Cancer and its treatment by Treatment Type)

The risk of physical long-term and late effects following therapy for HNC is associated with several factors, including: a) type
of treatment, b) duration and dose of treatment(s) (increasing cumulative dose and duration of therapy increases the potential risk), c) specific type of chemotherapy, and d) age of patient during treatment. Modalities of treatment include surgery, radiation therapy, chemotherapy, and targeted therapy. Primary care clinicians should refer to the patient’s cancer treatment summary, if available, for specific drugs and doses (See Recommendation 5.1).

The treatment of HNC creates severe pain and disability both temporary and permanent. This can manifest in many ways including loss of saliva, pain, dysphagia, sleep difficulty, obstructive sleep apnea, weight loss, and loss of work. Pretreatment psychological status and caregiver support play a significant role in the magnitude of distress during and after treatment. It is critical that surveillance of the psychological status from both survivor and caregiver’s perspective be assessed. In addition, the impact on the survivor’s financial status, family responsibilities, and support for the survivor impacts the patient’s posttreatment psychological status.

Table 3 lists potential physical and psychosocial long-term and late effects associated with surgery, radiation and chemotherapy. Long-term effects are medical problems that develop during active
treatment and persist after the completion of treatment; whereas, late effects are medical problems that develop or become apparent months or years after treatment is completed. While varying levels of evidence exist to demonstrate the presence of these effects during survivorship, there is limited information on the time interval or prevalence in the posttreatment phase among survivors. The guidelines combine evidence with expert consensus to assist primary care clinicians in managing HNC survivorship. Recommendations for the assessment and management of specific physical and psychosocial long-term and late effects most commonly experienced by HNC survivors are detailed in Table 4.

(Table 4: Guidelines for Assessment and Management of Physical and Psychosocial Long-term and Late Effects of Head and Neck Cancer and Its Treatment)

PHYSICAL EFFECTS: MUSCULOSKELETAL AND NEUROMUSCULAR

Accessory Nerve Palsy

Recommendation 3.1: It is recommended that primary care clinicians should refer patients with accessory nerve palsy resulting from post-
radical neck dissection to physical and/or occupational therapy to improve range of motion and ability to perform daily tasks. (LOE = IA)

Damage to the spinal accessory nerve (SAN) and subsequent perturbation of shoulder motion is a major cause of shoulder dysfunction and pain in HNC. Preservation of the SAN during modified radical neck dissection (MRND) has been associated with improved shoulder function. One study demonstrated denervation and neurogenic compromise of the SAN at 4 to 6 months postoperatively in all groups of patients who underwent neck dissection including radical neck dissection (RND), MRND, and selective neck dissection (SND). Electromyographic activity of the upper trapezius and middle trapezius is significantly decreased compared with the unaffected side in patients who have undergone neck dissection. Mild upper limb dysfunction was reported by 54%, moderate by 15%, and severe by 8%, while only 23% reported no issues. Patients with SAN should be referred to physical therapy to strengthen the affected shoulder girdle muscles, improve or maintain range of motion, and to improve overall function. Patients with impaired ability to perform activities of daily living (ADLs) should be referred to physical and/or occupational therapy.
**Cervical Dystonia/ Muscle Spasms/ Neuropathies**

Recommendation 3.2: It is recommended that primary care clinicians
(a) Should assess patients for cervical dystonia, which is characterized by painful dystonic spasms of the cervical muscles and can be caused by neck dissection, radiation, or both. (LOE = 0) (b) Should refer patients to physical therapy for primary treatment if cervical dystonia or neuropathy is found. (LOE = 0) (c) Should prescribe nerve stabilizing agents such as pregabalin, gabapentin, and duloxetine or Botulinum toxin Type-A injections into the affected muscles for pain management and spasm control as indicated. (LOE = 0, IIA)

Painful dystonic spasms of the cervical muscles are common in HNC survivors. The sternocleidomastoid (SCM) (if preserved), scalene, and trapezius muscles are most often involved. This painful condition is best termed cervical dystonia but is different clinically and pathophysiologically from the cervical dystonia that results from central nervous system disorders and degenerative conditions. Cervical dystonia in HNC patients can result from neck dissection that disrupts the cervical anatomy and damages the cervical plexus and nerve roots. Subsequent uncontrolled ectopic activity in these
neural structures causes painful spasms in the muscles they innervate. The condition may worsen as scarring progresses. Radiation to the neck can cause progressive fibrosis of the nerve roots and plexus as well as any peripheral nerves and muscles in the radiation field with adverse effects on these structures that further exacerbate propensity for painful spasm. The effect of spasm and progressive radiation fibrosis can lead to severe neck contracture. Radiation fibrosis syndrome is the clinical manifestations of progressive tissue fibrosis that results from radiation.\textsuperscript{30}

Radiation treatment techniques can impact side effects. A prospective, randomized study comparing the outcomes and toxicities of intensity-modulated radiotherapy (IMRT) vs. conventional two-dimensional radiotherapy (2D-CRT) for the treatment of nasopharyngeal carcinoma reported the percentage of patients with neck fibrosis as 2.3\% following IMRT and 11.3\% following 2D-CRT.\textsuperscript{31} The mean follow-up was 42 months (range 1-83 months). Another study evaluating late toxicity following conventional radiation in nasopharyngeal carcinoma found that 169 of 771 patients (22\%) had neck fibrosis.\textsuperscript{32}

No definitive diagnostic criteria are available for the diagnosis of neck fibrosis making it difficult to accurately ascertain incidence
rates. The signs and symptoms of cervical dystonia in HNC include pain and spasm with tenderness to palpation in the SCM, scalene, and/or trapezius muscles.\textsuperscript{30} Other muscles such as the pectoralis major muscles and cervical paraspinal (paraspinous) muscles may be involved. Restricted range of neck motion is common. Patients may occasionally demonstrate torsion dystonia such as torticollis.\textsuperscript{30}

The primary treatment modality for cervical dystonia is physical therapy. Emphasis is on neuromuscular re-education, proprioceptive retraining, myofascial release, lymphedema management, and restoration of range of motion. A life-long exercise program should be encouraged to maintain function. Nerve stabilizing agents such as pregabalin, gabapentin, and duloxetine may be added to control neuropathic pain and spasm. Opioids may be necessary in severe cases.

Botulinum toxin has both analgesic and muscle relaxing properties.\textsuperscript{33} While several formulations of botulinum toxin are FDA approved for the treatment of cervical dystonia, there is little data on the use of botulinum toxin to treat radiation-induced cervical dystonia or cervical dystonia associated with neck dissection. Botulinum toxin type-A has demonstrated efficacy in treating radiation-induced cervical dystonia in HNC patients in a small
A smaller retrospective review demonstrated improvement of cervical disability scores (33 to 23; \( p=0.01 \)) in six HNC cancer patients who were injected with botulinum toxin type-A (BTX-A) into the SCM and three patients who were injected into the pectoralis major pedicle flap. Another small study demonstrated the efficacy of BTX-A infiltration in alleviating muscle spasms in pectoralis major flaps following reconstruction of HNC patients. BTX-A may also be useful in alleviating the neuropathic pain associated with neck dissection in HNC patients.

**Shoulder Dysfunction**

Recommendation 3.3: It is recommended that primary care clinicians (a) Should conduct baseline assessment of patient shoulder function posttreatment and continue to assess ongoing complications or worsening condition. (LOE = IIA); (b) Should refer patients to physical therapy for improvement to pain, disability and range of motion where shoulder morbidity exists. (LOE = IA)

Shoulder pain and dysfunction are present in as many as 70% of patients following neck dissection. While there are many contributing factors to shoulder pain and dysfunction, the primary cause is likely damage to the SAN from neck dissection.
Perturbation of shoulder motion from weakness of the trapezius and other denervated shoulder girdle muscles can lead to rotator cuff tendonitis and adhesive capsulitis. Radiation therapy can also damage the SAN and other neuromuscular structures. The clinical manifestations of radiation may take months or years to develop. Clinicians should assess shoulder function following HNC treatment and continue to assess patients for emerging pain or functional impairment.

