J Prev Epidemiol. 2026;e39327 Review

doi 10.34172/jpe.2026.39327 Journal of Preventive Epidemiology http jprevepi.com

Global perspectives on pain management in ENT cancers; a narrative review study

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Received: 5 Dec. 2025
Revised: 6 Jan. 2026
Accepted: 16 Feb. 2026
ePublished: 4 Apr. 2026

Keywords: Head and neck cancer, Otorhinolaryngologic neoplasms, Pain management, Analgesics, Opioid analgesics, Adjuvant analgesics, Palliative care

Abstract

Pain in ear, nose, and throat (ENT) cancers is common and highly debilitating, resulting from tumor invasion, treatment toxicity, and complex neurophysiological mechanisms, making effective management essential for maintaining quality of life (QoL) and treatment adherence. This narrative review synthesizes global evidence on pain mechanisms, assessment methods, and management strategies, covering pharmacological, interventional, and non-pharmacological approaches while highlighting major regional disparities in access to care. Pain in these cancers arises from nociceptive, neuropathic, and inflammatory pathways, with opioids as the primary therapy supported by adjuvant medications and complementary non-pharmacological interventions. However, low- and middle-income countries face significant barriers, including limited opioid availability, inadequate training, and cultural obstacles, that hinder effective pain control. Emerging options such as targeted therapies, immunotherapy-related pain management, neuromodulation, and personalized analgesic strategies show promise but remain unevenly accessible. Overall, improving pain outcomes in ENT cancers requires a multidisciplinary, culturally sensitive, and equity-focused approach supported by strengthened palliative care systems and coordinated global efforts.

Citation: Mosleh H, Abbasi Z, Abniki M. Global perspectives on pain management in ENT cancers; a narrative review study. J Prev Epidemiol. 2026;x(x):e39327. doi: 10.34172/jpe.2026.39327.

Introduction

Pain is a pervasive and debilitating symptom in patients with cancers of the ear, nose, and throat (ENT), collectively referred to as head and neck cancers (HNC), and its management remains a critical challenge in oncology worldwide (1,2). The HNCs encompass a heterogeneous group of malignancies arising from the oral cavity, pharynx, larynx, salivary glands, nasal cavity, and related structures, globally representing the sixth most common cancer type (3). The annual incidence of HNC continues to rise, with over 900,000 new cases and nearly 500,000 deaths reported worldwide in 2022, and projections indicate a further 30% increase by 2030, particularly in low- and middle-income countries (LMICs) (1,3).

Pain in ENT cancers is not only highly prevalent, affecting up to 80% of patients at some point during their disease trajectory, but also multifactorial, resulting from tumor invasion, nerve compression, treatment-related tissue injury, and complex neurobiological mechanisms (2, 4). The burden of pain is compounded by its profound impact on quality of life (QoL), functional capacity, psychological well-being, and even survival outcomes (3,5,6). Despite advances in cancer therapies and supportive care, pain remains inadequately controlled in a significant proportion of patients, with up to 40% experiencing moderate to severe pain that is undertreated or refractory to standard interventions (7,8).

Effective pain management in ENT cancers necessitates a nuanced understanding of the underlying pain mechanisms, comprehensive assessment strategies, and the integration of pharmacological, non-pharmacological, interventional, and palliative approaches tailored to individual patient needs. However, global disparities in access to pain care, socioeconomic and cultural barriers, and evolving regulatory landscapes further complicate the delivery of optimal pain relief, particularly in resource-limited settings (9,10). This narrative review synthesizes current evidence on the epidemiology, mechanisms, assessment, and management of pain in ENT cancers, with a focus on global perspectives, emerging therapies, and future directions.

