

# Barriers to Adherence to Cancer Treatments Among Head and Neck Cancer Patients

JENNIFER LYNN MILLER, PhD, RN, CMSRN, and  
JULIANNE EVERS, DNP, APRN, AGACNP-BC, CCRN

From Bellarmine University Department of Nursing, Louisville, Kentucky

Authors' disclosures of conflicts of interest are found at the end of this article.

Correspondence to: Jennifer Lynn Miller, PhD, RN, CMSRN, Bellarmine University, 2001 Newburg Road, Louisville, KY 40205  
E-mail: [jmiller2@bellarmine.edu](mailto:jmiller2@bellarmine.edu)

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## Abstract

Head and neck cancer patients often undergo a demanding treatment schedule requiring radiation and chemotherapy. Adherence to these treatment schedules is affected by several issues, including socioeconomic factors, characteristics of the disease and treatment plan, symptoms, and side effects. Oncology advanced practitioners (APs) work directly with patients with head and neck cancer (HNC) during active treatment, often screening for and managing side effects and providing referrals. Evidence-based interventions and innovative strategies for the oncology AP to improve HNC patients' quality of life and treatment adherence include frequent distress screening, AP-led educational interventions and symptom management clinics, and incorporating technology to allow for close contact with patients during treatment.

**H**ead and neck cancer (HNC) includes cancers of the mouth, throat, larynx, nasal cavity, and sinuses. The American Cancer Society (2021a) estimates there were over 54,000 new cases and 10,000 deaths attributed to HNCs in 2021. The most common risk factors for HNC include alcohol and tobacco use, and human papillomavirus (HPV; National Comprehensive Cancer Network [NCCN], 2021). The 5-year relative survival rate for oral cavity and pharynx cancers is 64.1% (Centers for Disease Control and Prevention, 2021).

Treatment options for HNC depend on the primary site, stage, and pathological features, and include surgery, radiation therapy, and/or chemotherapy (NCCN, 2021). Early stage (I or II) disease can be managed with a single modality treatment of surgery or radiation therapy (NCCN, 2021). Approximately 60% of patients present with locally or regionally advanced disease and require a combined modality approach. Often the regimen consists of radiation therapy 5 days a week alongside chemotherapy, usually cisplatin, given every 1 to 3 weeks

and multiple provider visits (NCCN, 2021; Szturz et al., 2019).

Literature reports that HNC patients do not adhere to the radiation treatment schedule in a range of 12% to 57% of the time (Miller et al., 2021; Chang et al., 2020; Naghavi et al., 2016; Ohri et al., 2015; Pujari et al., 2017; Rangarajan & Jayaraman, 2017). In the limited literature available on chemotherapy adherence in this population, between 30% to 60% of HNC patients missed at least one cycle of weekly cisplatin chemotherapy (Iqbal et al., 2017). A review of trials comparing low-dose weekly vs. high-dose cisplatin given every 3 weeks revealed that patients receiving high-dose cisplatin received all planned cycles 61% to 85% of the time (Szturz et al., 2021). Nonadherence to the treatment schedule is related to worse treatment outcomes such as tumor recurrence (Ferreira et al., 2016; Ohri et al., 2016). Missing more than 2 planned treatment days increased the risk of poor locoregional control and disease-free survival by up to fourfold (Ferreira et al., 2016).

Oncology advanced practitioners (APs) are involved in the care and management of HNCs. Oncology nurse practitioners and physician assistants report the majority of their time is spent in patient counseling, prescribing, treatment management, and follow-ups (Bruinooge et al., 2018). They have an important role in identifying patients at risk for nonadherence and assisting them in managing their symptoms. This article reviews the literature related to nonadherence to cancer treatment among people with HNCs and discusses the implications for the oncology AP.

## THE FIVE DIMENSIONS OF ADHERENCE FRAMEWORK

The Five Dimensions of Adherence conceptual framework from the World Health Organization (2003) suggests that adherence is a multidimensional phenomenon, influenced by five sets of factors or dimensions: socioeconomic, health-care team (HCT) and system-related, condition-related, therapy-related, and patient-related. This framework challenges the common misconception in health care that patients are solely responsible for adhering to agreed-upon treatment plans (World Health Organization, 2003). Table 1 provides examples of each dimension.

## CONTRIBUTORS TO NONADHERENCE IN THE HNC POPULATION

While all five dimensions have not been explored in the literature, the dimensions of socioeconomic, systems-related, condition-related, and therapy-related factors have been described among people with HNC. Most of the literature on adherence is retrospective; therefore, it is likely that most patient-related factors, such as the ones listed in Table 1, were not able to be explored in these associations. These important factors should be explored in future prospective studies.