HNC survivors with shoulder pain and dysfunction should be referred to physical therapy. Progressive resistance training (PRT) for HNC cancer patients with SAN neurapraxia/neurectomy related shoulder dysfunction seems to be better than standard physical therapy in a small randomized controlled trial in terms of improving active shoulder external rotation (p=0.001), shoulder pain (p=0.38), and overall score for shoulder pain and disability (p=0.045). HNC survivors with SAN damage and shoulder dysfunction who underwent a PRT program were found to have significantly reduced shoulder pain and disability (p = .001) as well as improved upper extremity muscular strength (p < .001) and endurance (p = .039) compared with those who underwent a standardized therapeutic exercise protocol.
A Cochran Review concluded that there was limited evidence that PRT is more effective than standard physical therapy for shoulder dysfunction in patients treated for HNC in terms of improving pain, disability, and ROM at the shoulder joint but not sufficient evidence to conclude that QOL is improved.\textsuperscript{40, 41, 42, 43}

\textit{Trismus}

Recommendation 3.4: It is recommended that primary care clinicians (a) Should refer patients to physical therapy, speech language pathologists, and dental professionals to prevent and treat trismus. (LOE = 0); (b) Should prescribe nerve stabilizing agents to combat pain and spasms, which may also ease physical therapy and stretching devices. (LOE = IIA)

Trismus is defined as the inability to fully open the mouth. Quantitatively a \( \leq 35\)mm cut-off point for defining trismus has a sensitivity of 0.71 and a specificity of 0.98.\textsuperscript{44} Other studies have validated the \( \leq 35\)mm cut-off point for defining trismus.\textsuperscript{45} The 3-finger test is a quick clinical surrogate (where trismus is suspected
in any patient who cannot place 3 vertically stacked fingers between the incisors).

Trismus is a common complication of the treatment of HNC and has a deleterious impact on QoL in this population.\textsuperscript{46} Patients with trismus may have difficulty with eating, speaking, maintaining oral hygiene, being examined for cancer recurrence, engaging in oral intimacy, and a variety of other important aspects of daily life. One study found the incidence of trismus in pretreatment was 9\% and 28\% 1-year posttreatment, when defined as a maximum inter-incisor opening (MIO) \(\leq 35\text{mm}\).\textsuperscript{47} The highest incidence of trismus (38\%) was found 6 months after treatment. Patients with tonsillar tumors were most likely to develop trismus.\textsuperscript{47} Another study demonstrated that about half of patients who underwent primary treatment for oral or oropharyngeal cancer developed trismus (MIO <36mm) and reported problems opening the mouth, dental occlusion, eating, drinking, dry mouth, voice, or speech.\textsuperscript{48} Trismus in patients treated for oral and oropharyngeal cancer is strongly associated with clinical T stage (Tis/T1-2 35mm, T3-4 24mm), radiotherapy (no 30mm, yes 27mm) and type of primary surgery (primary closure 38mm, soft tissue flaps 30mm, composite flaps 24 mm).\textsuperscript{49}
Physical therapy is often primary treatment for trismus; however, trismus due to HNC is difficult to treat with physical therapy alone.\textsuperscript{50} A combination of physical therapy and stretching with a Therabite\textsuperscript{®} appliance has been shown to slow progression of trismus in patients with nasopharyngeal carcinoma after radiotherapy.\textsuperscript{51}

Nerve stabilizing agents such as pregabalin, gabapentin, and duloxetine may be helpful in treating neuropathic pain and spasm associated with radiation-induced trismus. Opioids may be added as second line agents in select cases.\textsuperscript{30} Botulinum toxin type A showed benefit as an adjunctive treatment for select neuromuscular and musculoskeletal complications of radiation fibrosis syndrome (RFS) related to cancer treatment including trismus in a small retrospective case series.\textsuperscript{30}

PHYSICAL EFFECTS: GENERAL

The physical effects and consequences of treatment are highly prevalent in HNC survivors and complicated by aging, comorbid issues, and lack of close surveillance and management.

*Dysphagia/Aspiration/Stricture*
Recommendation 3.5: It is recommended that primary care clinicians (a) should refer patients presenting with complaints of dysphagia, postprandial cough, unexplained weight loss, and/or pneumonia to an experienced speech-language pathologist for instrumental evaluation of swallowing function to assess and manage dysphagia and possible aspiration. (b) Should recognize potential for psychosocial barriers to swallowing recovery, and refer patients to appropriate clinician if barriers are present.; (c) Should refer patients with stricture to a gastroenterologist or head and neck surgeon for esophageal dilation. (LOE = IIA)

*Dysphagia*

Persistent or chronic dysphagia in HNC survivorship is a challenging clinical problem. The type, severity, and risk of dysphagia vary depending on the site of HNC and treatment regimen. Chronic dysphagia is relatively infrequent in patients who were treated with small field single modality surgery or radiation for early stage (T1-T2 N0) HNC, but is frequently encountered after multimodality treatment for advanced stage HNC. Even in modern practice with highly conformal radiotherapy (eg, IMRT) and less invasive surgical techniques (eg, transoral surgery) it is estimated
that almost half of patients treated with multimodality therapy for locoregionally advanced stage disease suffer some degree of chronic dysphagia.\textsuperscript{52} Psychosocial barriers and sensory changes such as altered taste may also interfere with oral intake in HNC survivorship.

\textbf{Aspiration}

Dysphagia in HNC survivors is most commonly characterized by inefficiency moving a solid food bolus through the mouth or pharynx, but in more severe cases may result in chronic aspiration. Aspiration typically occurs when drinking liquids. Primary care clinicians should be alert to a high risk of subclinical ("silent") aspiration. More than 50\% of chronic aspirators after HNC treatment do so silently with no outward cough or symptom of airway entry.\textsuperscript{53, 54, 55} Silent aspiration is only detected and effectively treated using instrumental swallowing studies (eg, the videofluoroscopic swallow study – also known as the modified barium swallow, or the fiberoptic endoscopic evaluation of swallow). Aspiration detected on instrumental testing is an independent predictor of pneumonia in cancer survivorship,\textsuperscript{56} and can be lessened with training in individualized (typically straightforward) compensatory techniques by a speech language pathologist. On the basis of numerous level II-A studies, it is
recommended that patients presenting with complaints of dysphagia, postprandial cough, unexplained weight loss, and/or pneumonia be referred to an experienced speech-language pathologist for instrumental evaluation of swallowing function to assess and manage dysphagia and possible aspiration. Early recognition and referral is recommended.\textsuperscript{57, 58, 59} Time posttreatment is a significant, negative predictor of response to swallowing therapy. Sudden onset or rapidly progressing dysphagia may be a symptom of locoregional tumor recurrence or second primary HNC; primary care clinicians refer to the head and neck surgeon to rule out new disease.

\textit{Stricture}

Risk of stricture (structural narrowing of the pharynx and/or esophagus) occurs in 7\% in patients treated with head and neck radiotherapy based on a meta-analysis pooling over 4,700 patients treated with a variety of radiotherapy techniques using single or multi-modality treatment regimens for HNC. Higher risk groups include those treated with IMRT who had 16\% risk of stricture in the meta-analysis, perhaps explained by differences in dose distributions at the esophageal inlet.\textsuperscript{60} Risk of stricture is also higher
among patients treated with total laryngectomy (19%).⁶¹ Most
treatment-related strictures are effectively managed by esophageal
dilation. Serial dilation is often required for long-term management.
Solid food dysphagia, difficulty belching/vomiting, and pharyngeal
sticking are common symptoms of patients with stricture. Based on
numerous level IIA studies, it is recommended that patients with
striction be referred to a gastroenterologist or head and neck
surgeon for esophageal dilation. Videofluoroscopy should be
considered as the first-line referral for patients with suspected
striction because of the high degree of co-existing physiologic
dysphagia.

