REVIEW

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Development of depression in patients with oropharyngeal cancer: a systematic review

Cover figure. Depression in patients with oropharyngeal cancer: represents a significant issue in contemporary head and neck oncology (Created in BioRender. Salskov, I. (2025) https://BioRender.com/i21h75z).

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Summary

Objective. The incidence of oropharyngeal cancer (OPC) has increased in the Western world. OPC affects quality of life, although the risk of depression in patients with OPC remains unknown. We investigated the risk of developing depression in patients with OPC.
Methods. Studies were identified through a systematic search in PubMed and EMBASE following Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines.
Results. Four studies comprising 3,736 OPC patients (range, 130-2,497 patients) from the United States (US/SEER and US/Texas), Australia, and the United Kingdom (UK) were included. The studies differed in methodology. The UK study showed that 47% of OPC patients had depressive symptoms compared to 14% of OPC patients with mild, moderate, or severe depression in the Australian study at 12 months after diagnosis. The US/SEER study found a cumulative probability of 19% for develop-ing depression within 5 years after diagnosis, while the US/Texas study found that 15% of the OPC patients had symptoms of major depression after OPC diagnosis but before radiotherapy. **Conclusions**. Overall, this study indicates that OPC patients are at risk of developing depression, although studies are heterogenous. Screening for depression among OPC patients should be con-sidered in future treatment regimens.

Keywords: depressive symptoms, depression, oropharyngeal cancer, squamous cell carcinoma, human papilloma virus

Introduction

The incidence of oropharyngeal cancer (OPC) has been increasing in the Western world for the last few decades, primarily driven by infection with oncogenic human papillomavirus (HPV) [1-4]. HPV-positive (HPV+) OPC exhibits a distinct biological, epidemiological, and histopathological profile compared to HPV-negative (HPV-) OPC, which is driven by tobacco and alcohol [5-7]. Most importantly, HPV+ OPC patients have a more favourable prognosis [1,7,8].

The treatment regimen comprises, per tradition, most often chemoradiotherapy (CRT) but also surgery, radiotherapy (RT), or chemotherapy (CT) either in combination or as monotherapy [9-12]. Treatment-related side effects include dysphagia, xerostomia, difficulties with chewing, fatigue, and appetite loss, which severely and negatively impact the quality of life (QoL) [13-18]. Furthermore, OPC survivors have been shown to experience sexual health problems and psychological distress post-treatment [19,20].

A recent study showed that patients with oral cancer, a nearby location to OPC, are at risk of developing depressive symptoms (DS) post-treatment [21], in parallel with cancer patients in general [22,23]. Additionally, studies found that cancer patients with depression are associated with a higher mortality rate than cancer patients without depression [24].

However, there is a lack of knowledge regarding the risk of depression in patients with OPC, comprising the 2 clinical phenotypes, i.e., HPV or tobacco and alcohol induced OPC. Therefore, the aim of this systematic review was to investigate the risk of depression in patients with OPC.

Materials and methods

This systematic review was conducted according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) [25] (Fig. 1). Two reviewers (CJK and IS) independently screened the articles. Eligible studies were identified through a systematic search in the PubMed and EMBASE databases.

Inclusion criteria were: 1) patients treated for oropharyngeal cancer (including CRT, surgery, CT, RT, or combinations thereof); 2) depression diagnosis and/or DS evaluated either by validated depression questionnaires, International Classification of Diseases (ICD) codes, or diagnosed by a psychiatrist; 3) language in Danish, Swedish, Norwegian, or English; and 4) published within the last 10 years.

Studies were excluded if they included less than 5 patients. If the same study cohort was used twice, only one study was included.

To build the search string, the following keywords were used: "oropharyngeal cancer" and "depression" or "post-traumatic stress disorder (PTSD)" or "quality of life" and "cancer survivors" or "aftercare". Possible synonyms for the keywords were employed. Supplementary 1 contains extended details on the electronic search. The last search was conducted on September 29, 2023.

The following data were extracted: authors, publication year, country, centre/database, inclusion period, number of patients, age, gender, follow-up time, measurement of depression, anatomical subsite, histology, HPV status/definition, treatment regimen, and tumour stage at diagnosis.

