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REVIEW

# Psychological Factors Related to Treatment Outcomes in Head and Neck Cancer

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## ABSTRACT

***Background***: Patients with head and neck cancer (HNC) often demonstrate stress, distress, anxiety, depression, and are at risk for suicide. These affect their quality of life (QoL) but less attention has been given to psychological variables that may impact response to treatment.

***Objectives***: This study aims to systematically review publications during 2013–2023 to collate evidence on the effects of psychological variables on HNC treatment outcomes.

***Methods***: We searched Ovid Medline, PubMed, Scopus, and Web of Science for articles that examined psychological factors related to treatment outcomes in patients with HNC.

***Results***: There were 29 studies (5 before treatment, 2 during, 17 after, and 5 covering the whole management trajectory) including 362,766 patients. The psychological factors were either behavioral (adjustment and coping strategy, unrealistic ideas, self-blame), cognitive (elevated risk of psychiatric co-comorbidity), or emotional (distress, depression, anxiety, nervousness, and fear of disfigurement and complications). It was found that there was a relationship

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between depression and decreased survival in patients with HNC. Pretreatment pain was an independent predictor of decreased survival in a large sample of patients. The distress level was approximately 54%, emotional problems ranged between 10 and 44%, while financial difficulties were identified in 54% of the patients. Sixty-nine percent of patients were reported to have used at least one cost-coping strategy within 6 months after treatment initiation. During post-treatment period, depression increased from 15% at the baseline to 29%, while the fear of recurrence was found among at least 35% of patients.

***Discussion and Conclusion*:** Several psychological factors predict QoL and survival among HNC survivors. Distress encompasses depression and anxiety, and physical burden from HNC diagnosis and treatment. Routine screening and early interventions that target distress could improve HNC survivors' QoL. A systematic and standardized measurement approach for QoL is warranted to homogenize these findings and to understand the underlying relationships.

**Keywords:** Stress; Distress; Psychology; Head and neck cancer; Systematic review

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**Key Summary Points**

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|---|
| *What was already known about the topic* |
| Patients with head and neck cancer (HNC) experience high symptom burden, which affects their daily functions and quality of life. |
| HNC exerts psychological impacts on its patients. This affects their quality of life and disease management. |
| The association between psychological factors on HNC treatment outcomes remains unclear. |
| *What this article adds to the existing knowledge* |
| We analyzed all the published studies between 2013 and 2023 examining the associations of HNC with psychological variables and treatment outcomes. The main outcome was the quality of life of patients with HNC during the treatment process and thereafter. |
| The psychological factors affecting treatment outcomes were found to be behavioral, cognitive, or emotional. |
| Psychosocial distress related to HNC includes both psychological and social factors. |
| Systematic and standardized measurement approaches for psychological factors in patients with HNC are warranted. |
| A multidisciplinary intervention is needed to properly address the prevalence of psychological factors in HNC during the entire disease trajectory. |

## INTRODUCTION

The diagnosis of head and neck cancer (HNC) presents a significant challenge for patients [1]. The challenges include treatment-related toxicity, its long-term consequences, secondary side effects, and fear of recurrence, making this cancer one of the most psychologically traumatic cancers [2, 3]. Impairments in chewing and

swallowing can induce psychological stress in patients with HNC [2]. Continuous support from diagnosis through the treatment trajectory and long-term follow-up is necessary [4–6].

Stress in patients with HNC stems from multiple factors such as cancer-related issues, functional impairments, and psychosocial concerns [7]. These factors are closely linked to increased distress in patients with HNC [7]. Increased distress can lead to decreased quality of care, noncompliance with treatment, and reduced survival rates [8]. Additionally, certain treatments may exacerbate distress which could further negatively impact patient outcomes [9]. Therefore, the experience of distress is considered a sign of sub-optimal treatment outcomes in cancer care [2, 10].

The psychological impact of HNC diagnosis extends beyond stress reactions, persisting well after treatment [11]. It has been reported that patients with HNC experience both post-traumatic stress symptoms and even clinical post-traumatic disorder following treatment [11]. Therefore, it is important to monitor HNC patient stress level at diagnosis, during treatment, and after treatment to optimize functioning and quality of life (QoL). This paper systematically reviews studies on psychological factors that influence HNC treatment outcomes, typically measured by tumor response, length of stay, complication rates, QoL, or survival. We aim to address three main questions. First, how does distress, commonly associated with HNC diagnosis, affect treatment responses? We hypothesize that there is variability in experiencing distress among patients with HNC and that higher levels of distress correlate with poorer treatment outcomes. Second, how do patients' pre-existing psychological characteristics—such as personality, temperament, social factors, or history of psychological problems—affect treatment outcomes? We hypothesize that traits such as neurotic personality, low social support, and a history of other psychological problems are associated with worse treatment outcomes. This knowledge is important, as it can be used in screening patients at high risk for psychological distress and in planning multidisciplinary interventions aiming to improve treatment outcomes in patients with HNC. And, third, how do these psychological factors impact the survival and QoL of HNC survivors after treatment? We hypothesize that knowing these psychological factors will help to define methods to assist HNC survivors deal with these adverse symptomatic sequelae, which are capable of imposing significant psychological and physical burdens on them after treatment.

## MATERIALS AND METHODS

### Study Design

We performed a systematic review of the published studies on psychological factors related to the treatment response in patients with HNC. Preferred Reporting Items for Systematic Review and Meta-Analysis (PRISMA) were followed [20, 21]. The first two authors regularly discussed the review's breadth, comprehensiveness, and clarity of purpose [21–23].

### Databases and Search Duration

We systematically searched PubMed, Ovid via Medline, Scopus, and Web of Science databases for the last 10 years (from 2013 until the end of November 2023) to retrieve all original studies that had examined psychological factors related to treatment response in patients with HNC (Fig. 1). To minimize omission of any potential study, the reference lists of all the potentially eligible articles were manually searched.

### Search Terms

The potentially relevant articles were retrieved by combining search keywords: ['psychological factor' AND 'treatment response' AND 'head and neck cancer'].

### Inclusion and Exclusion Criteria

This review includes all studies during the 10-year period which examined psychological factors and their impact on treatment responses in HNC. We included studies that assessed