**Gastroesophageal Reflux Disease (GERD)**

Recommendation 3.6: It is recommended that primary care clinicians
should (a) Should monitor patients for developing or worsening
GERD, as it prevents healing of irradiated tissues and is associated
with increased risk of HNC recurrence or second primary. (b) Should
counsel patients on an increased risk of esophageal cancer and the
associated symptoms. (c) Should recommend proton pump inhibitors
or antacids, sleeping with a wedge pillow or 3-inch blocks under the
head of the bed, not eating or drinking fluids for 3 hours before
bedtime, tobacco cessation and limiting alcohol intake. (d) Should refer patients to a gastroenterologist if symptoms are not relieved by common treatments. (LOE = IIA)

Gastroesophageal reflux is a very common in HNC survivors. With compromise of the airway from treatment modalities, strictures of the hypopharynx, dysphagia with silent or apparent aspiration, and swelling of the aerodigestive anatomy, reflux during the daytime or sleep can worsen these already challenging problems. If symptoms of reflux are present or persist with common remedies prior to treatment, endoscopy by a gastroenterologist might be indicated. Reflux can also injure the teeth by damaging the enamel.

**Lymphedema**

Recommendation 3.7: It is recommended that primary care clinicians (a) Should assess patients for lymphedema using the National Cancer Institute’s Common Toxicity Criteria for Adverse Events (CTCAE) v.4.03, endoscopic evaluation of mucosal edema of the oropharynx and larynx, tape measurements, sonography, or external photographs. (b) Should prescribe primary treatment of manual lymphatic drainage (MLD). If compression bandaging can be tolerated, it can also be used for treatment. (LOE = IIA)
Secondary lymphedema is a common late effect of the treatment of HNC. This is often underdiagnosed and neglected complication and can develop both externally (face, neck, chest) or internally (larynx, pharynx, oral cavity). Lymphedema not only has adverse cosmetic and psychosocial consequences but can cause infections, breathing or swallowing difficulties, or a variety of other profound sequelae.\textsuperscript{62}

There are few studies to determine the incidence of head and neck lymphedema in HNC patients. In one study of 81 HNC patients, 75.3\% (61 of 81) were found to have some form of late effect secondary lymphedema. Of those 9.8\% (6 of 61) had isolated internal lymphedema (IL) and 39.4\% (24 of 61) had isolated external lymphedema (EL). 50.8\% (31 of 61) had combined EL/IL.\textsuperscript{63}

The severity of IL and EL in HNC patients has been found to be associated with physical and psychosocial symptoms.\textsuperscript{64} Patients with more severe EL are more likely to have decreased neck rotation.\textsuperscript{64} The more severe combined EL and IL is associated with hearing impairment and decreased QoL.\textsuperscript{64} Several factors were found to be associated with the presence of secondary EL and IL in HNC patients including: (1) tumor location with EL (p = .009) and combined EL/IL (p = .032); time since end of HNC treatment with EL (p = .004) and
combined EL/IL ($p = .005$); (3) total dosage of radiation therapy ($p = .010$) and days of radiation ($p = 0.17$) with the presence of combined EL/IL; (4) radiation status of the surgical bed with the presence of IL, including surgery with postoperative radiation ($p = .030$) and salvage surgery in the irradiated field ($p = .008$); and (5) the number of treatment modalities used with EL ($p = .002$), IL ($p = .039$) and combined EL/IL ($p = .004$).  

There are no standard diagnosis criteria for head and neck lymphedema in HNC patients making it challenging to diagnose. Methods that have been used include (a) the National Cancer Institute’s (NCI) *Common Toxicity Criteria for Adverse Events* (version 4.03), (b) endoscopic evaluation of mucosal edema of the oropharynx and larynx, (c) tape measurements, (d) sonography, and (e), external photographs.  

There are no trials demonstrating the efficacy of isolated manual lymphatic drainage (MLD) in the management of lymphedema of the head and neck in HNC patients. Despite this, MLD remains the standard of care. One trial has demonstrated the efficacy of sequential therapy of MLD and compression garments.  

A large cohort of 700 HNC survivors suggests 60% response to complete decongestive therapy combining MLD and compression.
Compression garments, however, can be poorly tolerated and customization may be required for routine use.\textsuperscript{62}

\textit{Fatigue}

Recommendation 3.8: It is recommended that primary care clinicians (a) Should follow NCCN\textsuperscript{®} guidelines for monitoring and treating cancer-related fatigue. (b) Should recommend interventions according to fatigue score including: counseling, strategies for management, pharmacologic and nonpharmacologic interventions. (LOE = 0)

The fatigue these patients experience is the same as in most cancer patients and increase with multimodal therapy. This can interfere with recovery especially in the first year. Treatment with medication (ie, amphetamines) is frequently used although the level of evidence has not been well studied.

Cancer-related fatigue is very common among those treated for cancer, especially those who undergo treatment with radiation therapy and chemotherapy.\textsuperscript{67} For some, fatigue lasts long after treatment and can significantly interfere with QoL. Treatable causes of fatigue include anemia, thyroid dysfunction, and cardiac dysfunction.\textsuperscript{14} For those who do not have an identifiable physical
cause of fatigue (ie, anemia), contributing factors, such as mood disorders, sleep disturbance, and pain, should be addressed.\textsuperscript{14} A regular exercise regimen can reduce fatigue, help patients feel better physically and emotionally and help them cope.\textsuperscript{14, 68} Cognitive behavioral therapy may also lessen fatigue.\textsuperscript{69, 70} There are minimal data to support use of pharmacologic agents for management of fatigue in this population.\textsuperscript{14} Interventions should be tailored to the needs and abilities of the individual HNC survivor.

ASCO has more detailed information on the management of fatigue for cancer survivors (http://www.instituteforquality.org/screening-assessment-and-management-fatigue-adult-survivors-cancer-american-society-clinical).\textsuperscript{14}

\textit{Sensory Late Effects}

Recommendation 3.9: It is recommended that primary care clinicians (a) Should refer patients to appropriate specialists for loss of taste, and refer to dietary counseling for assistance in additional seasoning of food, avoiding unpleasant food, and expanding dietary options. (b) Should refer patients to appropriate specialists for loss of hearing related to treatment. (LOE = IIA)
Taste

Dysgeusia, or altered taste, is among the most common and burdensome acute toxicities of head and neck radiotherapy.\textsuperscript{71, 72} Dysgeusia is dependent on dose and volume of the irradiated tongue.\textsuperscript{73, 74} Taste disturbance is most pronounced around 2 months after the end of radiotherapy, and partial recovery is expected over the course of years. No pharmacological therapy is proven effective for dysgeusia in HNC survivors. Collectively, level III evidence suggest significant burden of taste disturbance early after HN radiotherapy with negative implications on QOL and oral intake in survivorship. Refer patients for dietary counseling for assistance with food seasoning, selection, and expansion of food choices in the setting of taste disturbance.

