



# American Head and Neck Society - Journal Club

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### Survivorship, Supportive Care & Rehabilitation Service Edition

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**Table of Contents** – [click the page number to go to the summary and full article link.](#)

<i>Head and Neck Cancer Survivorship Care: A Review of the Current Guidelines and Remaining Unmet Needs</i>	<i>page 1</i>
<i>Prevention of Depression with Escitalopram in Patients Undergoing Treatment for Head and Neck Cancer Randomized, Double-blind, Placebo-Controlled Clinical Trial</i>	<i>page 2</i>
<i>Impact of positron emission tomography/computed tomography surveillance at 12 and 24 months for detecting head and neck cancer recurrence</i>	<i>page 3</i>
<i>Long-term toxicities in 10-year survivors of radiation treatment for head and neck cancer</i>	<i>page 5</i>
<i>Systematic Review of the Impact of Cancer Survivorship Care Plans on Health Outcomes and Health Care Delivery</i>	<i>page 6</i>

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### **[Head and Neck Cancer Survivorship Care: A Review of the Current Guidelines and Remaining Unmet Needs](#)**

*Nguyen NA, Ringash J*

*from **Current Treatment Options in Oncology**, July 2018*

A larger proportion of patients with head and neck cancers (HNC) are now surviving, constituting up to 3% of all cancer survivors. This is likely due in part to the increase in HPV-related oropharyngeal cancers affecting younger individuals and with a better prognosis and to the improved outcomes of other HNCs as well over the last two decades. Most studies have previously been focusing on improving risk stratification, treatment and disease-related outcomes. Over the last decade, there has been an evolving interest in the field of survivorship care. Despite the collaborative efforts from a multidisciplinary team in managing cancer and treatment-related side-effects and in improving survivors' overall quality of life (QOL), it has been reported that up to 60–65% of patients have at least one unmet need. The purpose of this article is to review current guidelines for HNC survivorship care and identify areas of unmet need. Over the last 5 years, multiple groups have published guidelines describing survivorship care issues and their possible management. Although a very comprehensive and informative first initiative, multiple issues need to be further evaluated. These include how to best support patients and their partners' fear of



cancer recurrence, to provide coordinated care among all physicians, to identify and meet patients' needs in local multidisciplinary teams and to institute measures to ensure every individual's access to high-quality patient-centered care. Furthermore, experts may consider engaging in further dialog with primary care physicians (PCP) to improve sharing of survivorship care. More should be learned about PCPs' comfort levels in providing such care and whether further steps are required to facilitate a seamless transition of care and accessibility to specialized care as needed.

#### Summary statements

- There is increasing interest in formalized survivorship care in patients with head and neck cancer
- The prevalence of survivors of head and neck cancer has increased due to improved therapies and increase in HPV-related oropharyngeal cancer
- Three survivorship guidelines for patients with head and neck cancer have recently been published.
- Unmet needs remain and optimal model for survivorship is not yet clear

#### Strengths

- Comprehensive review of 3 recent survivorship guidelines: the American College of Surgeons guideline, Cancer Care Australia guideline and United Kingdom National Multidisciplinary Guideline.
- Clear table comparing the recommendations of each guideline
- Addresses future challenges

#### Weaknesses

- Despite lengthy review of each guideline, practical advice of implementation and best practices is lacking
- While there is acknowledgement of the infancy of the field of survivorship in patients with head and neck cancer, the conclusions simply point to the need for future studies.

[back to top](#)

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## [Prevention of Depression With Escitalopram in Patients Undergoing Treatment for Head and Neck Cancer Randomized, Double-blind, Placebo-Controlled Clinical Trial](#)

*Lydiatt WM, Bessette D, Schmid KK, Sayles H, Burke WJ.*

*From JAMA Otolaryngology – Head & Neck Surgery, July 2013*

**Importance:** Major depressive disorder develops in up to half the patients undergoing treatment for head and neck cancer, resulting in significant morbidity; therefore, preventing depression during cancer treatment may be of great benefit.

**Objective:** To determine whether prophylactic use of the antidepressant escitalopram oxalate would decrease the incidence of depression in patients receiving primary therapy for head and neck cancer.

**Design, Setting, and Participants:** A randomized, double-blind, placebo-controlled trial of escitalopram vs placebo was conducted in a group of nondepressed patients diagnosed as having head and neck cancer who were about to enter cancer treatment. Patients were stratified by sex, site, stage (early vs advanced), and primary modality of treatment (radiation vs surgery).

**Main Outcome and Measure:** The primary outcome measure was the number of participants who developed moderate or greater depression (scores on the Quick Inventory of Depressive Symptomology–Self Rated of  $\geq 11$ ).