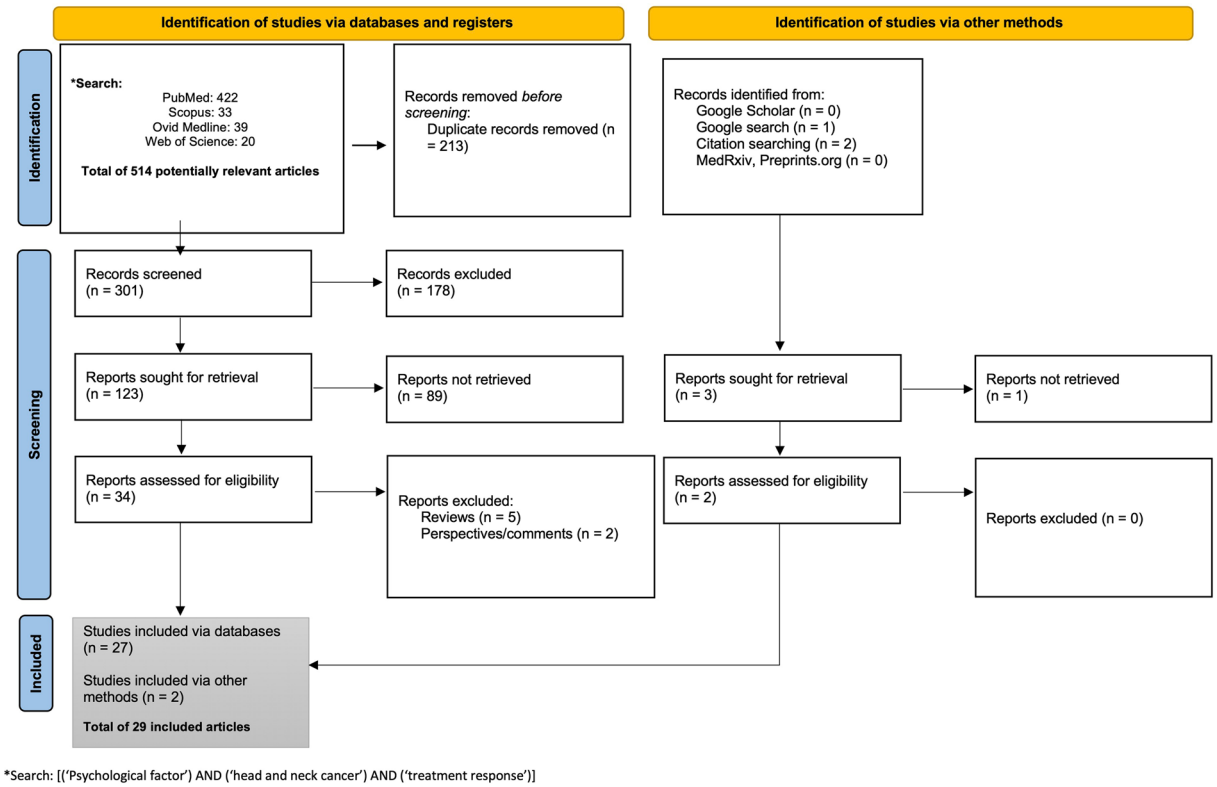


**Fig. 1** PRISMA flow chart

psychological distress, burden, anxiety, personality, social factors, or depression at any point during the treatment trajectory, including prior to diagnosis, at diagnosis, or during treatment. The primary outcomes were QoL, health-related quality of life (HRQoL), tumor response, length of hospital stay, complication rate, and survival. We excluded commentaries, opinions, reviews (including systematic reviews) perspectives, guidelines, editorials, and non-English language articles. Studies concerning psychological factors in caregivers, family members, or relatives of patients with HNC, as well as those focusing on coping mechanisms, screening, and interventions aimed at mitigating psychological factors in patients with HNC, were also excluded.

## Search Analysis and Screening

The articles were retrieved from the database search and were exported to Zotero (Cooperation for Digital Scholarship, VA, USA) for further analysis to remove duplicates and irrelevant studies. Access to the Zotero project group for this study was granted to the first two authors of this study, who independently of each other screened all the potential articles' titles and abstracts for relevancy based on the inclusion and exclusion criteria.

## Data Extraction and Synthesis

Following the initial screening process, full-text articles were independently reviewed to determine their eligibility for inclusion. A data extraction sheet was used to minimize the omission of potentially eligible studies. Any disagreements on inclusion and exclusion of specific articles were resolved through consensus. Thus, the interobserver reliability between the two independent researchers was measured using Kappa Cohen's coefficient ($k = 0.93$). All eligible studies to be included were summarized in Table 1.

**Table 1** Characteristics of the included studies

| Study (Country/Region) | Population | Assessment point in disease trajectory | Questionnaire/QoL outcome measure | Psychological variables assessed | Results | Effect on treatment outcome \| Conclusion |
|---|---|---|---|---|---|---|
| Beisland et al. 2013 [14] (Norway) | 139 | After treatment (RT) | GHQ, EPQ, Self-reported coping response EORTC QLQ-C30, EORTC QLQH&N35 | Distress, personality, and coping | Neuroticism and avoidant coping contributed to distress and low HRQoL | HRQoL \| Distress and HRQoL (to some extent) were found to be stable during follow-up |
| Chiou et al. 2013 [15] (Taiwan) | 73 | After treatment (RT and chemoRT) | EORTC QLQ-C30, EORTC QLQH&N35, BDI-II | Depression | Depression adds to poor QoL and affect most functional aspects of day-to-day activities of patients with HNC | HRQoL \| Depressed patients with HNC were noted to have poorer HRQoL in almost every functioning symptom |
| Ghazali et al. 2013 [16] (United Kingdom) | 189 | After treatment (Surgery alone, surgery + RT, RT + /or CT.) | UW-QoL | Fear of recurrence | Anxiety/mood and young age were predictors of fear of recurrence | Well-being \| The fear of recurrence was present in patients with HNC either intermittently or consistently |

**Table 1** continued

| Study (Country/Region) | Population | Assessment point in disease trajectory | Questionnaire/QoL outcome measure | Psychological variables assessed | Results | Effect on treatment outcome \| Conclusion |
|---|---|---|---|---|---|---|
| Gunn et al. 2013 [17] (United States) | 270 | Before treatment (surgery) | MDASI-HN | Fatigue, sleep disturbance, distress, pain, problem chewing, and swallowing | Burden includes fatigue, sleep disturbance, distress, pain, problem chewing, and swallowing substantially affected patients with HNC. Poorer performance status, higher T classification, and receipt of previous treatment correlated with higher symptom burden | HRQoL \| Substantial patients with HNC experience high symptom burden |
| Lebel et al. 2013 [18] (Canada) | 99 | After treatment (surgery) | Self-administered | Stigma | Stigma highly correlates with psychosocial impact | Well-being \| Stigmatization exerts a powerful and deleterious psychosocial impact on patients with HNC |
| Llewellyn et al. 2013 [19] (United Kingdom) | 103 | Treatment trajectory | SF-12, EORTC QLQ-C30 | Coping, benefit finding, and optimism | Moderate to high levels of benefit finding were reported. Anxiety, depression and quality of life were not related to benefit finding | QoL \| Optimism and coping strategies were associated with patients identifying positive consequences of a diagnosis of HNC |

**Table 1** continued

| Study (Country/Region) | Population | Assessment point in disease trajectory | Questionnaire/QoL outcome measure | Psychological variables assessed | Results | Effect on treatment outcome \| Conclusion |
|---|---|---|---|---|---|---|
| Neilson et al., 2013 [20] (Australia) | 101 | After treatment (RT, chemoRT, surgery + RT, surgery + chemoRT) | HADS, Functional Assessment of Chronic Illness Therapy for HNC (Additional Concerns subscale) | Distress and anxiety Sociodemographic (younger age) | Depression increases following cancer treatment<br>Anxiety increases before treatment and about 1 year after treatment<br>Depression was 15% at baseline, increasing to 29% 3 weeks post-treatment, falling to 8% at 18-month follow-up. The number of probable cases of anxiety was 20% at baseline, 17% at 3 weeks post-treatment and 22% at 18-month follow-up | QoL \| Anxiety level was higher in the pre-treatment, lower immediately after treatment, and increases to pretreatment level at about one year after treatment |
| Badr et al., 2014 [21] (United States) | 49 | During treatment (intensity-modulated RT; the majority received concurrent chemoRT, or surgery followed by chemoRT | MDASI-HN and NCCN DT | Distress | Both HNC patients and caregivers experience heightened level of distress during the course of radiotherapy | Distress increases steadily over the course of treatment |