Ototoxicity

HNC survivors with a history of ototoxic drug exposure (eg, cisplatin >100 mg/m\textsuperscript{2}) are at risk for chronic, potentially progressive sensorineural hearing loss.\textsuperscript{75} Ototoxic agents first affect the high-frequency range (frequencies above those needed for
speech processing). For this reason, hearing loss may not be detected until it progresses to the lower frequency range and interferes with routine communication. Hearing loss may also occur from local effects of surgery or radiotherapy. Treatment related hearing loss can progress over time. Late neurotoxic effects of both cytotoxic agents and radiotherapy on the cochlear nerve, over and above normal age-related hearing loss, are implicated as the source of progressive hearing loss years after initial treatment in long-term HNC survivors. On the basis of level III studies, it is recommended that HNC survivors with hearing loss be referred to an audiologist. Proactive baseline and on treatment ototoxic monitoring is favored for early recognition and management of hearing loss. Complete audiologic examination includes tympanometry, pure tone testing (air conduction and bone conduction), speech reception threshold and word recognition testing, and distortion product otoacoustic emissions. Audiologic intervention may include education to reduce noise exposure or fitting of hearing aids.

**Trouble Sleeping/Sleep Apnea**

Recommendation 3.10: It is recommended that primary care clinicians (a) Should screen patients for sleep disturbance using
Insomnia Severity Index, Clinical Sleep Assessment, and Patient-Reported Outcome Measurement Information System. (b) Should assess patients for snoring and ask partner about symptoms of sleep apnea. (c) Should refer patients to a sleep specialist for a sleep study (polysomnogram) if sleep apnea suspected. (d) Should manage sleep disturbance similar to patients in the general population. (e) Should recommend nasal decongestants, nasal strips, and sleeping in the propped-up position to reduce snoring and mouth-breathing. Room cool mist humidifiers can aid sleep as well by keeping the airway moist. (f) Should test fit of dentures to ensure proper fit, and counsel patients to remove them at night to avoid irritation. (LOE = 0)

Obstructive sleep apnea (OSA) is a common abnormality in patients being treated for HNC. Swelling of the airway occurs in most of these patients. Reconstructive techniques especially flaps replacing the posterior tongue can compromise the airway even after a tracheostomy is removed. Primary radiation or chemoradiotherapy can create long term swelling of the tongue and larynx. Recognition of any preexisting airway difficulties should be assessed, as these patients will be especially at risk.
The complications of OSA include hypoxia, hypertension, cardiac arrhythmias, and cardio-pulmonary stress. It can lead to myocardial infarction, pulmonary hypertension, heart failure, and stroke. Sleep deprivation from the consequences of apnea will create excessive fatigue, daytime drowsiness, and cognitive difficulties. OSA can amplify recovery difficulties in HNC survivors.

Interventions can include: referral to behavioral therapy, education, exercise, complementary therapy (eg, aromatherapy, guided imagery), and possible managed pharmacologic interventions.

Speech/Voice

Recommendation 3.11: It is recommended that primary care clinicians (a) Should assess patients for speech disturbance. (LOE = 0) (b) Should refer patients to an experienced speech language pathologist if communication disorder exists. (LOE = IA, IIA)

Speech, voice, and/or resonance disturbance may alter understandability or acceptability of verbal communication in HNC survivorship. New or progressive hoarseness or dysarthria can indicate new cancer, and should be first evaluated by the head and
neck surgeon. While rare (prevalence <5%), de novo radiation-associated lower cranial neuropathies may cause delayed speech or voice deterioration in long-term survivors (eg, typically nerve XII palsy causing dysarthria, and nerve X causing dysphonia).\textsuperscript{80, 81} Behavioral voice/speech therapies and prosthetic rehabilitation options should be considered. On the basis of a two level IA RCTs and various level IIA studies, HNC survivors with communication disorders should be referred to a speech pathologist for assessment and management of speech, voice, and resonance disturbance. Early assessment and intervention is preferred.\textsuperscript{82, 83} Prosthetic rehabilitation is, in certain clinical scenarios, supported by numerous level IIA studies. Tracheoesophageal (TE) voice using a valved voice prosthesis optimizes QoL and intelligibility of speech after a total laryngectomy.\textsuperscript{84} TE prostheses are managed by speech pathologists. Prosthetic obturators fabricated by maxillofacial prosthodontists can improve speech resonance in patients with palatal defects, and palatal drop prostheses can improve articulation after subtotal or total glossectomy.\textsuperscript{85} Prosthetic rehabilitation can be costly and outcomes are highly dependent on familiarity of the provider (level 0), thus referring clinicians are encouraged to seek expert teams for these specialty services.
Hypothyroidism

Recommendation 3.12: It is recommended that primary care clinicians (a) Should evaluate patient thyroid function by measuring thyroid stimulating hormone (TSH) every 6-12 months. (LOE = III)

In patients whose treatment has included radiotherapy of the neck, hypothyroidism is a significant and frequent permanent sequela. Hypothyroidism can occur as early as 4 weeks and as late as 10 years following treatment with a median time to hypothyroidism of 1.8 years.86 Following radiotherapy the prevalence is 20% at 5 years and 27%-59% in 10 years (depending on the technique of RT)86, 87, 88 Following surgery the prevalence is 7% at 5 years and 39% at 10 years.88 [LOE III] Radiotherapy to both sides of the neck increase the risk of hypothyroidism as does the addition of surgery, or when surgery involves the thyroid.86 [LOE III].

PHYSICAL EFFECTS: ORAL HEALTH

Close oral and dental surveillance of the HNC survivor is critical. Although chemotherapy for any type of cancer can cause oral side effects acutely as well as long-term, HNC patients frequently must undergo both chemotherapy and radiation for the
best survival rates, which create a cumulative effect on the oral physiology causing a more severe reaction even in the face of maximum prophylactic care.

The oral changes that will occur are greatly affected by the patient’s oral and dental pretreatment status. Comorbid states that will potentially increase the severity of oral side effects must be considered. General nutritional status, diabetes, alcohol abuse, tobacco use, and general health status must be assessed. Pretreatment assessment and treatment for abnormalities are mandatory. During adjuvant treatment, there will be a need for intensive evaluation, prophylactic care, and careful surveillance for side effects.

The main issues to be evaluated include dental caries, gingival status, periodontal abnormalities, oral mucosal health, taste, production of saliva, pain from mucositis, and ability to initiate swallowing.

Ongoing and diligent attention to oral health is essential in HNC survivors previously treated with radiation therapy. Many of the effects of radiotherapy to the head and neck may endure throughout the survivor’s lifetime and present clinically challenging situations that necessitate ongoing communication and collaboration between
primary care clinicians and dental professionals. Dental specialists with sufficient training and experience with HNC patients provide optimal oral care for these patients. The dental specialist should be included from the time of diagnosis to prevent and treat dental complications that arise. Treatment side effects include neurosensory alteration, loss of saliva and taste, and other functional changes. Oral and dental infections are not uncommon especially in patients receiving either radiation or chemotherapy. Osteonecrosis is rare, but a devastating side effect of treatment. Pretreatment assessment of dental status and treatment of preexisting dental and gingival disease can prevent osteonecrosis.

**Oral and Dental Surveillance**

Recommendation 3.13: It is recommended that primary care clinicians (a) Should request written instructions from the dental professional. (b) Should counsel patients that preventive care can help reduce caries and gingival disease, and to maintain close follow-up with the dental professional. (c) Should counsel patients to avoid tobacco, alcohol (including mouthwash containing alcohol), spicy or abrasive foods, extreme temperature liquids, sugar
containing chewing gum or sugary soft drinks, and acidic or citric liquids. (c) Should refer patients to an oral surgeon for extractions and consideration for hyperbaric oxygen treatment both pre- and post-extraction. (LOE = 0)

Instructions should include: a) Brushing with a very soft toothbrush and using dental floss after each meal; b) Daily fluoride treatments using prescription 1.1% sodium fluoride toothpaste as a dentifrice or in customized delivery trays; c) Exercises to prevent trismus and loss of oral excursion; d) Timing and frequency of visual examinations, a check on dental occlusion, dental cleanings by a dental hygienist, dental X-rays, and inspection for recurrence and/or new oral primary cancers.