Search strategy

A comprehensive literature search was

Key point

Pain management in ear, nose, and throat (ENT) cancers is a complex, multidimensional challenge that requires a global, integrative, and patient-centered approach, particularly as clinicians must tailor interventions to address tumor-related pain, treatment toxicity, and functional impairments affecting speech, swallowing, and airway protection. Advances in pharmacology, interventional techniques, rehabilitation, and psychosocial care offer meaningful opportunities to improve patient outcomes, yet persistent disparities, knowledge gaps, and systemic barriers highlight the need for coordinated education, policy development, and research initiatives. In clinical practice, applying multimodal analgesia, early palliative care integration, and individualized rehabilitation strategies can significantly reduce symptom burden and support treatment adherence. By embracing innovation, collaboration, and equity, the oncology community can transform pain care for patients with ENT cancers worldwide, alleviating suffering and enhancing quality of life (QoL) across the cancer continuum.

conducted across major biomedical databases—PubMed/Medline, Scopus, Embase, Web of Science, and Google Scholar search engine—to identify peer-reviewed studies related to pain management in ENT cancers. The search strategy combined Medical Subject Headings (MeSH) and free-text terms using Boolean operators, with the core keywords including 'otorhinolaryngologic neoplasms', 'pain management', 'analgesics', 'opioid analgesics', 'adjuvant analgesics', and 'palliative care'. Filters were applied to include human studies, English-language publications, and articles published from inception to the present. Reference lists of relevant reviews and original studies were also screened to ensure comprehensive coverage of the available evidence.

Epidemiology of pain in ENT cancers

Pain is a hallmark symptom of ENT cancers, with prevalence estimates ranging from 50% to 80% during the disease course and reaching up to 70% among post-treatment survivors (4,11). The incidence and severity of pain are influenced by tumor site, stage, treatment modality, and patient-specific factors such as age, sex, comorbidities, and psychosocial context (1,5,6). For example, oral cavity and oropharyngeal cancers are associated with higher baseline pain prevalence (up to 48%) compared to thyroid or nasopharyngeal cancers, and pain intensity often peaks during multimodal treatments such as chemoradiotherapy (3-5). Longitudinal cohort studies have demonstrated that pain persists in a substantial subset of HNC survivors, with 20–30% reporting moderate to severe pain two to five years post-diagnosis, and one-third experiencing worse pain after treatment than before (3,4,6). Persistent pain is particularly prevalent in patients with advanced-stage disease, those undergoing multimodal therapy, and those with comorbid depression or socioeconomic deprivation (3-5). Global epidemiological analyses reveal marked regional disparities, with the highest burden of HNC and associated pain observed in LMICs, where late-stage presentation, limited access to analgesics, and inadequate palliative care infrastructure exacerbate suffering; the age-standardized incidence rate for HNC has escalated in low- and middle-income regions, and projections indicate continued increases in incidence and pain-related disability-adjusted life years (DALYs) in these settings through 2030 (1,9).

Pain mechanisms in ENT cancers

Nociceptive pain

Nociceptive pain in ENT cancers arises from actual or threatened tissue injury due to tumor invasion, inflammation, or treatment-related trauma, and is typically described as sharp, throbbing, or aching (2,4). Tumor growth can infiltrate mucosal surfaces, bones, and soft tissues, leading to the release of inflammatory mediators (e.g., bradykinin and prostaglandins) that sensitize peripheral nociceptors and amplify pain signaling (2,7,12). Acute nociceptive pain is common at diagnosis and during interventions such as surgery or radiotherapy, often responding to nonsteroidal anti-inflammatory drugs (NSAIDs) and opioids (4, 3).

Neuropathic pain

Neuropathic pain, defined as pain caused by a lesion or disease of the somatosensory nervous system, is prevalent in ENT cancers, particularly following nerve compression by tumors or iatrogenic injury from surgery, radiotherapy, or chemotherapy (4,14). Neuropathic features—burning, tingling, electric shocks- are reported in 13–65% of patients, and up to 40% of cancer pain cases have a neuropathic component (4). Mechanistically, neuropathic pain involves aberrant neuronal firing, altered expression of ion channels, and neuroinflammation, with glial cell activation and cytokine release contributing to central sensitization (7,12,15). Oral mucositis-induced pain, a frequent complication of radiotherapy, exemplifies the interplay between mucosal injury, neuroinflammation, and neuropathic pain generation (4,14).