**Table 1** continued

| Study (Country/Region) | Population | Assessment point in disease trajectory | Questionnaire/QoL outcome measure | Psychological variables assessed | Results | Effect on treatment outcome \| Conclusion |
|---|---|---|---|---|---|---|
| Schaller et al., 2015 [22] (Sweden) | 26 | After treatment (RT and RT + CT) | Qualitative semi-structured | Pain, fatigue, altered mood, and preoccupied mind | Pain influences their social lives but not their psychological suffering | Physical pain, psychological distress, and social withdrawal were prominent in patients with HNC |
| Wells et al. 2015 [23] (United Kingdom) | 280 | After treatment (surgery alone, RT or CT) | DT, PCI | Distress and unmet needs<br>Sociodemographic (younger age, unemployed, & living alone) | The unmet needs included oral and eating problems, fear of recurrence and fatigue | QoL \| Being younger, out of work but not retired, having a feeding tube and living alone were associated with high levels of distress, concerns, and unmet needs |
| Ninu et al. 2016 [23] (Italy) | 86 | After treatment (surgery, chemo-/radiotherapy, and combined treatment) | DT, EORTC QLQC30, EORTC QLQH&N35 | Distress<br>Sensory problems, social eating, and dry mouth | 41% showed high level of distress<br>Distress was higher in patients with a tracheotomy or with previous cancer in another part | QoL \| Monitoring of the QoL during the treatment trajectory could be useful in planning the rehabilitation and follow-up visit |
| Threader & McCormack, 2016 [25] (Australia) | 9 | After treatment (surgery + RT, surgery + RT and CT) | Interpretative Phenomenological Analysis | Distress, stigma due to facial disfigurement and psychological growth | HNC is associated with multiple layers of distress including stigma | Stigmatization and devalued social identity contributed to stress |

**Table 1** continued

| Study (Country/Region) | Population | Assessment point in disease trajectory | Questionnaire/QoL outcome measure | Psychological variables assessed | Results | Effect on treatment outcome \| Conclusion |
|---|---|---|---|---|---|---|
| Ghiggia et al. 2017 [26] (Italy) | 21 | After treatment (chemoRT) | DT, EORTC QLQC30, EORTC QLQH&N35, Mini-MAC | Anxiety and depression | Clinically relevant anxiety symptoms & clinically relevant depressive symptoms | QoL \| Patients with high level of anxiety and depressive symptoms showed high level of hopelessness, helplessness, and anxious preoccupation |
| De Souza et al. 2017 [27] (United States) | 73 | During treatment (chemoRT) | Self-reported data | Financial stress | Patients with HNC experience financial stress | Interventions should be investigated in patients who may suffer from financial stress |
| Elaldi et al. 2021 [28] (France) | 72 | After treatment (surgery, RT, chemoRT, and surgery + chemoRT) | QoL questionnaire EORTC QLQC30, EORTC QLQH&N35 | Treatment-related stressor and emotional factors | Fear of recurrence was the main stressor<br>Other stressors include dental, salivary, fatigue, speech, and eating problems | QoL \| Psychological distress was the main determinant of QoL outcomes. Thus, multidisciplinary management of persistent symptoms and psychological distress is essential steps towards improving QoL of patients with HNC |

**Table 1** continued

| Study (Country/Region) | Population | Assessment point in disease trajectory | Questionnaire/QoL outcome measure | Psychological variables assessed | Results | Effect on treatment outcome \| Conclusion |
|---|---|---|---|---|---|---|
| Hueniken et al. 2021 [29] (Canada) | 430 | After treatment (surgery, RT, chemoRT, and surgery + RT and/or chemoRT) | FIT | Financial stress<br>Financial strain<br>Loss of productivity | Post-treatment lost income and financial concerns were source of financial stress and strain in patients with HNC | HRQoL \| Treatment of HNC may cause financial stress to HNC patients |
| Jella et al. 2021 [30] (United States of America) | 710 | Treatment trajectory | National Health Interview survey | Financial | Patients with HNC experience financial stress that is related to medical bills and exogenous expenses | Financial stress may impede patients' ability to access and adhere to treatment or make a trade-off between healthcare and other essential needs |
| Lewis et al. 2021 [31] (India) | 600 | After treatment (RT or concurrent chemoRT) | DT | Socioeconomic status | About 56% of HNC showed significant baseline distress<br>Patient with low socioeconomic status | QoL \| There is a need for interventions to mitigate this type of distress in patients with HNC, especially those with low socioeconomic value |

**Table 1** continued

| Study (Country/Region) | Population | Assessment point in disease trajectory | Questionnaire/QoL outcome measure | Psychological variables assessed | Results | Effect on treatment outcome \| Conclusion |
|---|---|---|---|---|---|---|
| Cerea et al. 2022 [32] (Italy) | 51 | Before treatment (surgery, RT, CT, or concomitant RT and CT) | Self-report | Physical factors (body image distress) and psychological variables such as coping strategies, social anxiety, self-esteem, intolerance of uncertainty, pain, and distress) | Physical QoL was associated with body image distress than psychological variables. Similarly, pain was associated with mental QoL above other psychological variables such as coping strategies, social anxiety syndrome, and self-esteem. Intolerance of uncertainty, pain and distress | QoL \| Body image distress and pain are associated with poor quality of life |
| Eastburn et al. 2022 [33] (United States) | 228 | After treatment (surgery, RT, CT, or concomitant RT and CT) | Eating Assessment Tool, Generalized Anxiety Disorder–7, Patient Health Questionnaire–8 | Dysphagia, anxiety, depression | Dysphagia was associated with increased symptoms of anxiety and depression | Anxiety and depression in survivors of HNC can be monitored for symptoms of dysphagia |
| Braga Mendonça et al. 2022 [34] (Brazil) | 118 | Treatment trajectory (chemoRT) | Phenomenological interview, Suffering inventory | Distress | Distress originated from health services, diagnosis confirmation, the commencement of treatment, and interruption of life projects | Distress was greater in patients who are yet to commence their chemotherapy treatment<br>Feeling of nearness of death |

**Table 1** continued

| Study (Country/Region) | Population | Assessment point in disease trajectory | Questionnaire/QoL outcome measure | Psychological variables assessed | Results | Effect on treatment outcome \| Conclusion |
|---|---|---|---|---|---|---|
| Mott et al., 2022 [35] (United States) | 357,052 HNC 21.4 million for other cancer | After treatment | National Health Interview survey, Annual cross-sectional household survey | Financial and emotional | HNC reported higher level of coping hardship Psychology financial hardship | QoL \| Cancer patients generally have similar levels of psychological financial hardship. However, HNC exhibit higher coping hardship |
| Van Beek et al., 2022 [36] (Netherlands) | 558 | Treatment trajectory (surgery, RT, or a combination of chemoRT, or surgery and [chemo]radiotherapy) | Care use and costs | Physical and emotional factors | Distress, symptoms of anxiety and depression, fear of cancer recurrence, and/or anxiety disorder were associated with higher use of primary care | QoL \| Patients with HNC with psychological problems make more use of healthcare and informal care. Thereby, resulting in higher costs |
| Al-Salool et al., 2023 [37] (Germany and United States) | 213 | Before treatment (surgery, RT, chemoRT, and CT) | DT | Emotional factors (worry, fear, sadness, depression, sadness, and loss of interest) | A significant number of patients developed emotional distress due to the toxicities from treatment. At least one of the emotional problems (sadness, fear, worry, depression, loss of interest, and nervousness) was found in one of the patients | Patients with emotional risk factors are likely to require psycho-oncological assistance |