Caries
Recommendation 3.14: It is recommended that primary care clinicians (a) Should counsel patients to seek regular professional dental care for routine examination and cleaning, and immediate attention to any intraoral changes that may occur. (b) Should counsel patients to minimize intake of sticky and/or sugar-containing food and drink to minimize risk of caries. (c) Should counsel patients on dental prophylaxis including brushing, the use of
dental floss, and fluoride use (prescription fluoride toothpaste and or dental trays). (LOE = 0)

Head and neck cancer survivors are at increased risk of dental caries secondary to disruption of salivary flow and composition as well as direct damage to dental structures from treatment (eg, chemotherapy-associated vomiting). Close monitoring of dental and oral health should continue as long as salivary flow is reduced or salivary composition is abnormal as caries can progress rapidly with these changes.

**Periodontitis**

Recommendation 3.15: It is recommended that primary care clinicians (a) Should examine patient teeth for visible signs of plaque and calculus, especially on the lingual surface of the mandibular anterior teeth and in between molar teeth. (b) Should refer patients to a dentist or periodontist for thorough evaluation. (c) Should counsel the patient to seek regular treatment from and follow recommendations of a qualified dental healthcare professional and reinforce that proper examination of the gingival attachment is a normal part of ongoing dental care. (LOE = 0)
Early intervention for changes in the lining of the mouth or teeth may prevent more serious complications.

Loss of gingival attachment within the radiation field can lead to subsequent dental infections, loss of teeth, and osteonecrosis, which can become a systemic health issue.\textsuperscript{90} This condition can go unnoticed by the patient as it is not usually painful and signs of advancement cannot be readily detected upon visual examination of the oral cavity. Rapid deterioration of the supporting structures of the teeth is sometimes seen following head and neck radiation therapy and may lead to deep periodontal pockets that can subsequently lead to infection or tooth loss.\textsuperscript{91} This situation can increase the risk of osteoradionecrosis, a devastating complication with loss of the jawbone requiring debridement, hyperbaric oxygen treatments, and eventually reconstruction. Pre- and post-extraction hyperbaric oxygen treatments from a certified facility should be considered if a tooth extraction becomes necessary. Management of advancing periodontal disease requires intervention and ongoing management by a qualified dental professional.

\textit{Xerostomia}
Recommendation 3.16: It is recommended that primary care clinicians (a) Should encourage use of alcohol-free rinses if patient requires mouth rinses. (b) Should counsel patients to consume a low-sucrose diet, avoid caffeine, spicy and highly acidic foods. (c) Should encourage patients to avoid dehydration by drinking fluoridated tap water, but explain that consumption of water will not eliminate xerostomia. (d) Should refer patients to psychosocial support who are unable to practice swallowing or complete behavioral therapies. (LOE = 0)

One major issue affecting most HNC survivors treated with radiation therapy is xerostomia or reduction in salivary flow. While some salivary gland tissue can be spared with newer techniques, dry mouth complications should still be expected. The direct effect of ionizing radiation on the salivary glands may be transient or permanent and is dependent upon a variety of factors including location of the primary tumor, the total amount of radiation received by the salivary glands, any other oncology treatments (eg, chemotherapy), comorbidities, and current medications. Patients who experience surgical ablation of the salivary glands or associated ducts will most often present with a lifetime of salivary hypofunction. While the condition may affect QoL, the effects of
xerostomia can have catastrophic effects on the dental and oral health and subsequently the patient’s general health.

Saliva, in its appropriate composition, offers many necessary protective benefits to dentition and oral homeostasis. Salivary changes, whether resulting in dry mouth or thick ropey saliva, compromises these protective features and can result in increased incidence of dental caries, sensitivity of non-decayed teeth, attrition and erosion of the dentition, mucosal injury, dysgeusia and hypogeusia, inability to wear dental prostheses, and increased incidence of oral infection. Primary care clinicians should not consider the presence of some saliva as resolution of the dry mouth issue and should refer patients complaining of thick or ropey saliva to a dental specialist trained to manage such conditions. Patients with decreased salivary flow are candidates for rapid development of cervical and interproximal dental caries, many of which cannot be easily detected upon simple visual inspection of the oral cavity until the condition is advanced.

Xerostomia can create great difficulty in wearing dentures or dental appliances. Xerostomia increases the likelihood of mucosal injury from loss of proper dental occlusion or even rough foods.
Primary care clinicians should rely upon the skills of a dental professional to procure and review dental radiographs to properly assess the presence or risk for such dental caries to potentially avoid costly restorations, and the possibility of tooth loss and its associated risks in this population. Late stage dental caries can quickly advance to a dental infection or abscess and become a systemic health risk if not adequately and properly treated. Dental pain may be a late symptom, therefore, patients should be educated about subtle dental signs or symptoms, such a strange taste or gum swelling.

**Osteonecrosis**

Recommendation 3.17: It is recommended that primary care clinicians (a) Should monitor patients for swelling of the jaw, indicating possible osteonecrosis, from 6 months to 2 years post-RT.; (b) Should administer conservative treatment protocols, such as antibiotics and daily saline irrigations for early-stage lesions. (c) Should consider hyperbaric oxygen therapy for early and intermediate lesions. (LOE = 0)

Osteonecrosis occurs usually from dental complications, lack of proper dental care, and tooth extraction. Radiotherapy to the oral cavity and salivary glands increases the risk of osteonecrosis.
Osteoradionecrosis can become a serious condition and disease progression may ultimately lead to pathologic mandible fracture. Early osteoradionecrosis may manifest itself as small areas of intraoral exposed mandible. Early management of the condition with antibiotics, appropriate dental care by a dentist, and hyperbaric oxygen treatment can prevent disease progression. Referral to head and neck surgeon is recommended as treatment may require debridement of necrotic bone while undergoing conservative management. External mandible bony exposure through the skin is recommended to be immediately referred to the care of head and neck surgeon.

*Oral Infections/Candidiasis*

Recommendation 3.18: It is recommended that primary care clinicians (a) Should refer patients to a qualified dental professional for treatment and management of complicated oral conditions and infections. (b) Should consider systemic fluconazole and/or localized therapy of clotrimazole troches to treat oral fungal issues. (LOE = 0)

Oral antibiotics for any systemic infection will increase the likelihood of fungal overgrowth and infection in the oral cavity. This
must be considered by the primary care clinician anytime antibiotics are contemplated.

There are many aerobic, anaerobic, and facultative anaerobic Gram-positive and Gram-negative bacteria that exist as part of the normal flora of the oral cavity. With treatment-related mucositis and ultimately xerostomia, the normal bacterial flora of the mouth is disturbed\textsuperscript{95} resulting frequently in fungal overgrowth in the oral and hypopharyngeal areas, which may cause aggravation or recurrence of mucositis during or after treatment and present as a red or gray membrane that may easily bleed and be very painful. This mucositis may be aggravated by preexisting dental and gingival disease and may make eating and swallowing very difficult. Although pain medicine will likely be necessary, topical and or systemic treatments that may be necessary include antibacterial and antifungal medications.

There are instances when oral candidiasis presents in an erythematosus form that is almost invisible upon visual inspection of the oral cavity. Patients with this form will often complain of a burning or scalding sensation on the tongue and the oral mucosa with little or no clinical manifestation visibly apparent. Similarly, patients presenting with persistent angular cheilitis may be
suffering from an underlying untreated fungal infection, which can be resolved with proper anti-fungal therapy.