### Socioeconomic Factors

Socioeconomic factors, including some demographic characteristics, are useful to help identify at-risk groups. Some of these factors are not modifiable, so interventions may only include screening and early education. Groups identified at risk for nonadherence among the HNC population include older adults, females, those with lower education levels, and people who experience transportation issues or live far from the treatment site (Miller et al., 2021; Graboyes et al., 2017; Rangarajan & Jayaraman, 2017; Chang et al., 2020; Schwam et al., 2015; Cosway et al., 2017; Thomas et al., 2017; Costas-Muniz et al., 2016).

One study reported that patients over the age of 65 years were more likely to be nonadherent to treatment plans (Chang et al., 2020), while other studies found no significant association between age and adherence (Miller et al., 2021; Ohri et al., 2015; Naghavi et al., 2016).

Race and marital status were examined in relationship to nonadherence to radiation therapy among HNC patients, but no significant associations were reported (Miller et al., 2021; Ohri et al., 2015; Naghavi et al., 2016). One retrospective study identified a significant difference in biological sex related to adherence: females made up only 22% of the study population (N = 262) but accounted for nearly 40% of patients who missed three or more radiation appointments (Miller et al., 2021).

Two studies identified a low level of education to be related to nonadherence but had significant limitations. One study suggested HNC patients that graduated high school were more likely to adhere to the treatment timeline, while the risk of nonadherence increased in the zip codes with lower high

**Table 1. The Five Dimensions of Adherence and Associated Examples**

Dimension	Examples of contributors to nonadherence
Socioeconomic factors	<ul style="list-style-type: none"> <li>• Poverty</li> <li>• Illiteracy</li> <li>• Low level of education</li> <li>• Unemployment</li> <li>• Transportation issues</li> <li>• Lack of support</li> <li>• Age (especially children and the elderly)</li> <li>• Race</li> </ul>
Health-care team and system-related factors	<ul style="list-style-type: none"> <li>• Poor relationship with provider</li> <li>• Poorly developed health services</li> <li>• Lack of or poor health insurance plan</li> <li>• Lack of knowledge and training on disease management and addressing adherence among health-care team</li> <li>• Short consultations</li> <li>• Lack of follow-up or education provided to patients</li> </ul>
Condition-related factors	<ul style="list-style-type: none"> <li>• Symptoms due to disease process</li> <li>• Levels of disability</li> <li>• Progression and severity of disease</li> <li>• Availability of effective treatments</li> </ul>
Therapy-related factors	<ul style="list-style-type: none"> <li>• Complexity and duration of the medical regimen</li> <li>• Side effects</li> <li>• Ability to see benefit from treatment</li> <li>• Medical support</li> </ul>
Patient-related factors	<ul style="list-style-type: none"> <li>• Forgetfulness</li> <li>• Psychosocial stress</li> <li>• Anxiety</li> <li>• Low motivation</li> <li>• Lack of education and understanding about the disease trajectory and treatment</li> <li>• Perceptions that treatment is not necessary, or the disease is not serious</li> <li>• Low expectations</li> <li>• Frustrations with the health-care team</li> <li>• Feeling stigmatized by the disease</li> </ul>

Note. Information from World Health Organization (2003).

school graduation rates (Graboyes et al., 2017). However, in this study, US high school graduation rates were estimated by zip codes. Another study from India that included all cancer populations reported that among 61 nonadherent patients, 51% had only a primary school education and 44% were illiterate (Rangarajan & Jayaraman, 2017).

The last and most significant socioeconomic factor reported in the literature is related to distance from the treatment center and transportation issues. Several studies reported that distance traveled to the treatment center was a barrier or predictive of nonadherence or refusal of radiation therapy or chemotherapy appointments (Chang et al., 2020; Schwam et al., 2015; Cosway et al., 2017; Thomas et al., 2017; Costas-Muniz et al., 2016). These studies relied on subjective reports by patients and families or notes in the electronic health record that

described transportation problems or location of the treatment center as the reason for refusing or missing treatment. One study defined extended distance to travel by living more than 50 miles from the treatment site but did not find a significant association with nonadherence (Miller et al., 2021).

The at-risk groups here can be identified early and offered referrals to social work and other support services such as ride programs, local lodging options, and more. Providing patient and family-centered education at the patient's education level is also important to ensure patients understand the treatment schedule and the importance of adhering to treatment.