**Table 1** continued

| Study (Country/Region) | Population | Assessment point in disease trajectory | Questionnaire/QoL outcome measure | Psychological variables assessed | Results | Effect on treatment outcome \| Conclusion |
|---|---|---|---|---|---|---|
| Deenadayalan et al. 2023 [38] (India) | 754 | Before treatment | Structured Pro Forma | Emotional factors | Unawareness of prognosis is associated with higher level of distress | QoL \| Higher educational levels and better socioeconomic status increases the likelihood of being aware of their diagnosis and prognosis |
| McDowell et al., 2023 [39] (Australia) | 182 | Treatment trajectory (RT and chemoRT) | MDASI-HN, HADS, Functional Assessment of Cancer Therapy-General | Emotional factor (support) | Sociodemographic (age, gender, marital status, and level of education are factors that affects the anxiety and burden level of patients with HNC before, during, and after radiotherapy | HRQoL \| Patients with HNC need support before, during, or after chemoradiotherapy patients with HNC differ in terms of their response to treatment trajectories. Therefore, it may be useful to identify patients in need of additional support during treatment to reduce patient suffering acutely and in the longer term |

**Table 1** continued

| Study (Country/Region) | Population | Assessment point in disease trajectory | Questionnaire/QoL outcome measure | Psychological variables assessed | Results | Effect on treatment outcome \| Conclusion |
|---|---|---|---|---|---|---|
| Reyes et al., 2023 [9] (Spain & United States) | 56 | After treatment (surgery, surgery + RT, surgery + RT and CT, RT, or chemoRT) | Sequelae after treatment of HNC,<br>State-Trait Anxiety Inventory | Physical and psychological factors<br>The physical factors include cancer itself and associated treatment sequelae<br>Psychological factors (cognitive and emotional) in the form of anxiety, stigmatization, and discomfort | Anxiety because of stigmatization. The level of anxiety was slightly dependent on gender | QoL \| Treatment of HNC generates physical and psychological burden on the patients |
| Smith et al., 2023 [40] (Australia) | 57 | After treatment (chemoRT ± surgery, RT alone or surgery + RT) | FIT | Financial burden | Financial challenge is associated with poorer HRQoL | QoL \| Interventions aimed at reducing financial challenge should be incorporated in routine clinical care |
| Sunderland et al., 2023 [41] (New Zealand) | 167 | Before treatment | Free form text | Emotional (anxiety and depression) and financial factors | Patients with high anxiety and depression showed increased unmet needs and decreased HRQoL<br>They find it challenging to travel for treatment<br>They also experience financial difficulties | QoL \| Patients with HNC should be monitored for psychological distress and ease of access to health services after treatment |

**Table 1** continued

+ Disease trajectory also extended to include during and after treatment

*BDI-II* Beck Depression Inventory-II (BDI-II), *CT* Chemotherapy, *ChemoRT* Chemoradiotherapy, *DT* Distress Thermometer, *EPQ* Eysenck Personality Questionnaire, *EORTC QLQ-C30* European Organisation for Research and Treatment of Cancer Quality-of-Life-Questionnaire-C30, *EORTC QLQ-H&N35* European Organisation for Research and Treatment of Cancer Quality-of-Life Questionnaire-Head and Neck 35, *FIT* financial Index of Toxicity, *GHQ* General Health Questionnaire, *HADS* Hospital Anxiety and Depression Scale, *HRQoL* Health Related Quality of Life, *Mini-MAC* Mental Adjustment to Cancer Scale, *NCCN DT* National Comprehensive Cancer Network Distress Thermometer, *MDASI-HN* M.D Anderson Survey Inventory for Head and Neck, *PCI* Patient Concerns Inventory, *QoL* Quality of Life, *RT* Radiotherapy, *SF-12* Short Form Survey, *UW-QoL* University of Washington Head and Neck Quality of Life Questionnaire

### Assessment of Methodological Quality and Risk of Bias

The quality of the potentially relevant studies was assessed using an adapted version of the Mixed Methods Appraisal Tool (MMAT) [12]. The MMAT contains a total of 9 items with each assigned a single point. Therefore, the adapted version of the MMAT had a total score of 18 [12]. The presence of the criterion within the study was indicated by +1 (Yes), while its absence by a score of 0 (No) and nothing when it was unclear (?) (Table 2) [12, 13].

### Eligible Studies

In each eligible study, the first author's name, year of publication, country, size of the series, stage of assessment of psychological variables in the disease trajectory, questionnaire or methods used to assess the psychological variables, main results, and a summary were extracted (Table 1).

### Ethical Approval

This article is based on previously conducted studies and does not contain any new studies with human participants or animals performed by any of the authors.

## RESULTS

### Results of the Database Search

A total of 514 hits were retrieved. After deleting duplicates ($n$ = 213), and irrelevant papers ($n$ = 272), there were 29 studies eligible with a total of 362,766 patients with HNC to be included, as shown in Fig. 1 [9, 14–41].

### Characteristics of Relevant Studies

The studies showed high-quality assessment scores (Table 2). Ten (34.5%) of them had been carried out in Europe [14, 16, 19, 22–24, 26, 28, 32, 36], 9 (31.0%) in the United States [17, 18, 21, 27, 29, 30, 33–35], 8 (27.6%) in Asia [15,

**Table 2** The quality of the included studies using the Mixed Methods Appraisal Tool

| Study | Methodological quality criteria | | | | | Total score (25 points) | Quality interpretation |
|---|---|---|---|---|---|---|---|
| | Qualitative (5 points) | Quantitative randomized controlled trials[a] (5 points) | Quantitative non-randomized (5 points) | Quantitative descriptive (5 points) | Mixed methods (5 points) | | |
| #1 | 5 | 0 | 4 | 4 | 3 | 16 | High |
| #2 | 5 | 0 | 3 | 4 | 4 | 16 | High |
| #3 | 5 | 0 | 4 | 4 | 4 | 17 | High |
| #4 | 5 | 0 | 4 | 5 | 4 | 18 | High |
| #5 | 5 | 0 | 5 | 5 | 4 | 19 | High |
| #6 | 5 | 0 | 5 | 5 | 5 | 20 | High |
| #7 | 5 | 0 | 5 | 5 | 5 | 20 | High |
| #8 | 5 | 0 | 5 | 5 | 5 | 20 | High |
| #9 | 5 | 0 | 3 | 3 | 2 | 13 | Satisfactory |
| #10 | 5 | 0 | 4 | 4 | 2 | 16 | High |
| #11 | 5 | 0 | 4 | 4 | 4 | 17 | High |
| #12 | 5 | 0 | 4 | 4 | 4 | 17 | High |
| #13 | 5 | 0 | 3 | 3 | 2 | 13 | Satisfactory |
| #14 | 5 | 0 | 2 | 3 | 3 | 13 | Satisfactory |
| #15 | 5 | 0 | 4 | 4 | 4 | 17 | High |
| #16 | 5 | 0 | 5 | 5 | 5 | 20 | High |
| #17 | 5 | 0 | 4 | 4 | 3 | 16 | High |
| #18 | 5 | 0 | 4 | 4 | 4 | 17 | High |
| #19 | 5 | 0 | 5 | 5 | 5 | 20 | High |
| #20 | 5 | 0 | 2 | 2 | 2 | 11 | Poor |
| #21 | 5 | 0 | 5 | 5 | 5 | 20 | High |
| #22 | 5 | 0 | 3 | 3 | 3 | 14 | Satisfactory |
| #23 | 5 | 0 | 5 | 5 | 5 | 20 | High |
| #24 | 5 | 0 | 3 | 3 | 3 | 14 | Satisfactory |
| #25 | 5 | 0 | 5 | 5 | 5 | 20 | High |