Nociplastic pain and central sensitization

Nociplastic pain refers to pain arising from altered nociceptive processing without clear evidence of tissue damage or somatosensory system lesion, and is increasingly recognized in chronic cancer pain syndromes (4,15). Central sensitization, characterized by the heightened responsiveness of central neurons to peripheral input, manifests as widespread pain, allodynia, and hyperalgesia and may persist long after the initial insult has resolved; studies have identified features of central sensitization in up to 36% of HNC survivors, with systemic symptoms such as fatigue, cognitive dysfunction, and sleep disturbances clustering with widespread pain (7,15).

Assessment and measurement of pain in ENT cancers

Accurate assessment of pain in ENT cancers is essential

for effective management, yet remains challenging due to the heterogeneity of pain mechanisms, subjective reporting, and communication barriers (2). The most commonly used tools for quantifying pain intensity are the visual analog scale (VAS) and numeric rating scale (NRS), which provide simple, validated measures for clinical and research settings (4, 14). For neuropathic pain, screening questionnaires such as the Leeds Assessment of Neuropathic Symptoms and Signs (LANSS) and Douleur Neuropathique 4 (DN4) are valuable for identifying neuropathic components and guiding adjuvant therapy selection (14).

Multidimensional instruments, including the Brief Pain Inventory (BPI), McGill Pain Questionnaire (MPQ), and the European Organisation for Research and Treatment of Cancer QoL Questionnaire (EORTC QLQ-C30 and QLQ-H&N35), assess pain interference with function, emotional well-being, and overall QoL (3,5,6). Patient-reported outcomes are increasingly recognized as critical endpoints in clinical trials and routine care, enabling personalized treatment planning and longitudinal monitoring (3). However, heterogeneity in assessment tools and lack of standardized pain phenotyping limit data comparability and hinder precision pain medicine approaches.

Pharmacological management

Opioids and analgesics

Opioids remain the cornerstone of moderate to severe cancer pain management, endorsed by international guidelines from the World Health Organization (WHO), American Society of Clinical Oncology (ASCO), European Society for Medical Oncology (ESMO), and European Association for Palliative Care (EAPC) (16,17). The WHO analgesic ladder, originally a three-step framework, recommends progression from non-opioid analgesics (e.g., acetaminophen, NSAIDs) to weak opioids (e.g., codeine, tramadol) and then to strong opioids (e.g., morphine, oxycodone, fentanyl) as pain severity increases (13,17). Recent updates incorporate a fourth step for interventional procedures and advocate a bidirectional, individualized approach (17).

Oral morphine and transdermal fentanyl are the most widely used strong opioids, with >90% of patients achieving meaningful pain relief within two weeks, though side effects such as constipation, drowsiness, and dry mouth are common (13,18). Opioid rotation, dose titration, and the use of adjuvant medications are strategies to optimize analgesia and minimize toxicity (18). However, 10–20% of patients may require changes in therapy due to inadequate response or intolerable side effects (13,18). The opioid crisis has prompted reassessment of opioid use in cancer pain, with concerns about dependence, misuse, and regulatory restrictions impacting prescribing practices, particularly in high-income countries (8,10,19). Nonetheless, opioids are designated as essential medicines for palliative care, and their judicious use remains vital for alleviating suffering in ENT cancer patients (8,9,16).