Results

The literature search retrieved 1,042 studies after exclusion of duplicates (Fig. 1). Four studies met the inclusion criteria with a total of 3,736 patients (range, 130-2,497 patients; Tab. I). Jansen et al. included 973 patients with OPC from 2011-2014 [26]. Shinn et al. included 130 patients with OPC from 2005-2007 [27] and Bigelow et al. included 2,497 patients with OPC from 2004-2011 [28]. While the US/Texas study only included patients from Texas [27], the US/SEER study included patients from Surveillance, Epidemiology, and End Results (SEER)-Medicare-linked databases from 12 states of the United States of America [28]. McDowell et al. included 136 patients with HPV+ OPC from 2018-2019 [29].

Clinical characteristics

The overall M:F ratio was 4:1. The US/Texas and Australian studies reported a mean age of 56 and 61 years, respectively [27,29], while the US/SEER study reported a median age of 72 years [28]. The UK study did not further specify age but included 3 patients 16 years old [26]. See Table I.

In the Australian study the palatine tonsils were the most common sublocation (n = 84, 62%) [29], while the base of the tongue was most common in the US/SEER study (n = 1288, 52%) [28]. Two studies did not specify the anatomical subsite [26,27]. In the US/Texas study most patients were American Joint Committee on Cancer (AJCC) Stage III-IV (AJCC version not specified) (n = 119, 91.5%) [27], in the US/SEER study most patients were AJCC 6th Stage IV (n = 1392, 64.8%) [28], and in the Australian study most patients were UICC8 Stage I (n = 74, 54%) [29]. Stage was not defined in the UK study [26] (Tabs. I-II).

HPV status

Most patients in the UK study were HPV+ OPC (n = 603, 62%) based on an enzyme-linked immunosorbent assay (ELISA) [26]. The US/Texas study reported HPV data on 22 OPC patients (17%), with 15 being HPV+ OPC (68%) and 7 being HPV- OPC (32%), with no specification on the