With an increasingly painful mouth, patients may become reluctant to maintain proper dental hygiene. Light use of a very soft dry toothbrush, and irrigation with recommended alcohol-free rinses may be of benefit until a normal hygiene routine can resume. Dental consultation is indicated if resolution does not occur. Treatment with systemic fluconazole or topical therapy with clotrimazole troches may be recommended. Commonly prescribed nystatin may not necessarily be the preferred treatment for these cases since the drug is administered in suspension with high sugar content. Regular administration of a high sugar solution in a xerostomic mouth is contraindicated due to the risk of increased dental caries.

If a patient wears a denture or dental appliance, it must be treated simultaneously with the mouth to avoid reinfection. Similarly, the patient should be instructed to change the toothbrush and remove the very end of any lip balm stick or lip cosmetics applicator.

Oral infections are not solely due to fungal species. While herpes simplex viruses 1 and 2 have not been shown to reactivate specifically by oropharyngeal radiation, if immunosuppressive
agents are used, reactivation may occur.\textsuperscript{94} Bacterial infections may be encountered due to the high population of cariogenic and periodontal bacterial pathogens that are normally present in the oral cavity. Proper management of infections of any kind is especially important in HNC survivors.

PSYCHOSOCIAL EFFECTS

Psychosocial long-term and late effects in HNC survivors require awareness and management from both the specialist and the primary care clinician.

Health-related QoL (HRQoL) concerns include altered eating, speech, aesthetics, social disruption, depressive symptoms and general health. In one study of HNC survivors, even among the highest functioning group, social disruption was reported at 80.8% and depressive symptoms at 71.5%. Disruption of the control of daily life can lead to feelings of diminished self and subsequent negative psychosocial impacts.\textsuperscript{97}

Body and Self-Image

Recommendation 3.19: It is recommended that primary care clinicians (a) Should assess patients for body and self-image
concerns. (LOE = IIA); (b) Should refer for psychosocial care as indicated. (LOE = IA)

Head and neck cancer and its treatment may change both body appearance and alter the HNC survivor’s perception of self. These concerns may decrease QoL outcomes related to sexual function; intimacy and social role disturbances. Such concerns when blended with possible physical changes may also contribute to employment and financial challenges.98

Prevalence of body image concerns and diminished self-perception among HNC survivors is high. Fingeret et al99 studied body image in 280 HNC patients undergoing surgical interventions and found that younger HNC patients were at a higher risk for body image concerns. Approximately 75% of HNC patients surveyed felt “concerned or embarrassed” by body changes after diagnosis. 50% had frequent thoughts about appearance changes; 38% reported avoiding social activities and 33% had behavioral concerns regarding grooming. Importantly, 69% indicated dissatisfaction with information provided by clinicians related to body image.

In a meta-analysis, Lang et al97 found that diminished sense of self was associated with impairments in functions, alterations to
self-beliefs in one’s destiny, encounters of rejection and injustice and self-blame for the disease.97

Distress/Depression/Anxiety

Recommendation 3.20: It is recommended that primary care clinicians (a) Should assess patients for distress, depression and/or anxiety periodically (3 months posttreatment and at least annually) ideally using a validated screening tool. (b) Should offer in-office counseling and/or pharmacotherapy and/or refer to appropriate psycho-oncology and mental health resources as clinically indicated if signs of distress, depression, or anxiety are present. (c) Should refer patients to mental health specialists for specific QoL concerns, such as to social workers for issues like financial and employment challenges or to addiction specialists for substance abuse. (LOE = I)

Many cancer survivors report ongoing difficulties in recovery and returning to “normal” following treatment.1,100,2 Some survivors of cancer experience fear of recurrence101 contributing to significant mental health problems for which they already have an increased risk, including distress, depression, and anxiety.102,103 Prevalence estimates for anxiety, depression, and distress in cancer survivors
are widely variable, the result of inconsistency in the use of measurement tools and differences in methodological approaches, such as the choice of comparators from the general population. However, among cancer survivors generally, the estimated prevalence of anxiety and depression is 17.9% and 11.6%, respectively.\textsuperscript{104}

Distress for HNC patients is prevalent and includes worry, anxiety, sadness, emotional concerns\textsuperscript{105}, social disruption\textsuperscript{98}, fear of recurrence and posttraumatic distress disorder.\textsuperscript{106} In one study, Lydiatt et al\textsuperscript{107} reported that HNC patients had a rate of 15 to 50% for depressive disorders compared to 15-25% prevalence for cancer patients generally. Buchmann et al\textsuperscript{105} studied distress in 89 HNC patients and found that 75% reported emotional concerns and over 50% acknowledged feelings of worry. In a study by Devins et al\textsuperscript{108} (n = 774 HNC patients), the most commonly reported reasons for distress were interpersonal relationships, uncertainty and interference in activities. HNC patients also identified distress related to disease and treatment, stigma and existential stress with moderate frequency. Fear of recurrence is also a concern among HNC survivors since the risk of recurrence and/or second primaries for HNC survivors is high at 36%.\textsuperscript{109}
To provide timely and appropriate support for patients with a history of HNC, primary care clinicians should be familiar with the mental health concerns they may experience, the tools to screen for and assess these problems, and the resources to care for patients. (See Table 7: Validated Tools to Assess for Distress/Depression/Anxiety)

The NCCN® Guidelines for Distress Management provide an algorithm for distress and depressive orders (DIS-6). The NCI also publishes a PDQ Guideline for care of depression (http://www.cancer.gov/about-cancer/coping/feelings/depression-pdq). The American Psychosocial Oncology Society website (http://www.apos-society.org/) can help primary care clinicians identify resources for patients.

HEALTH PROMOTION
(Table 5: Guidelines for Health Promotion)

Information
Recommendation 4.1: It is recommended that primary care clinicians (a) Should assess the information needs of the patient related to
HNC and its treatment, side effects, other health concerns, and available support services. (b) Should provide or refer patients to appropriate resources to meet these needs. (LOE = 0)

The information needs of HNC survivors and caregivers should be routinely assessed and information about the long-term and late effects of HNC treatment, as well as information on risk reduction and health promotion, should be provided. Resources that may be beneficial to share with patients include the ACS Survivorship Center website (cancer.org/survivorshipcenter), the ACS website, Journey Forward (journeyforward.org), the ASCO survivor and caregiver site (cancer.net), and the NCCN patient and caregiver resources (http://www.nccn.org/patients/default.aspx). Community-based organizations and patient advocacy groups often have helpful information for your local community.

**Healthy Weight**

Recommendation 4.2: It is recommended that primary care clinicians (a) Should counsel patients to achieve and maintain a healthy weight. (LOE = III) (b) Should counsel patients on nutrition strategies to maintain a healthy weight for those at risk for cachexia. (LOE = 0) (c) Should counsel patients if overweight or
obese to limit consumption of high-calorie foods and beverages and increase physical activity to promote and maintain weight loss. (LOE = IA)

The ACS Nutrition and Physical Activity Guidelines for Cancer Survivors are a resource for all cancer survivors, and the guidelines include recommendations to address the unique needs of HNC survivors. HNC survivors experience significant, highly visible facial disfigurement and notable treatment-induced problems with eating, swallowing, breathing, and speech. HNC survivors may also experience loss of taste and smell, excessive dry mouth, and other deficits of functioning in the oral cavity. These effects of treatment can be debilitating for patients as they may negatively impact appearance, communication, and ability to eat. As a result, HNC survivors may have difficulty gaining, and maintaining a healthy weight. Avoiding wasting should be a primary aim of health promotion with these patients.

Primary care clinicians should intervene early to address eating issues, swallowing problems, and pain management to help HNC survivors maintain a healthy weight.