**Table 2** continued

| Study | Methodological quality criteria | | | | | Total score (25 points) | Quality interpretation |
|---|---|---|---|---|---|---|---|
| | Qualitative (5 points) | Quantitative randomized controlled trials[a] (5 points) | Quantitative non-randomized (5 points) | Quantitative descriptive (5 points) | Mixed methods (5 points) | | |
| #26 | 5 | 0 | 5 | 5 | 5 | 20 | High |
| #27 | 5 | 0 | 3 | 3 | 2 | 13 | Satisfactory |
| #28 | 5 | 0 | 5 | 5 | 4 | 19 | High |
| #29 | 5 | 0 | 4 | 5 | 4 | 18 | High |

[a]There were no randomized controlled trials in any of the included studies

*High* 16 points and above, *Satisfactory* between 13 and 16 points, *Low* less than 13 points

20, 25, 31, 38–41], and 2 (6.9%) were international multicenter studies [9, 37]. From the included studies, 13 (44.8%) reported that the patients included in their studies received surgery, radiotherapy, chemoradiotherapy, and surgery + radiotherapy and/or chemoradiotherapy [9, 16, 20, 21, 24, 25, 28, 29, 32, 33, 36, 37, 40], 4 (13.8%) studies reported that the included patients received either radiotherapy or chemoradiotherapy [15, 22, 31, 39], 1 (3.4%) highlighted that the patients received either surgery alone or radiotherapy or chemotherapy, 1 (3.4%) study reported that the patient received only radiotherapy [14], 2 (6.9%) studies mentioned that the included patients received surgery only [17, 18], 3 (10.3%) studies highlighted that the included patients in their studies received chemoradiotherapy alone [26, 27, 34], and 5 (17.2%) studies mentioned the treatment modalities of the patients [19, 30, 35, 38, 41]. Several assessment scales were used to measure the psychological factors as predictors of treatment outcomes. These included Distress Thermometer, European Organization for Research and Treatment of Cancer Quality-of-Life-Questionnaire-C30, European Organisation for Research and Treatment of Cancer Quality-of-Life Questionnaire-Head and Neck 35, Mental Adjustment to Cancer Scale, University of Washington-QoL, MD Anderson Symptom Inventory-Head and Neck Module, Patient Concerns Inventory, Financial Index of Toxicity, National Health Interview survey, Hospital Anxiety and Depression Scale, Eating Assessment Tool, Generalized Anxiety Disorder–7, Patient Health Questionnaire–8, and Suffering Inventory.

### Psychological Consequences of HNC Diagnosis and Association with Treatment Outcome

The diagnosis of patients with HNC have been found to have various psychological consequences such as distress (Section "Psychological Consequences of HNC Diagnosis") [9, 20, 26, 32, 33, 36, 39, 41]. These psychological factors have been found to correlate with poorer treatment outcomes such as the patients' well-being [16, 18], quality of life [9, 19, 20, 23, 24, 26, 28, 31, 32, 35, 36, 38, 40, 41], and health-related quality of life [14, 15, 17, 29, 39] (Section "Effects of Psychological Factors on Treatment Outcome"). The findings of these studies (summarized in Table 1) indicate that psychological variables may interfere with the ability of patients with HNC to cope with the disease [14, 19, 32], its associated physical symptoms [15, 17, 20, 26, 33], and treatment-related issues such as often a remarkable and highly visible disfigurement

**Table 3** Brief overview of psychosocial distress in head and neck cancer patients

| Factors | Sub-factors | | Examples |
|---|---|---|---|
| Psychosocial | Psychological | Behavioral | ■ Adjustment and coping with HNC<br>■ Unrealistic ideas<br>■ Excessive cravings<br>■ Preoccupied mind and altered mood<br>■ Loss of interest in things<br>■ Neuroticism<br>■ Self-blame |
| | | Cognitive | ■ Elevated risk of psychiatric co-morbidity |
| | | Emotional | • Distress<br>• News of cancer<br>• Treatment toxicities<br>• Comorbidity<br>• Unpredictability of the disease<br>• Fear of disfigurement<br>• Fear of complications<br>• Successful management concerns<br>• Fear of recurrence<br>• Nervousness<br>• Discomfort<br>• Prolonged hospital stay<br>• Insufficient information about cancer and treatment<br>• Depression<br>• Worry, fear, sadness, and loss of interest<br>• Existential issues (fear of death and suicide thought)<br>• Fatigue<br>• Hopelessness<br>• Helplessness<br>• Illness intrusiveness<br>• Post-traumatic growth |

**Table 3** continued

| Factors | Sub-factors | Examples |
|---|---|---|
| | Social | ■ Stigmatization<br>■ Low self-esteem<br>■ Unmet needs<br>■ Body image and disfigurement<br>■ Speech<br>■ Interpersonal issues (relationship with others such as partners, friends, families and relatives)<br>■ Dental and salivary<br>■ Dependence on others<br>■ Pain, taste, smell, and odor<br>■ Day-to-day impairments (eating, swallowing, sleeping, and breathing)<br>■ Interference with activities<br>■ Financial (unemployment, inability to return to work, paying medical bills, transportation burden, health insurance, and exogenous financial challenges)<br>■ Low social economic status (living alone, younger age, and social support) |

*HNC* Head and Neck Cancer

and disruptions of essential functioning, such as difficulty in eating, swallowing, breathing, and speech [14], which are indicated by QoL measures (Table 3).

### *Psychological Consequences of HNC Diagnosis*

Studies addressing our first research question (summarized in Table 1) demonstrated that psychological distress was common after receiving a HNC diagnosis and that distress interfered with treatment outcomes, as indicated by QoL measures (Table 3) [9, 19, 20, 23, 24, 26, 28, 31, 32, 35, 36, 38, 40, 41]. Patients with HNC manifested a variety of psychological responses to cancer diagnosis and its treatment, most often reported as feeling anxious or depressed. Specific issues reported were worrying about unpredictability of the disease and about the consequences of treatment toxicities, as well as fears of disfigurement or complications [25]. Depressive symptoms (e.g., fatigue, hopelessness, helplessness, and suicidal thoughts) were common and had co-comorbidity with other conditions, such as having alcohol use disorder or anxiety disorder [42]. Additionally, HNC diagnosis had many functional or social consequences. The social consequences included, for instance, fear of being stigmatized, low self-esteem, negative body image (due to speech impairment, dental and salivary problems), and increased dependence on others. Functional consequences were susceptibility to pain, taste, smell, and odor, and difficulties in everyday life included financial difficulties, difficulties arising from low social economic status, living alone, and having low social support (Table 3). We did not find any studies on the effect of psychological factors on such therapeutical outcomes as tumor response, length of stay, or complication rate.