### Condition-Related Factors

Condition-related factors that have been examined in the literature include cancer stage and

cancer-related symptoms. Adherence depends on factors related to the disability of the patient (including physical, psychological, social, and vocational considerations), prevalence and severity of symptoms, severity of the disease, and availability of effective treatments (World Health Organization, 2003). Comorbidities such as depression and substance abuse disorders are modifiers of adherence behavior (World Health Organization, 2003). There is more literature available about condition-related factors and nonadherence to treatment among HNC patients than any of the other factors.

Symptoms that interfere with treatment adherence could be condition- or therapy-related factors. Head and neck cancer causes symptom burden in patients, including fatigue, nausea, pain, dysphagia, and respiratory problems (American Cancer Society, 2021b). The cancer and its treatment can also impede patients' abilities to communicate and take oral nutrition. These symptoms can affect the HNC patient's actual and perceived abilities to complete radiation therapy (Edmonds & McGuire, 2007). One retrospective study of 1,095 HNC patients in Taiwan reported that one of the top reasons for missing treatment was due to concerns with treatment side effects (Chang et al., 2020). Coordinating interdisciplinary care, social work referrals, community-based organizations (World Health Organization, 2003), and telephone navigation to check in with patients can help resolve issues to avoid adherence problems (Percac-Lima et al., 2015).

Psychosocial distress appears or increases in the HNC population over the course of radiation therapy (Chen et al., 2018; Sawada et al., 2012). Increased depression scores were related to worse rates of completion of adjuvant therapy in HNC patients undergoing surgery (Barber et al., 2015) and were also related to worse radiation therapy adherence among HNC patients in the US and China (Miller et al., 2021; Chen et al., 2018). Another study examining all cancer populations undergoing radiation therapy found a significant association between missing at least one appointment and distress scores between 7 and 10 out of 10 (Anderson et al., 2019).

Fatigue is one of the most common side effects of radiation therapy, commonly increasing throughout the radiation therapy course and

causing distress among people receiving radiation (Sawada et al., 2012). Patients with HNC had a greater risk of disturbance to their daily functioning due to fatigue compared with other cancers (Poirier, 2011; Sawada et al., 2012). Patients with HNC have also reported sleep and fatigue to be among the top causes of distress during radiation therapy (Badr et al., 2014). Tiredness was a predictor of nonadherence to radiation therapy appointments in one retrospective study; as the score for tiredness increased, so did the likelihood of missing appointments (Miller et al., 2021). Interventions for cancer-related fatigue can be found in Table 2.

Some HNC patients experience a cumulative effect from multiple symptoms, but the health-care team may not recognize this during routine distress screening. In a retrospective study (N = 262), patients who missed three or more radiation appointments rated almost all of their weekly symptoms at higher levels than those who missed two or fewer appointments (Miller et al., 2021). However, even in the nonadherent group, most mean scores were 4 or less out of 10, suggesting that multiple symptoms at a lower level can be distressing enough to interfere with treatment adherence (Miller et al., 2021). Reviewing distress screening results at each administration is important, instead of relying on cutoff scores to signal that the patient may need intervention.

When multiple symptoms are present, HNC patients may also be experiencing symptom clusters. One example of a symptom cluster includes symptoms of pain, dry mouth, lack of appetite, sleep disturbance, fatigue, drowsiness, distress, and sadness (Chiang et al., 2018). Another encompasses nausea, vomiting, numbness, shortness of breath, and difficulty remembering (Chiang et al., 2018). Recognizing symptom clusters can assist the provider in further evaluating the cumulative effect on the patient, their treatment, and their outcomes.

Spiritual well-being was identified as protective against nonadherence; as the patient reported a higher level of spiritual well-being, their chance of being nonadherent to their radiation schedules decreased (Miller et al., 2021). This is an opportunity for the health-care team to encourage patients to practice spiritual care, which can be different for each individual. Supporting a patient's spiritual

care includes discussing the patient's religious or spiritual background, considering the patient's culture and beliefs in the decision-making process, or making referrals to social work or chaplaincy providers (Lee, 2019; Balboni et al., 2014).

### Therapy-Related Factors

Treatment plan recommendations for HNC depend on the size, location, and grade of the primary tumor (NCCN, 2021). Advanced cancer stage has been associated with nonadherence to cancer treatment plans among HNC and other cancer populations (Chang et al., 2020; Rangarajan & Jayaraman, 2017).