Adjuvants and neuropathic agents

Adjuvant analgesics are integral to the management of neuropathic and refractory pain in ENT cancers. Tricyclic antidepressants (TCAs; e.g., amitriptyline, nortriptyline), serotonin-norepinephrine reuptake inhibitors (SNRIs; e.g., duloxetine, venlafaxine), and anticonvulsants (e.g., gabapentin, pregabalin) are first-line agents for neuropathic pain, often used in combination with opioids (4,14). Meta-analyses demonstrate that adding antidepressants or anticonvulsants to opioids reduces pain more effectively than opioids alone, though side effects such as sedation, dizziness, and cognitive impairment may limit tolerability (13,20). Methadone, a μ-opioid receptor agonist effective for complex pain syndromes and opioid switching but requiring specialist oversight due to variable pharmacokinetics, along with tapentadol, a noradrenaline reuptake inhibitor shown to be non-inferior to morphine and oxycodone with fewer gastrointestinal effects and benefits in mixed pain states, and ketamine, used at sub-anesthetic doses for refractory pain with central sensitization despite limited evidence and the need for careful toxicity monitoring, represent key options in managing challenging cancer-related pain (13,14). Topical agents such as lidocaine patches and high-concentration capsaicin are recommended for localized neuropathic pain, while cannabinoids have shown limited efficacy and uncertain long-term safety in cancer pain (4,13). Pharmacogenetic considerations may influence opioid responsiveness and adverse effect profiles, underscoring the potential for personalized analgesic regimens (13,21,22).

Non-pharmacological approaches

Physical and rehabilitation interventions

Physical therapy and rehabilitation are essential components of multimodal pain management in ENT cancers, addressing both nociceptive and functional impairments (23,24). Exercise interventions, including aerobic and resistance training, have demonstrated benefits in improving muscle strength, cardiorespiratory fitness, and QoL during and after cancer treatment (3,6,23). Targeted physiotherapy programs are effective for managing trismus, shoulder dysfunction, and fibrosis following surgery or radiotherapy, and may reduce pain intensity and disability (24). Manual therapies, low-level laser therapy, heat therapy, and cryotherapy are adjunctive modalities for managing musculoskeletal pain, lymphedema, and radiation-induced complications (4,23). Early and individualized rehabilitation is associated with better functional outcomes and reduced long-term morbidity (6,23).

Psychological and behavioral interventions

Psychological distress, including anxiety, depression, and

pain catastrophizing, is highly prevalent in ENT cancer patients and exacerbates pain perception and disability (25,26). Cognitive-behavioral therapy, mindfulness-based stress reduction, and psychoeducation are evidence-based interventions that alleviate emotional distress, enhance coping, and improve QoL; studies indicate that cognitive-behavioral therapy significantly reduces anxiety and depression scores, though its impact on overall QoL may be variable and influenced by intervention design and patient characteristics (6,25,26). Integrating psychological support into routine care, including nurse-led interventions and peer support groups, fosters resilience and addresses the multidimensional nature of cancer pain (25,26). Training healthcare providers in emotional intelligence and communication skills further enhances the delivery of holistic pain management (5,27).

Complementary and integrative therapies

Complementary therapies such as acupuncture, massage, aromatherapy, reflexology, and music therapy are increasingly incorporated into integrative oncology programs for pain management; the systematic reviews and randomized controlled trials demonstrate that acupuncture reduces pain intensity and analgesic consumption in HNC patients undergoing radiotherapy, with minimal adverse effects (28,29). Massage therapy, reflexology, and aromatherapy provide additional benefits for pain relief, anxiety reduction, and improved well-being, though methodological heterogeneity warrants further research (28). Mind–body practices, including meditation, hypnosis, yoga, and tai chi, have shown promise in reducing pain severity, emotional distress, and fatigue, supporting their integration into multimodal care plans (4,26).

Interventional and procedural pain management in ENT cancers

Interventional pain management techniques are indicated for patients with refractory or localized pain unresponsive to pharmacological and non-pharmacological therapies. Nerve blocks, including facial, glossopharyngeal, sphenopalatine ganglion, and stellate ganglion blocks, provide targeted analgesia for breakthrough neuropathic pain syndromes, with studies reporting significant pain relief lasting several weeks; the efficacy of nerve blocks is enhanced when combined with adjuvant medications such as amitriptyline (30).