### *Effects of Psychological Factors on Treatment Outcome*

The psychological variables affecting treatment response may be behavioral, cognitive, or emotional [43, 44]. Behavioral variables include adjustment difficulties and avoidant

coping strategy for HNC. Emotional variables include preoccupied mind (worry) and altered mood, loss of interest, unrealistic ideas, self-blame, and excessive cravings (Table 3). Patients with HNC may often present with a variety of both psychological characteristics (distress, depression, anxiety) and consequences of cancer diagnosis, the disease itself, and its treatment (nervousness, sadness, worry of the unpredictability of the disease, consequences of treatment toxicities, fear of disfigurement, recurrence, and complications). Insufficient information about the status of the disease may lead to fatigue, hopelessness, helplessness, and existential matters (fear of death and suicidal thoughts). Compared to lung cancer patients, there was an elevated risk of psychiatric co-comorbidity among patients with HNC such as alcohol use disorder, adjustment disorder, and depressive disorder [42].

Another important aspect of the psychosocial variables found was the social consequences of HNC. This includes stigmatization, low self-esteem, body image and disfigurement, speech impairment, dental and salivary problems, increased dependence on others, susceptibility to pain, taste, smell, and odor, and day-to-day impairments (eating, swallowing, sleeping, and breathing), all of which may negatively affect relationships with others (such as partners, friends, families, and relatives). There may also be many practical daily challenges including financial difficulties (unemployment, inability to return to work, paying medical bills, transportation burden, health insurance, and exogenous financial challenges), and difficulties arising from low social economic status such as living alone, younger age, and social support (Table 3).

Of the aforementioned psychological variables coping [43, 44], adjustment difficulties, and depressive symptoms (Table 3) were associated with poorer treatment outcomes, as indicated by QoL. Psychological variables were associated with QoL or HRQoL at several points during the disease trajectory – before treatment, during treatment, and after treatment [9, 14–41]. Of the 29 included studies, 5 (17.9%) each examined psychological variables before treatment [17, 32, 37, 38, 41], 2 (6.9%) during treatment [21, 27], 17 (58.6%) after the treatment [9, 14–16, 18, 20, 22–26, 28, 29, 31, 33, 35, 40], and 5 (17.9%) during the entire treatment trajectory [19, 30, 34, 36, 39].

***Patterns of Psychological Variables Before Treatment Outcome*** Before radiotherapy, 33% of the patients had high symptom burden (moderate–severe), i.e., fatigue, sleep disturbance, distress, pain, and problems chewing and swallowing [17]. Previous treatment and cancer stage correlated with the high burden [17]. Distress was seen among 54.1% [38], emotional problems among 10–44% [37], and financial difficulties among 54% [41]. Pre-treatment pain was an independent parameter affecting survival in a large sample of HNSCC [45]. None of these studies had investigated the effect of psychological intervention before treatment.

***Patterns of Psychological Variables During Treatment Trajectory*** Distress was found in 77% of the cases during radiotherapy [21]. Furthermore, 69% of the patients used at least one cost-coping strategy within 6 months of treatment initiation [27]. Of note, distress was found to reduce compliance to radiotherapy, and hence reducing survival rates [46, 47].

***Psychological Variables After Treatment and During Follow-Up*** High level of neuroticism (considered as perhaps the most complex health-relevant personality factor which involves a pattern of anxiety, worrying, moodiness, and negative emotions [48]), avoidant coping strategy, advanced stage of cancer, and smoking history affected the distress level and HRQoL of patients with HNC [14]. Specifically, treatment-related factors seem to affect HRQoL [14]. Depressed patients with HNC showed the worst symptoms (except constipation and finance-related) [15]. Depression was likely to lead to poor QoL and to affect almost all functional aspects of the daily activities of patients with HNC [15]. Prevalence of depression increased from 15% at baseline to 29% at post-treatment state and fell back to 8% during follow-up [20, 26]. The prevalence of fear of recurrence (FoR) was at least 35% in patients with HNC [16, 23, 28] and was predicted by young age and anxiety [16]. Stigma and disease

intrusiveness were especially prevalent in men, and correlated significantly and uniquely with negative psychosocial impact in men [18, 25]. Distress was prevalent in at least 33% of HNC survivors [23, 31], with 70–74% having unmet needs and concerns (oral and eating problems, salivary, speech, dental, and fatigue) [23, 28, 33]. In addition, about 21–72% reported difficulty in paying their healthcare costs and other exogenous financial expenses [29, 30, 40]. About 31% of the patients with HNC struggle to cope with their cancer [35].

### Effects of Pre-existing Psychological Factors on Treatment Outcome

Patients with HNC with neurotic personality were found to have higher distress and lower health-related QoL [14]. Loneliness from living alone without social support, level of education, and worry from unemployed status were found to increase the anxiety level and poor QoL of patients with HNC [19, 38, 39].

### The Association of Psychosocial Variables with Survival

Depression was associated with a reduced survival rate in patients with HNC [46, 49–55]. Similarly, experienced distress was associated with an increased risk of cancer-related mortality [56]. Self-reported physical and social functioning after cancer diagnosis were associated with lower overall mortality [57, 58]. Socioeconomic status also played a role, with higher socio-economic status associating with a higher survival rate [59, 60]. Specifically, higher socioeconomic status (measured by income) correlated significantly with greater survival in Canada [60], Germany, and Taiwan [59, 61]. Factors such as low education, low personal income, and living in low-income areas were associated with poorer survival [62, 63]. Additionally, a history of alcohol-related health problems was associated with decreased survival [64, 65]. Having social support, such as being married, was associated with higher odds of survival in patients with HNC [66].

## DISCUSSION

In this systematic review, we have examined several key psychological and psychosocial factors that are a consequence of HNC diagnosis and its treatment. We discuss how these factors interfere with QoL and survival of patients with HNC. These patients have been specifically characterized by having high levels of psychosocial distress, which, in turn, may interfere with the ability of the survivors to cope with the disease symptoms and the treatment [44, 67, 68]. Patients with HNC are psychosocially distressed, manifested and too often have high levels of anxiety and depression during their radiotherapy, which may decrease their compliance to treatment and thus impact their survival [46, 47]. This review has further examined the association of social and socioeconomic factors on treatment outcomes and found that higher socioeconomic status and higher levels of social support were associated with better chances of survival and better QoL. Of note, our review did not identify studies that would have reported on the impact of psychological factors on such outcomes as tumor response, complication rate, or length of hospital stay.