*Physical Activity*
Recommendation 4.3: It is recommended that primary care clinicians should counsel patients to engage in regular physical activity consistent with the ACS guideline and specifically: (a) Should avoid inactivity and return to normal daily activities as soon as possible following diagnosis (LOE = III); (b) Should aim for at least 150 minutes of moderate or 75 minutes of vigorous aerobic exercise at least 2 days per week. (LOE = I, IA); (c) Should include strength training exercises at least 2 days per week. (LOE = IA)

Approximately 32% of cancer survivors meet the recommendations for physical activity. HNC survivors should be advised to return to normal daily activities as soon as possible following diagnosis and continue to engage in regular physical activity. HNC survivors should strive to exercise at least 150 minutes moderately or 75 minutes vigorously per week and include strength training exercises at least 2 days per week, as is recommended for the general population.\textsuperscript{68}

Few studies have focused specifically on strategies to help HNC survivors meet recommended physical activity guidelines. HNC introduces unique and debilitating problems that may inhibit survivor’s ability to meet recommended levels of exercise. McNeely et al\textsuperscript{110} conducted a randomized controlled trial in which HNC
survivors were assigned to either a 12-week progressive resistance exercise training program or a standardized therapeutic exercise program meant to address should pain and dysfunction. The results indicated generally good adherence to the resistance program (91%), although the authors acknowledge that the generalizability of study findings to community-based settings is limited. Independent predictors of reduced adherence included having received more extensive neck dissection procedures and daily alcohol consumption. Higher adherence was associated with HNC survivors who had undergone nerve-sparing neck dissection and who were not regular drinkers.

Other studies have also found that higher levels of alcohol consumption interfere with adherence to self-care behaviors in non-cancer populations. The authors recommend that tailored interventions to increase exercise should address alcohol use and other unhealthy behaviors (eg, smoking). Primary care clinicians are also encouraged to note the degree of neck dissection treatment patients have received, recognizing there may be added problems with adherence among those who received radical neck dissection, compared to those who underwent modified or selective neck dissection. Attention should be paid to anxiety, depression, and
QoL, which also emerged as significant predictors of poorer exercise adherence. In lieu of an acceptable level of HN-specific studies, primary care clinicians are encouraged to rely upon research with survivors of other cancer when counseling patients of HNC around physical activity.

**Nutrition**

Recommendation 4.4: It is recommended that primary care clinicians (a) Should counsel patients to achieve a dietary pattern that is high in vegetables, fruits, and whole grains, and low in saturated fats, sufficient in dietary fiber and limited in alcohol consumption. (LOE = IA, III) (b) Should refer patients with nutrition-related challenges (eg, swallowing problems that impact nutrient intake) to a registered dietician or other specialist. (LOE = 0)

According to most sources, about 75% of all head and neck cancers are related to tobacco and alcohol use. Thus, in addition to encouraging healthful eating, it is particularly important to emphasize limiting alcohol to no more than 2 drinks per day for men or 1 drink per day for women.

Dietary counseling should take into account common functional problems that impact eating in HNC survivorship (eg, dry mouth, dysphagia, taste disturbance). Patients with dysphagia have
particular difficulty consuming vegetables and whole grains and more easily eat high calorie foods. Patients with nutrition-related challenges such as dry mouth, taste disturbance or swallowing problems that impact nutrient should be referred to a registered dietitian for assessment and personalized dietary counseling. Primary care clinicians should be aware that trouble with eating can result from multiple sources, and lead to social isolation, depression, and other negative health consequences. Some of these sources include: dysphagia, stricture, dental extractions, trismus, xerostomia, taste disturbance, or psychological issues. Refer according to the source of eating problems.

**Tobacco Cessation**

Recommendation 4.5: It is recommended that primary care clinicians should counsel patients to avoid tobacco products and offer or refer to cessation counseling and resources. (LOE = I)

Tobacco use is implicated in approximately 85% of HNC incident cases. While a large proportion of HNC patients will attempt to quit smoking before or during treatment, 14-60% will relapse. Continued smoking is associated with a number of negative outcomes including increased risk of other
smoking-related illnesses (eg, coronary artery disease) as well as higher rates of SPCs and recurrence of the original primary cancer.\textsuperscript{117, 118, 119} In addition, smoking reduces treatment efficacy\textsuperscript{120, 121}, worsens treatment side effects,\textsuperscript{122, 123, 124, 125} and, ultimately, negatively impacts QoL, morbidity, and mortality.\textsuperscript{126, 117} Due to the numerous medical and psychosocial advantages of smoking cessation, primary care clinicians should encourage and support patients to quit or maintain abstinence.

Berg et al\textsuperscript{127} found that, after controlling for a number of demographic and psychosocial variables, depression was a significant predictor of continued smoking among HNC survivors, even more important than hope, QoL, and social support. In fact, among cancer survivors who continued to smoke, the rates of depression where much higher (63.8\%), compared to only 26.7\% among those who quit smoking after cancer diagnosis. Other research supports this finding – depressed smokers are 40\% less likely to quit than smokers who are not depressed. Continued post-surgery abstinence has been associated with lower levels of depression among HNC survivors.\textsuperscript{128} Collectively, these results suggest that primary care clinicians should pay keen attention to depressive symptoms in HNC survivors attempting to maintain
abstinence from smoking. When counseling patients primary care clinicians are encouraged to emphasize the negative consequences of smoking on medical and psychosocial outcomes.\textsuperscript{127}

Timing of cessation appears to be critically important – in a study by Simmons et al\textsuperscript{129}, only 13% of the patients who were abstinent before surgery relapsed whereas there was a 60% relapse rate among those patients who reported smoking in the week prior to cancer surgery. What’s more, there were different predictors of relapse for these two groups. Among those who quit smoking before surgery, higher perceived difficulty and lower cancer-related risk perceptions predicted smoking relapse. For those who smoked before surgery, the biggest predictors were lower quitting self-efficacy, higher depression, and greater fears of cancer recurrence. Thus, primary care clinicians should encourage early cessation at diagnosis, address potential barriers to maintain abstinence (eg, quitting self-efficacy), and continue to provide support in order to promote long-term success of cessation efforts.

The majority of these recommendations for primary care clinicians are consistent across all forms of HNC. However, it should be noted that there are important differences between survivors of HPV-related and non-HPV related HNC. Overall prognosis is worse
among current or former smokers with HPV-related cancers, and they may be at increased risk for recurrence compared to HPV-related survivors who never smoked, therefore encouraging survivors of HPV-related cancers to quit using tobacco products support survival outcomes.

**Personal Oral Health**

Recommendation 4.6: It is recommended that primary care clinicians (a) Should counsel patients to maintain regular dental care including frequent visits to dental professionals, early interventions for dental complications, and meticulous oral hygiene. (b) Should test fit of dentures to ensure proper fit, and counsel patients to remove them at night to avoid irritation. (c) Should counsel survivors that nasal strips can reduce snoring and mouth-breathing, and that room humidifiers and nasal saline sprays can aid sleep as well. (LOE = 0)

Much has been said previously in this article about the importance of oral health in HNC survivors. (See Physical Effects: Oral Health section) It should be noted that the primary care clinician should emphasize the importance of meticulous dental hygiene practices at home in addition to regularly scheduled dental visits, as the patient is the one on the front line of dental and oral
health. Patients should not discontinue the use of prescription fluoride until instructed to do so by the dental professional. Patients are often lulled into a false sense of security that once any moisture reappears in the mouth following treatment that everything is fine. This is most often not the case as the first saliva to return following head and neck radiation therapy is not protective to the teeth or the oral mucosa.

If the patient is edentulous or partially edentulous and wears removable appliances such as a denture or partial denture, it is important that proper fit be evaluated on a regular basis. Many HNC survivors with edentulous areas will experience a remodeling of the supportive ridge for the appliance, causing the denture to become loose and ill-fitting, and rub the gums, tongue, or oral mucosa to the point of ulceration. Dentures or partials still in good repair may be relined by the dental professional to improve fit. The patient should be encouraged to take the appliances out overnight to give the oral tissues a rest and prevent nocturnal bruxing if the dentures are ill-fitting. The dentures should be kept moist while out of the patient’s mouth.