Neuromodulation techniques, including spinal cord stimulation, dorsal root ganglion stimulation (DRG-S), and peripheral nerve stimulation, are emerging modalities for intractable neuropathic and mixed pain in cancer survivors; the spinal cord stimulation modulates pain signaling at the dorsal column, providing ≥50% pain relief and reducing opioid requirements in selected patients; the DRG-S offers focal analgesia with superior electrical efficiency and is FDA-approved for complex regional pain syndromes, with case series demonstrating efficacy in cancer-related pain (7,31). Intrathecal drug delivery systems enable targeted administration of opioids and adjuvants, minimizing systemic side effects and improving pain control in advanced cancer (7). Other interventional options include percutaneous neurolysis, radiofrequency ablation, vertebroplasty, and kyphoplasty for bone metastasis pain and vertebral compression fractures (7).

Radiation and surgery-related pain syndromes

Pain syndromes related to cancer treatment are common and often complex, involving both nociceptive and neuropathic mechanisms (4). Acute postoperative pain arises from surgical trauma, nerve injury, and inflammation, while chronic postsurgical pain may persist due to peripheral and central sensitization (15,32). Shoulder pain following radical neck dissection, trismus, glossopharyngeal neuralgia, and first bite syndrome are notable chronic pain syndromes requiring multidisciplinary management (33).

Radiotherapy-induced oral mucositis is a devastating complication, characterized by mucosal ulceration, neuroinflammation, and severe pain that impairs nutrition, speech, and QoL (4,14). Management includes topical agents (e.g., sucralfate, lidocaine), systemic analgesics, cryotherapy, low-level laser therapy, and nutritional support (4). Chemotherapy-induced peripheral neuropathy and radiation-induced fibrosis further contribute to chronic pain and functional impairment (4,15).

Palliative care integration and multimodal interprofessional management

Palliative care is integral to the management of pain and other distressing symptoms in ENT cancers, emphasizing early identification, comprehensive assessment, and multidisciplinary intervention (34,35). Early integration of palliative care alongside disease-directed therapy improves symptom control, QoL, patient and family satisfaction, and reduces healthcare utilization (3,34,35). Multimodal interprofessional pain management aligns with the biopsychosocial model, incorporating medications, restorative therapies, interventions, behavioral health, and complementary medicine, delivered through coordinated teamwork (34). Barriers to effective palliative care include misconceptions, prognostic uncertainty, late referrals, and limited access in LMICs (9,34,35). Addressing these challenges requires education, policy reform, and the establishment of collaborative care pathways that prioritize patient-centered goals and advance care planning (34,35).

Conclusion

Pain management in ENT cancers is a complex, multidimensional challenge that demands a global, integrative, and patient-centered approach. Advances in pharmacology, interventional techniques, rehabilitation, and psychosocial care offer hope for improved outcomes,

but persistent disparities, knowledge gaps, and systemic barriers must be addressed through coordinated education, policy, and research initiatives. By embracing innovation, collaboration, and equity, the oncology community can transform pain care for patients with ENT cancers worldwide, alleviating suffering and enhancing QoL across the cancer continuum.

Authors' contribution

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Writing–original draft: All authors.
Writing–review and editing: All authors.

Conflicts of interest

The authors declare that they have no competing interests.

Declaration of generative AI and AI-assisted technologies in the writing process

During the preparation of this work, the authors utilized Grammarly and Copilot to refine grammar points and language style in writing. Subsequently, the authors thoroughly reviewed and edited the content as necessary, assuming full responsibility for the publication's content.

Ethical issues

Ethical issues (including plagiarism, data fabrication, and double publication) have been completely observed by the authors.

Funding/Support

None.

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