**Results:** From January 6, 2008, to December 28, 2011, 148 patients were randomized. Significantly fewer patients receiving escitalopram developed depression (24.6% in the placebo group vs 10.0% in the escitalopram group; stratified log-rank test,  $P = .04$ ). A Cox proportional hazards regression model compared the 2 treatment groups after controlling for age, baseline smoking status, and stratification variables. The hazard ratio of 0.37 (95% CI, 0.14-0.96) demonstrated an advantage of escitalopram ( $P = .04$ ). Patients undergoing radiotherapy as the initial modality were significantly more likely to develop depression than those undergoing surgery (radiotherapy compared with surgery group; hazard ratio, 3.6; 95% CI, 1.38-9.40;  $P = .009$ ). Patients in the escitalopram group who completed the study and were not depressed rated their overall quality of life as significantly better for 3 consecutive months after cessation of drug use.

**Conclusions and Relevance:** In nondepressed patients undergoing treatment for head and neck cancer, prophylactic escitalopram reduced the risk of developing depression by more than 50%. In nondepressed patients who completed the trial, quality of life was also significantly better for 3 consecutive months after cessation of drug use in the escitalopram group. These findings have important implications for the treatment of patients with head and neck cancer.

#### Summary Statements:

- Depression rates are high in patients being primarily treated for head and neck cancers.
- Compared to surgery, patients undergoing radiation therapy have a 3.6 increased likelihood of developing depression.
- Prophylactic escitalopram can mitigate the risks of developing depression in all patients being treated for head and neck cancer.
- Adverse events from taking escitalopram are low and most patients tolerate the medication very well.
- Patients taking escitalopram during therapy had significantly improved quality of life even 3 months after stopping the medication.

#### Strengths

- This was a randomized controlled, double blinded, placebo controlled trial
- There was a low drop out rate among participants allowing for appropriate comparisons.
- There was a low risk profile for taking the drug itself making adoption of its use in all patients a reasonable option.

#### Weaknesses

- The study was closed early due to slower than expected accrual and only 125 evaluable subjects out of the planned 150 patients were included in the study.
- Approximately 50% of the patients screened (298) declined to participate, due to unwillingness to take a study medicine and lack of time as the two main reasons.
- The vast majority of patients were white limiting the generalizability to the greater population.

[back to top](#)

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## [Impact of Positron Emission Tomography/Computed Tomography Surveillance at 12 and 24 Months for Detecting Head and Neck Cancer Recurrence](#)

Allen S. Ho, MD; Gabriel J. Tsao, MD; Frank W. Chen, BA; Tianjie Shen, MD; Michael J. Kaplan, MD; A. Dimitrios Colevas, MD; Nancy J. Fischbein, MD; Andrew Quon, MD; Quynh-Thu Le, MD; Harlan A. Pinto, MD; Willard E. Fee, Jr, MD; John B. Sunwoo, MD; Davud Sirjani, MD; Wendy Hara, MD; and Mike Yao, MD



from *Cancer*, April 2013

**Background:** In head and neck cancer (HNC), 3-month post-treatment positron emission tomography (PET)/computed tomography (CT) reliably identifies persistent/recurrent disease. However, further PET/CT surveillance has unclear benefit. The impact of posttreatment PET/CT surveillance on outcomes is assessed at 12 and 24 months.

**Methods:** A 10-year retrospective analysis of HNC patients was carried out with long term serial imaging. Imaging at 3 months included either PET/CT or magnetic resonance imaging, with all subsequent imaging comprised of PET/CT. PET/CT scans at 12 and 24 months were evaluated only if preceding interval scans were negative. Of 1114 identified patients, 284 had 3-month scans, 175 had 3- and 12-month scans, and 77 had 3-, 12-, and 24-month scans.

**Results:** PET/CT detection rates in clinically occult patients were 9% (15 of 175) at 12 months, and 4% (3 of 77) at 24 months. No difference in outcomes was identified between PET/CT-detected and clinically detected recurrences, with similar 3-year disease free survival (41% vs 46%,  $P = .91$ ) and 3-year overall survival (60% vs 54%,  $P = .70$ ) rates. Compared with 3-month PET/CT, 12-month PET/CT demonstrated fewer equivocal reads (26% vs 10%,  $P < .001$ ). Of scans deemed equivocal, 6% (5 of 89) were ultimately found to be positive.

**Conclusions:** HNC patients with negative 3-month imaging appear to derive limited benefit from subsequent PET/CT surveillance. No survival differences were observed between PET/CT-detected and clinically detected recurrences, although larger prospective studies are needed for further investigation.