This review revealed that anxiety, depression, and emotional distress were consistently associated with poorer QoL outcomes among post-treatment HNC survivors [9, 20, 26, 32, 33, 36, 39, 41]. In particular, depression and higher anxiety levels were associated with poorer QoL [41]. Anxiety may be caused by several factors, such as stigmatization, unmet needs (such as support, hospital needs, treatment plan, and financial difficulties), sociodemographic factors (such as poverty, low income, and level of education), FoR, impairments in daily activities, devalued social identity, hopelessness, and helplessness [9, 32, 36, 39, 41]. Stigma may lead to devalued social identity due to the effect of HNC on lifestyle, and the treatments may result in facial disfigurement [25]. The received information of the cancer diagnosis, uncertainty about the treatment (post-treatment and management), anxious preoccupation, helplessness, hopelessness, and physical symptoms such as dysphagia may cause depression in patients with HNC [15,

20, 26, 33]. Of note, a combination of anxiety and depression (distress) was associated with impaired QoL. This finding corroborates what is known in the literature for other cancer subtypes, such as lung, breast, and colorectal cancers [69]. However, during follow-up, both distress and HRQoL were found to be stable [14].

As has been observed previously among patients with HNC, depression and tendency to experience negative emotions are important psychological predictors of low QoL [69]. This review extends previous findings by providing evidence of psychological variables such as anxiety, distress, and depression as predictors of negative QoL outcomes in patients with HNC after treatment [9, 20, 23, 24, 26, 28, 36]. Moreover, their presence may exacerbate the physical burden of cancer [21]. The reasons for the association between HNC and adverse psychological outcomes remain unconfirmed, but they have been suggested to arise from difficulties faced in health care services, distress from waiting for diagnosis confirmation, HNC treatment and its sequelae, the practical life changes due to beginning of treatment, and interruption of life projects [34]. The presence of these psychological variables is significantly associated with higher use of primary care services, more physical complaints, and seeking supportive care and/or informal care [36].

Neuroticism, which is one of the notable personality traits, was found to be associated with lower HRQoL in patients with HNC [14]. By definition, persons with higher neuroticism scores experience high levels of distress across a variety of situations [70]. Thus, the finding that patients with HNC with high levels of neuroticism also had a low HRQoL was expected [14, 70]. A possible explanation is that neuroticism/neurotic patients have negative feelings about their health and self-doubt about various aspects related to the treatment. While neuroticism is one of the five essential personality traits, it would be interesting to see how the other remaining traits, openness, extroversion, agreeableness, and conscientiousness, may affect the QoL of patients with HNC during the entire episode of the disease trajectory. A large body of research has shown that people with high conscientiousness live longer and are healthier, but studies among patients with HNC are lacking.

Patients with HNC experience psychoneurological symptoms, such as depression, fatigue, sleep disturbance, pain, and fatigue, while receiving radiotherapy [21, 71–73]. However, depression and fatigue appeared to be the two core symptoms that are connected with various aspects of QoL. These symptoms decrease the patients' functional status, QoL, and survival ratio [73]. Stronger symptom networks were associated with female sex, higher stress levels, and no alcohol use [73]. Of note, patients with HNC experienced increased epigenetic age acceleration, which is associated with fatigue and inflammation (debilitating symptoms in patients with HNC), especially immediately after treatment completion [72]. These findings suggest that some of the associations could be explained through epigenetic or inflammatory pathways.

Patients with HNC have been reported to be more prone to distress compared with other cancer groups [21, 67, 69]. This is due to the disease affecting their daily lives in terms of pain, improper functioning, and its manifestation (e.g., dysphagia) and disfigurement [25, 33]. Therefore, the associated psychological suffering affects their social lives [22, 25]. Higher distress level was more prevalent in patients with advanced-stage HNC, not having begun chemotherapy, and in those receiving palliative chemotherapy [34]. Considering the overwhelming psychological burden associated with HNC, patients tend to use different coping strategies [14, 19, 32, 35]. As shown in this study, the coping approach has a compelling relationship with the QoL [19]. Typically, patients use coping mechanisms when trying to alleviate the psychological consequences of HNC [19, 35]. Generally, coping can be divided into avoidance coping (social distancing or avoiding thinking about the disease), or active coping (finding benefits from one's situation, being optimistic, and seeking knowledge). Avoidance coping was helpful to guarantee self-esteem but exacerbated the distress level of patients with HNC, therefore leading to a low HRQoL [14]. This aligns with prior studies which have shown that active coping

strategies are often (with some exceptions) more beneficial for health and well-being than avoidant strategies. However, active coping strategies such as benefit finding and optimism were associated with improved QoL [19, 32]. These were instrumental to the patients in identifying the positive consequences of HNC diagnosis such as receiving support and love from others, bringing family closer together, knowing more about adjustment strategies, and being strategic in one's approach to things (taking things as they come) [19, 32, 35]. It should be noted that a few studies in this review emphasized coping mechanisms [14, 19, 32, 32, 35]. Therefore, the finding should be interpreted with caution since the studies did not measure coping strategies at more than one time point, and it is possible that coping strategies employed by HNC survivors may change during the entire disease or treatment trajectories since they experience more coping hardship than other cancer survivors [35].

The FoR concern was another factor that can affect post-treatment QoL [16, 23, 28, 36]. This was corroborated by the fact that the anxiety level decreases after treatment and typically increases after about a year after treatment, possibly due to the FoR (mostly common in female patients with HNC below the age of 55 years), or concerns relating to returning to work [20, 74]. It was present in these patients either intermittently or consistently [16], and it represents one of the main concerns during the post-treatment period in the disease trajectory [28]. This is particularly important in HNC given that it is a malignancy characterized by aggressive behavior and a high chance of recurrence [54–56]. As a result, patients with HNC with a high level of FoR were associated with higher use of primary care services, resulting in higher costs [36]. Therefore, interventions by a multidisciplinary team aimed at alleviating the FoR in these patients would represent an essential step toward improving the QoL of patients with HNC. For example, in Germany, a certified HNC center is expected to offer all patients with HNC a psychologic assessment that will include a psychologist specialized in cancer care. Besides multidisciplinary interventions, other newer approaches that are beyond the adjustment to the fear, threat, or expectation of recurrence after intervention are warranted to allay FoR in patients with HNC [75].

Other psychological variables such as body image distress and pain have been touted to have significant association with QoL of patients with HNC [32]. The physical QoL of patients with HNC has been affected more by body image distress than other psychological variables [32]. Pain, on the other hand, affects the mental QoL above other psychological variables [32]. A substantial number of patients with HNC experience high symptoms of pain which affects their social lives (social withdrawal) [17, 22, 32]. The experience of constant pain persists even after receiving treatment such as definitive accelerated radiotherapy, thereby contributing to a lower QoL [76].