Receiving both chemotherapy and radiation therapy modalities concurrently was found to be associated with nonadherence among this population (Chang et al., 2020; Rangarajan & Jayaraman, 2017; Sharma et al., 2016), with one study suggesting that HNC patients receiving concurrent chemoradiation were nearly five times more likely to miss three or more radiation appointments, compared with patients receiving radiation alone (Miller et al., 2021). Concurrent chemoradiation was reported in 58% of HNC patients in a cohort study conducted by radiation oncologists in the Southeastern United States (Naghavi et al., 2016).

Therapy-related factors encompass treatment side effects. Radiation therapy toxicity is a major cause of treatment interruption (Ferreira et al., 2016). Mucositis is one such side effect indicating toxicity. Mucositis is characterized by inflammation of the oral mucosa, which may cause pain and burning sensations, consequently compromising oral intake in the HNC population while undergoing radiation therapy (Siddiqui & Movsas, 2017). In a systematic review of the literature, mucositis was found among 90% to 100% of HNC patients ( $n = 6,181$ ), and 11% of these patients experienced radiation treatment interruptions or modifications due to mucositis (Trotti et al., 2003). Patients with HNC participating in a qualitative study described that mucositis led to worsening oral intake, fatigue, and well-being (Pattison et al., 2015).

Interventions to help reduce or mitigate mucositis include coordinating dental evaluations before the start of treatment and educating the patient against smoking, drinking alcohol, or consuming acidic or spicy foods during treatment

**Table 2. Interventions for Cancer-Related Fatigue**

Assessment	Use of a valid, reliable screening tool for cancer-related fatigue Identify treatable contributing factors, such as: <ul style="list-style-type: none"> <li>• Pain</li> <li>• Emotional distress</li> <li>• Anemia</li> <li>• Sleep disturbance</li> <li>• Nutritional status</li> <li>• Activity level</li> <li>• Medication side effects</li> <li>• Alcohol or substance abuse</li> <li>• Comorbid conditions</li> </ul>
Pharmacologic interventions	Methylphenidate Dexamethasone
Nonpharmacologic interventions	Exercise <ul style="list-style-type: none"> <li>• Moderate to vigorous activity, as tolerated</li> <li>• Strength training</li> <li>• Stretching and flexibility exercises</li> <li>• Avoid exercising one to two days after chemotherapy or if experiencing neutropenia, low platelet counts, anemia, or fevers</li> </ul> Nutrition <ul style="list-style-type: none"> <li>• Nutrition consultation</li> <li>• Manage nausea or vomiting</li> </ul> Psychosocial interventions <ul style="list-style-type: none"> <li>• Provide education about cancer-related fatigue</li> <li>• Energy conservation and pacing activities</li> </ul> Optimize sleep <ul style="list-style-type: none"> <li>• Sleep hygiene, such as establishing routine, avoiding caffeine or alcohol near bedtime</li> <li>• Avoid long naps in the afternoon</li> </ul> Relaxation techniques <ul style="list-style-type: none"> <li>• Progressive muscle relaxation</li> <li>• Guided imagery</li> <li>• Meditation</li> <li>• Massage</li> <li>• Healing touch</li> <li>• Journaling</li> <li>• Yoga</li> <li>• Music</li> </ul>

*Note.* Information from McQuestion (2021); NCCN (2021).

(Edmonds & McGuire, 2007; Siddiqui & Movsas, 2017). Twice-daily brushing with a soft toothbrush, salt and soda rinses four to six times a day (especially after meals), and continuing dental care are important points of education for patients and families (McQuestion, 2021). If pain is severe, providers may prescribe pain-relieving medications (Edmonds & McGuire, 2007; Siddiqui & Movsas,

2017). However, taking opioids and related classes of medications can increase other risk factors for nonadherence, such as limiting the ability to drive and side effects such as tiredness and alterations in decision-making.

Patients who were nonadherent to their radiation schedules were also more likely to report inpatient admissions and outpatient IV administration (Miller et al., 2021), both of which can result from treatment toxicities or unmanaged side effects such as mucositis, pain, and nausea.

## DISCUSSION

The literature is largely descriptive about the problem of nonadherence among HNC patients. Although limited, the evidence does shed some light onto the problem. Because many factors associated with nonadherence are modifiable, the health-care team can focus on screening and symptom management as opportunities for improvement.