### Summary statements

- In a retrospective review of head and neck cancer patients with negative imaging at 3 months post-treatment, routine surveillance PET/CT at 12 months after treatment detects clinically occult disease in 9% of patients. Routine surveillance PET/CT at 24 months after treatment detects clinically occult disease in 4% of patients
- For patients with recurrent disease, there is no difference in outcome between those with recurrence detected by routine surveillance PET/CT or those with recurrence detected because of symptoms/signs of recurrence
- Nearly 75% of recurrences detected by routine surveillance PET/CT imaging at 12 or 24 months post-treatment are distant metastases

### Strengths

- Standard protocol that was applied universally to all patients in the retrospective cohort which increases internal validity
- Addresses clinically relevant question using clinically relevant comparison group (benefit of imaging relative to clinical detection) and clinically relevant outcome (effect of detecting occult disease through surveillance imaging on oncologic outcomes; not just diagnostic performance [e.g. sensitivity, specificity, etc.] of imaging test)
- Includes HPV-positive and HPV-negative patients

### Weaknesses

- Retrospective, single institution study design limits external validity and generalizability of results to other settings, practice patterns, patient populations
- Heterogeneous patient population (primary sites, AJCC stage, treatment modality)



- Limited # of events preventing subgroup analysis to see if specific patient groups may have derived benefit (based on some combination of site/stage/treatment modality)

[back to top](#)

## [Long-term toxicities in 10-year survivors of radiation treatment for head and neck cancer](#)

Dong Y, Ridge JA, Li T, Lango MN, Churilla TM, Bauman JR, Galloway TJ.

from **Oral Oncology**, August 2017

**OBJECTIVES:** To characterize the recognized but poorly understood long-term toxicities of radiation therapy (RT) for head and neck cancer (HNC).

**MATERIALS AND METHODS:** We retrospectively evaluated patients treated with curative-intent RT for HNC between 1990 and 2005 at a single institution with systematic multidisciplinary follow-up  $\geq 10$  years. Long-term toxicities of the upper aerodigestive tract were recorded and assigned to two broad categories: pharyngeal-laryngeal and oral cavity toxicity. Kaplan-Meier estimates and Chi-square tests were used for univariable analysis (UVA). Cox model and logistic regression were used for multivariable analysis (MVA).

**RESULTS:** We identified 112 patients with follow-up  $\geq 10$  years (median 12.2). The primary tumor sites were pharynx (42%), oral cavity (34%), larynx (13%), and other (11%). Forty-four percent received postoperative RT, 24% had post-RT neck dissection, and 47% received chemotherapy. Twenty-eight (25%) patients developed pharyngeal-laryngeal toxicity, including 23 (21%) requiring permanent G-tube placed at median of 5.6 years (0-20.3) post-RT. Fifty-three (47%) developed oral cavity toxicity, including osteoradionecrosis in 25 (22%) at a median of 7.2 years (0.5-15.3) post-RT. On MVA, pharyngeal-laryngeal toxicity was significantly associated with chemotherapy (HR 3.24, CI 1.10-9.49) and age (HR 1.04, CI 1.00-1.08); oral cavity toxicity was significantly associated with chemotherapy (OR 4.40, CI 1.51-12.9), oral cavity primary (OR 5.03, CI 1.57-16.1), and age (OR 0.96, CI 0.92-1.00).

**CONCLUSION:** Among irradiated HNC patients, pharyngeal-laryngeal and oral cavity toxicity commonly occur years after radiation, especially in those treated with chemotherapy. Follow-up for more than five years is essential because these significant problems afflict patients who have been cured.

### Summary statements

- The authors present a relatively large single institution retrospective series of head and neck cancer survivors with follow up of over 10 years with goal of assessing their level of late toxicities related to their therapy. They evaluated patients treated from 1990 to 2005 who underwent definitive multidisciplinary treatment that included radiation as either definitive or adjuvant therapy. Assessment was then made to determine the rate of different oral and pharyngolaryngeal late toxicities with additional evaluation of patient, disease, and treatment factors that may have influence their development.
- Overall, 112 patients were included with the majority of primary sites being in the pharynx and oral cavity. One quarter of patients developed pharyngolaryngeal late side effects with 21% requiring a permanent gastrostomy tube. Forty-seven percent of patients developed oral cavity late toxicity with 22% developing osteoradionecrosis. Of note, many of these severe side effects occurred more than 5 years after completion of the treatment.



- On multivariate analysis, it was noted that both permanent gastrostomy tube dependence and oral cavity toxicity were predisposed by advanced age as well as the addition of chemotherapy to the treatment regimen.
- The authors emphasize the importance of long term follow up to identify and address these late treatment-related side effects.

### Strengths

- A relative large single institution cohort with follow up over 10 years
- A regimented treatment approach as well as a detailed surveillance algorithm

### Weaknesses

- A retrospective review of a heterogenous patient population with an inability to completely control for all treatment and patient-related factors
- The treatment approach during that time period (2D and 3D RT) is less used now that intensity modulated radiation therapy has become more popular
- Those patient who died from their cancer or treatment-related toxicities may have resulted in an under-estimate of the true rate of side effects.