Mouth breathing can exacerbate xerostomia, recurrent oral mucositis, and oral infections, not to mention descanting of the teeth
and rapid advancement of dental caries. Dentulous patients who mouth breathe with notice a more rapid formation of dental plaque and calculus. Efforts should be made to facilitate nasal respiration. Patients using a CPAP or other similar device to treat sleep apnea should be aware that vigilant attention to dental and oral health is of the utmost importance to avoid caries leading to abscesses that could develop into risks of osteoradionecrosis.

Patients should also be trained to do at-home head and neck self-evaluations and be instructed to report any suspicions or concerns immediately.

CARE COORDINATION AND PRACTICE IMPLICATIONS

(Table 6: Guidelines for Care Coordination and Practice Implications)

There are no clear guidelines for the shared care and co-management of patients with HNC after the completion of active treatment. The time for optimal transition is unknown and should be based on the individual risk profile, the treating clinician’s expertise and resource restraints. HNC survivors may continue to see the oncology team for follow-up disease surveillance; however, they should also be seen by the primary care clinician for health
maintenance and management of comorbidities that may or may not be related to cancer diagnosis and treatment.\textsuperscript{130, 131}

\textit{Survivorship Care Plan (SCP)}

Recommendation 5.1: It is recommended that primary care clinicians should consult with the oncology team and obtain a treatment summary and SCP. (LOE = 0, III)

Survivorship care plans are recommended as an important tool to facilitate communication and allocation of responsibility during the transition from active treatment to survivorship care.\textsuperscript{4, 132} A summary of a patient’s diagnosis and treatment received should be provided by the oncology team when a patient with HNC transitions care to other providers; a treatment summary should describe the type and stage/side of the cancer, type of surgery, the name of the chemotherapy/hormones/biologics and cumulative doses of chemotherapy and the types and cumulative doses of radiation therapy, including the fields and extent of the radiation\textsuperscript{4, 133} Patients can initiate the building of a survivorship care plan process on the ASCO website: http://www.cancer.net/survivorship/follow-care-after-cancer-treatment/asco-cancer-treatment-and-survivorship-

Ideally, the oncology team should also work with the patient to develop an individualized cancer survivorship care plan that provides recommendations for the type and timing of follow up scans, laboratory tests, and office visits. The care plan should include information on the risk for late effects of treatment and what to watch for specifically based on the type of cancer and treatment received. Patients should be assessed for the presence of these physical and psychosocial effects and be referred to the appropriate providers and services as indicated in the recommendations in prior sections.

Communication with Other Providers

Recommendation 5.2: It is recommended that primary care clinicians (a) Should maintain communication with the oncology team throughout the patient’s diagnosis, treatment and posttreatment care to ensure care is evidence-based and well-coordinated. (LOE = 0) (b) Should refer patients to a dentist to provide diagnosis and treatment of dental caries, periodontal disease, and other intraoral conditions including mucositis and oral infections and communicate
with the dentist on follow-up recommendations and patient education. (c) Should maintain communication with specialists referred to for management of comorbidities, symptoms, and long-term and late effects. (LOE = 0)

Communication and cooperation among providers and HNC survivors is critical, with the oncology team providing concrete recommendations for care when needed or requested by other providers. Clear communication regarding the respective roles of different members of the healthcare team is critical to a successful transition to survivorship care.

The primary care clinician should serve as a general medical care coordinator throughout the spectrum of cancer detection and aftercare, focusing on evidence-based preventive care and the management of preexisting comorbid conditions, regularly addressing the patient’s overall physical and psychosocial status, making appropriate referrals for psychosocial, rehabilitative, or other specialist care as needed, and coordinating those components of survivorship care that are agreed upon with the treating clinicians. Treatment of HNC is complex, and, therefore, decisions about and coordination of cancer treatment should be left to the oncology team.
Inclusion of Caregivers

Recommendation 5.3: It is recommended that primary care clinicians should encourage the inclusion of caregivers, spouses, or partners in usual HNC survivorship care and support. (LOE = 0)

Caregivers have to cope with the physical aftermath of the survivors’ treatment and help manage long-term and late effects, in addition to the caregiver’s own psychosocial and physical unmet needs. \(^{134}\) Research has shown that for 14-24 months after a survivor’s cancer diagnosis, caregivers provide consistent, continuing care involvement \(^{135}\) for patients following breast cancer treatment. Successful coordination of care involves not only a comprehensive care team, including primary care clinicians, but also the informal caregivers (usually the spouse/partner/family member) who provide ongoing care to cancer survivors in the home. \(^{136}\) Furthermore most caregivers are older adults who are also managing health problems. When possible, primary care clinicians should include caregivers of HNC survivors in all follow-up care appointments to optimize survivor wellness.
LIMITATIONS

A significant limitation of this guideline is the limited evidence-base to provide clear and specific recommendations for the prevention and management of long-term and late effects of cancer survivors. There are few prospective, randomized controlled trials testing interventions among HNC survivors. The majority of the citations characterizing the risk and magnitude of risk of late effects and management recommendations rely predominantly on case-control studies with fewer than 500 participants and reviews that combine studies with varying outcome measures. There were several cohort studies that used population-based data to estimate the risk of late effects.

Another limitation is the reliance on previous guidelines for surveillance and symptom management. Additionally, the literature review was not managed by a clinical epidemiologist due to limited resources; and instead was conducted by project staff and an ACS librarian. Furthermore, the guidelines did not result directly from the development of specific clinical questions asked prior to the literature review; and guidelines included in the literature review were not evaluated through an instrument such as the Rigor of Development subscale of the Appraisal for Guidelines for Research
and Evaluation (AGREE II). Recommendations are based on current evidence in the literature, but most evidence is not sufficient to warrant a strong recommendation. Rather, recommendations should be largely seen as possible management strategies given the current limited evidence base.

**SUMMARY**

Head and neck cancer survivors face potentially significant impacts of cancer and its treatment and deserve high-quality, comprehensive, coordinated clinical follow-up care. Primary care clinicians must consider each patient’s individual risk profile and preferences of care to address physical and psychosocial impacts. Patients should be provided support to address fear of recurrence, depression, anxiety, cognitive impairment, body image issues, sexual concerns, functional changes and physical impairments, relationship changes, other social role difficulties, employment concerns, and financial challenges, among others. HNC survivors also need to be counseled on health promotion strategies to minimize and mitigate long-term and late effects, ameliorate comorbid health conditions and to potentially increase survival.
To clarify the roles of all clinicians working with cancer survivors, we concur with the IOM that cancer survivors and primary care clinicians receive a survivorship care plan, which includes a concise summary of treatment as well as a clinical follow-up care plan. Ideally, this plan would be constructed in partnership with the survivor to identify and prioritize goals for survivorship care and would be communicated to the patient to ensure understanding of individual risks; recommended tests, procedures and supportive care strategies; and how to optimize wellness. Survivorship care should be coordinated with treating cancer specialists.

RESOURCES

In addition to this guideline, tools and resources are available to assist primary care clinicians in implementing these recommendations. The CA Journal offers the CA Patient Page (Wiley insert URL) to help patients understand how to use this guideline to talk to the primary care clinician about surveillance and screening, symptom management, healthy behaviors and care coordination. The Survivorship Center also offers The GW Cancer Institute’s Cancer Survivorship E-Learning Series for Primary Care Providers (The E-Learning Series), a free, innovative online continuing
education program to educate primary care clinicians about how to better understand and care for survivors in the primary care setting. Continuing education credits are available at no cost to physicians, nurse practitioners, nurses and physician assistants for each 1-hour module. Learn more about The E-Learning Series at cancersurvivorshipcentereducation.org.

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