Sociodemographic parameters affect the level of anxiety in patients with HNC. Age (less than 45 years), sex (females), marital status (unmarried or living alone), and level of education (low level of education) are factors that affect the anxiety and burden level of these patients before, during, and after radiotherapy [39]. For example, younger age (less than 45 years) was associated with increasing distress and anxiety [20, 23]. This may be because of considering the treatment outcome and the unaccomplished future plans related to career, education, and marriage, among others. Deficits in social support negatively affect the overall QoL of patients with HNC. It was found that moderate to high levels of benefit finding, emotional support, optimism, living with a partner, high education, and active coping strategies may lead to positive consequences [19]. Smoking has been linked to a decreased ability to cope with stress [77]. Patients receiving palliative care may benefit from spiritual resources to reduce the associated higher level of stress at this stage [34]. In addition, living alone and unemployment were associated with higher anxiety and poor QoL [23]. This is evident considering the high level of burden, pain, and social isolation associated with HNC. Therefore, additional support from partners, spouses, and social caucus is imperative to reduce the patient's suffering acutely and in the longer term [23, 39]. If the patient is living without a partner or family members, there

should be support available through healthcare or the social system. The level of education plays a significant role in the level of distress of these patients [38, 39]. Patients with a low level of education may not have substantial information about their diagnosis and prognosis, and this increases their level of anxiety and depression [38, 39]. Low economic status limits the financial ability of the patients in terms of having medical insurance and being able to cover the medical costs, at least in some countries. This may increase the level of anxiety in terms of obtaining the protocol management of the disease [27, 29–31, 40, 41].

The negative effects of depression and anxiety on the QoL of these patients further corroborate the clinical HNC guidelines for recommending routine clinical screening for both depression and anxiety (or distress). Identification of patients at a high risk of distress is critical, because it could allow planning timely and targeted interventions [78–80]. Such a personalized approach could potentially lead to better oncological outcomes. Remarkably, depression and anxiety can occur at any stage of the disease trajectory. As a result, screening should be done at the time of diagnosis, during treatment, after treatment, and during follow-up to identify patients who exhibit clinical symptoms of distress. Prior to screening, it is important to standardize the QoL measuring tools to enhance their replicability, and to demonstrate that they are free from bias. One of the remarkable findings of this review showed a wide range of heterogeneity and diversity in the measurement tools for the arrays of psychological factors and QoL of HNC survivors [9, 14–41]. Therefore, there is currently no recognized gold standard measurement for these psychological factors and their effects on QoL. As a result, it may be challenging to properly understand the effects of these psychological variables on QoL.

The importance of investigating the impact of psychological factors on cancer treatment response has been recently highlighted in the study by Fraterman et al. [81]. They suggested that pretreatment emotional distress may be a marker associated with clinical responses after neoadjuvant immune checkpoint blockade in melanoma, which warrants further research. Our review found a relationship between depression and survival of patients with HNC, with depressed patients having a reduced survival ratio [46, 49–55]. This result is iconsistent with a recent systematic review that examined the effect of depression on the survival of patients with HNC [82]. The pooled analysis in this study demonstrated a statistically significant effect of depression on survival [82]. This finding is corroborated by the results of other reviews of depression in HNCs, breast, lung, brain, skin, and hematologic cancers [83–85]. Of note, depression may lead to treatment interruption and reduced compliance (behavioral effect), which affect treatment response (biological effect) [46, 51] and even increase suicidal thoughts [86]. Despite the establishment of an association between depression and survival in patients with HNC, it is important to emphasize that the strength, mechanisms, and etiology of this association remain unclear [83]. Therefore, a multi-institutional study is warranted to investigate this association, depression screening, and its management interventions [83]. Most importantly, it remains to be ascertained whether depression is an independent prognostic factor of outcome in patients with HNC [55]. This is particularly important considering other reports that have suggested no association between depression and overall survival in patients with HNC [87], so more evidence is thus needed to establish depression as a risk factor for disease progression [84].

Apart from receiving the diagnostic news of cancer, and uncertainty regarding treatment and its outcome, several other factors may exacerbate the level of depression in patients with HNC. These include demographic factors, such as sex, absence of active social network, and marital status (unmarried). For example, mental health disorders, treatment delays, and body image disturbance are prevalent in female patients. Remarkably, these are predictors for depression that can reduce the chance of survival [52, 88]. In addition, ineffective coping strategies [89], risk of suicide [90], unhealthy lifestyle, and continued alcohol use after diagnosis are reported to have an adverse effect on survival [91, 92]. Therefore, screening for depression [51, 87] and

mental health disorders [52] and depression intervention strategies are warranted to improve overall survival [50]. Also, social support should be considered as part of standard care for managing HNC, since patients with reduced or no social support from families were significantly more likely to develop depression [66, 93].

In studies conducted in Canada, Germany, and Taiwan, socioeconomic status correlated significantly with survival [59–61, 94]. Patients with HNC with higher income status were associated with higher survival, and this was especially seen in oropharyngeal cancer compared with other subsites [60]. The authors suggested that this may indicate indirect evidence of the prevalence of papillomavirus (HPV)-positive HNC in higher socioeconomic group, although there appears to be no evidence to suggest that HPV-positive HNC is more prevalent in patients with high social economic status [60]. However, this disparity between socioeconomic groups may further make a case for unequal treatment, and tends towards confirming the significant impact of socioeconomic deprivation on overall survival for patients with HNC, especially in Canada [60]. Hence, special attention should be paid to clinical care of patients with HNC with lower socioeconomic status [95].

Our review has summarized information about important psychological and psychosocial factors from the last decade that affect the QoL in HNC survivors, but it has a number of limitations. Firstly, the review considered the psychological factors throughout the disease trajectory. However, the level of psychological burden experienced by patients with HNC varies before, during, and after treatment, respectively. Therefore, each of these would merit a distinct study. In addition, not all the included studies were required to have measured the psychological factors prior to HNC treatment to rule out the possibility of reverse causality (the treatment affecting psychological factors). The efficacy of psychological (e.g., distress) intervention for patients with HNC is warranted in future studies. In summary, our review accepted the hypothesis that there is a variability in experiencing distress among patients with HNC, and that higher levels of distress correlate with poorer treatment outcomes. In addition, it further confirmed the hypothesis that traits such as neurotic personality, low social support, and a history of psychological problems are associated with worse treatment outcomes. Finally, our review accepted the hypothesis that knowing these psychological factors will help to define methods to assist HNC survivors deal with these adverse symptomatic sequelae that are capable of imposing significant psychological and physical burdens on patients with HNC after treatment.

## CONCLUSION

Our review demonstrated strong negative associations between psychological variables and both QoL and survival of patients with HNC during their treatment trajectory. Psychological aspects also affect patients' social life. Psychological distress may thus not only be present in patients but also in their caregivers. Therefore, multidisciplinary interventions become imperative to improve HNC survivors' QoL. Remarkably, a successful treatment or a patient's satisfactory medical care does not necessarily mean that the patient is free from psychological burden. As a result, continuous routine screening at every stage of the disease trajectory is encouraged to identify patients who are at a high risk of psychological burden. For reproducibility and homogenization of findings, a systematic and standardized QoL measurement framework should be developed. This will enhance a uniform understanding of the relationships between the QoL and psychological variables among post-treatment HNC survivors in various studies. Future studies should also examine the impact of distress interventions on treatment response. Such studies could inform the development of insightful interventions and supportive care strategies to improve QoL in this population.

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### *Declarations*

***Conflict of Interest.*** Antti A. Mäkitie, Rasheed Omobolaji Alabi, Laura Pulkki-Råback, Alhadi Almangush, Jonathan J Beitler, Nabil F Saba, Primož Strojan, Robert Takes, Orlando Guntinas-Lichius. Alfio Ferlito is an Editorial Board member of Oncology and Therapy. Alfio Ferlito was not involved in the selection of peer reviewers for the manuscript nor any of the subsequent editorial decisions.

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