[back to top](#)

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## [Systematic Review of the Impact of Cancer Survivorship Care Plans on Health Outcomes and Health Care Delivery](#)

Paul B. Jacobsen, Antonio P. DeRosa, Tara O. Henderson, Deborah K. Mayer, Chaya S. Moskowitz, Electra D. Paskett, and Julia H. Rowland

*from Journal of Clinical Oncology, July 2018*

**Purpose:** Numerous organizations recommend that patients with cancer receive a survivorship care plan (SCP) comprising a treatment summary and follow-up care plans. Among current barriers to implementation are providers' concerns about the strength of evidence that SCPs improve outcomes. This systematic review evaluates whether delivery of SCPs has a positive impact on health outcomes and health care delivery for cancer survivors.

**Methods:** Randomized and nonrandomized studies evaluating patient-reported outcomes, health care use, and disease outcomes after delivery of SCPs were identified by searching MEDLINE, Embase, PsycINFO, Cumulative Index to Nursing and Allied Health Literature, and Cochrane Library. Data extracted by independent raters were summarized on the basis of qualitative synthesis.

**Results:** Eleven nonrandomized and 13 randomized studies met inclusion criteria. Variability was evident across studies in cancer types, SCP delivery timing and method, SCP recipients and content, SCP-related counseling, and outcomes assessed. Nonrandomized study findings yielded descriptive information on satisfaction with care and reactions to SCPs. Randomized study findings were generally negative for the most commonly assessed outcomes (ie, physical, functional, and psychological well-being); findings were positive in single studies for other outcomes, including amount of information received, satisfaction with care, and physician implementation of recommended care.

**Conclusion:** Existing research provides little evidence that SCPs improve health outcomes and health care delivery. Possible explanations include heterogeneity in study designs and the low likelihood that SCP delivery alone would influence distal outcomes. Findings are limited but more positive for proximal outcomes (eg, information received) and for care delivery, particularly when SCPs are accompanied by





counseling to prepare survivors for future clinical encounters. Recommendations for future research include focusing to a greater extent on evaluating ways to ensure SCP recommendations are subsequently acted on as part of ongoing care.

### Summary Statements

- Although routine SCPs are endorsed, adoption has been limited and there is a perceived lack of evidence that SCPs actually improve outcomes.
- 1399 studies were identified; 24 met inclusion criteria (publication in English, involvement of SCP delivery to cancer survivors and/or their health care providers, and evaluation of patient reported outcomes, health care use or disease outcomes with respect to SCP delivery). There were 11 non-randomized and 13 randomized studies.
- Results of *non-randomized* (sample sizes 10-4021, median 142) studies consisted mainly of descriptive analyses that portrayed positive evaluations of SCP feasibility, survivors' satisfaction with receiving SCPs, and with providing info to SCPs. One study analyzed changes over time of psychological distress scores and found no statistically significant differences between those who received an SCP and those who did not.
- In seven of the *randomized* (sample sizes 41-968, median 224) studies, there were no statistically significance differences across SCP interventions. Four studies reported findings that suggested beneficial effect of SCPS in terms of fewer depressive symptoms, less health worry, greater satisfaction with care, and greater amount of info received. In terms of health care delivery, an additional 5 studies suggested SCP beneficial effects in: greater likelihood of identifying PCP as responsible for follow-up, greater adherence to cardiomyopathy screening, better implementation of SCP recommendations, and more cancer-related contact with PCP. One study depicted adverse effects of SCPs in more symptoms, illness concerns, and emotional impact of illness.

### Strengths

- It appears that this comprehensive review article is the one of the few that has compiled a broader group of cancer patients than what has been published in the past, and evaluates the impact of SCPs on overall cancer care.
- In spite of limitations, the study serves as a launching pad to model and improve future studies. Consistency of SCP content and delivery, quality of methods (ie clear statement of primary and secondary outcomes), specific outcomes that SCPs may influence (proximal vs distal outcomes and relation to timing of SCP delivery), maximizing impact of SCPs, and situating SCP research within the broader context of survivorship care delivery (what should be delivered, who should deliver it {PCP vs oncologist} and what information should be delivered) are a few of the parameters that should be included in future studies.

### Weaknesses

- Only English publications were used
- One SCP study does not reflect all tumor sites; Future studies may have more meaning if sorted by tumor site; eg HNC patients may benefit more from "distal" SCP vs patient with leukemia.
- Inherent methodology precluded quantitative synthesis of existing data, ie this is not a meta-analysis.
- All aspects of SCPs were not evaluated (survivor/provider preferences for content and delivery)