### Screening

The National Cancer Institute (NCI) and NCCN both advocate for frequent distress screening of some form at every patient encounter if possible (2021). Distress screening can be implemented using one of many available standardized tools. Model screening programs include a brief screening administration, scoring and evaluation, and referrals if indicated (NCI, 2021). The NCCN has a simple distress thermometer to capture the patient's current feelings of distress, which leads providers to further evaluate the specific symptoms the patient is experiencing (2021). There are more in-depth symptom assessment scales to obtain an overview of several symptoms in oncology patients, such as the Edmonton Symptom Assessment Scale (Watanabe et al., 2011).

In addition to distress, clinicians are encouraged to assess symptoms most commonly associated with the cancer diagnosis. For instance, HNC providers will assess for pain, mucositis, and dysphagia to ensure symptoms are managed well and are not interfering with treatment adherence. There are standardized tools to address the HNC population. The MD Anderson Symptom Inventory for Head and Neck Cancer (MDASI-HN) measures nine symptoms relevant to HNC such as mucus, difficulty swallowing or chewing,

skin pain, problems with tasting food, and mouth/throat sores, as well as other general symptom profiles (MD Anderson Cancer Center, 2021). The Functional Assessment of Cancer Therapy-Head and Neck (FACT-HN) assesses physical, social/family, emotional, and functional well-being, along with other additional concerns related to HNC (FACIT Group, 2020). Both instruments are lengthy and may be burdensome to administer at every encounter but could be used as a follow-up to a more simple screening such as the NCCN Distress Thermometer (NCCN, 2021).

### Roles of Oncology APs

Advanced practitioners practice in various HNC treatment settings, including radiation oncology and medical oncology settings. Twenty-two percent of radiation oncology practices reported employing APs in 2014 (Guidi & Kloos, 2015), and recommendations for adapting to the increased demand for radiation oncology providers included collaborating with more oncology APs to see more patients who need radiation and chemotherapy (Yang et al., 2014; Reckling, 2014).

The American Society for Radiation Oncology (ASTRO) defines the role of APs to include recognizing and managing treatment-related symptoms and toxicities under the supervision of the radiation oncologist (American Society for Radiation Oncology, 2020). This is an opportunity for the oncology AP to make an impact on treatment adherence, as patients with less symptoms and side effects are more likely to adhere to their treatment schedules (Miller et al., 2021).

Oncology APs are experienced and knowledgeable about managing the side effects of cancers and cancer treatments and can be leaders in this area of practice. Independent, AP-led symptom management clinics have been documented to be effective in improving symptoms and quality of life, lowering unplanned hospitalization admission and emergency department visits, improving treatment adherence, and saving money with health-care expenditures (Mason et al., 2013; Graze et al., 2014; Terzo et al., 2017; Periasamy et al., 2017). These clinics can be run independently by or in collaboration with APs.

Outpatient pharmacy consultation is also an important piece of the multidisciplinary team for

people receiving cancer treatment, particularly because people with HNC experience swallowing difficulties and polypharmacy. A study of HNC and lung cancer patients and health-care team members in a radiation oncology clinic found that providers, nurses, and pharmacists underestimated the need for patient education among these populations. The patients reported a 46% rate of non-adherence to their prescribed medications (Maleki et al., 2020), which could significantly impact their symptom management and treatment adherence. This illustrates an opportunity for oncology pharmacists to answer questions and provide relevant education about medications that patients are prescribed from various providers.

Technologies can also be leveraged to connect oncology APs with patients. Digital health tools, such as at-home daily digital symptom tracking systems, allow APs to view the patient's symptom scores in between clinic visits and intervene earlier. These tools potentially improve efficiency, workflow, and increase adherence to cancer treatments among oncology patients (Wilson & Mooney, 2020). Oncology APs can be advocates for implementing new technologies in their practice settings (Wilson & Mooney, 2020).

## CONCLUSION

Adherence to cancer treatment schedules is an important determinant in treatment outcomes. Factors associated with nonadherence to cancer treatment among HNC patients are multidimensional and include symptoms and toxicities and demanding treatment schedules, as well as socioeconomic factors such as education level and the distance traveled to receive treatment. Oncology APs in various settings have an important role in screening, management of symptoms and side effects, and counseling patients on the importance of treatment adherence. Examples of innovative management strategies include AP-led symptom management clinics, educational interventions, and utilizing technology to more closely screen for symptom burden. These interventions can have a meaningful impact on treatment adherence, quality of life, and treatment outcomes. ●

## Disclosure

The authors have no conflicts of interest to disclose.

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