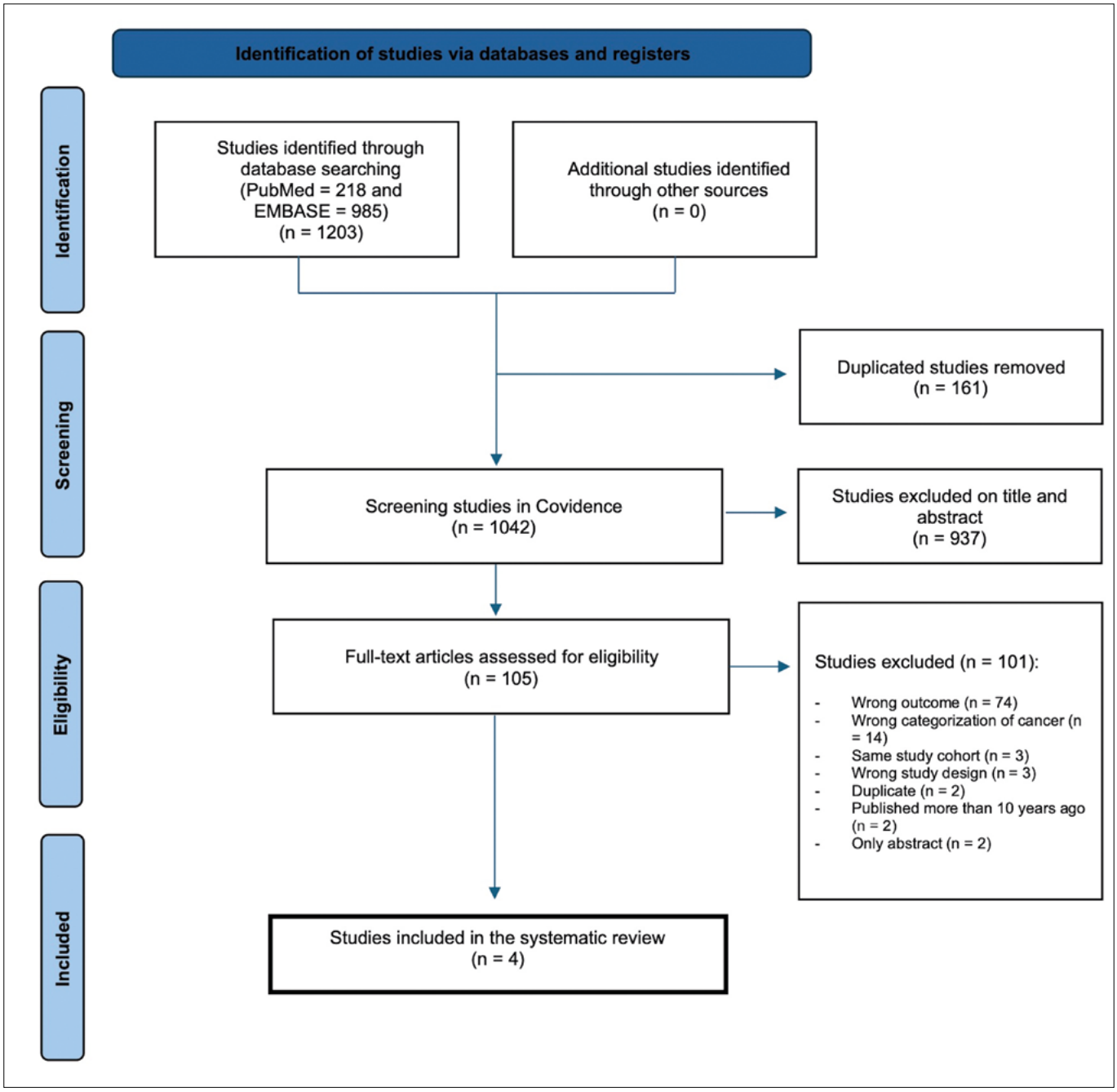

Figure 1. PRISMA flowchart of the study selection.

definition of HPV-positivity [27]. The Australian study only included HPV+ OPC patients based on p16 status [29], while the US/SEER study did not provide HPV status [28] (Tab. II).

Treatment

In the US/Texas, Australian, and US/SEER studies the majority of OPC patients underwent CRT with proportions of 75%, 87%, and 54%, respectively [27-29]. Treatment regimens were not specified in the UK study[26] (Tab. I).

Questionnaires

The UK study, the US/Texas study, and the Australian study used the following questionnaires to measure depression, respectively [26,27,29]: the Hospital Anxiety and Depression

Table I. Overview of study characteristics.

Author, publication year, country of the study	Centre/database	Inclusion period	Number of patients with oropharyngeal cancer
Jansen et al., 2018, the United Kingdom [26]	Head and Neck 5000 (HN5000) prospective clinical cohort study, 76 centres in the United Kingdom	April 2011 - December 2014	Baseline: 973 patients Follow-up: 567 (58%) patients (406 [42%] patients either died before end of the first year or had missing follow-up data)
Shinn et al., 2016, the United States, Texas [27]	The University of Texas M.D. Anderson Cancer Center (MDACC)	March 2005-June 2007	130 patients (18 [14%] patients either died from their cancer or the treatment during the study)
McDowell et al., 2021, Australia [29]	The Peter MacCallum Cancer Centre	November 8, 2018-May 8, 2019	Baseline: 136 patients Answered PROMIS questionnaire: 135 patients (missing response from one patient)
Bigelow et al., 2020, the United States [28]	The Surveillance, Epidemiology, and End Results SEER–Medicare-linked database	2004-2011	2,497 patients

NS: not specified; HADS: Hospital Anxiety and Depression Scale; PHQ-9: Physicians Health Questionnaire; CES-D: Center for Epidemiologic Studies Depression Scale; PROMIS-Emotional distress: Patient-Reported Outcomes Measurement Information System, Emotional Distress Depression Short Form 8a, RT: radiotherapy, ICD: International Classification of Diseases.

Scale (HADS), the Physicians Health Questionnaire (PHQ-9), and the Patient-Reported Outcomes Measurement Information System (PROMIS) questionnaire. None of the questionnaires are diagnostic for clinical depression, but PHQ-9 and PROMIS have a high sensitivity and specificity for detecting clinical depression [30-33].

The fourth study did not use a questionnaire but extracted data on depression from the SEER Medicare-Linked database based on ICD-9 coding.

Depression at diagnosis

At baseline, the proportion of depression and/or DS among OPC patients varied from 4.5% (n = 112) in the US/SEER study [28] to 17.8% (n = 173) in the UK study [26]. In the UK study it was further divided, corresponding to 15.7% (n = 95) of HPV+ OPC patients, 22.3% (n = 53) of HPV- OPC patients, and 18.9% (n = 25) with unknown HPV status [26].

In the US/Texas study 15% (n = 19) had depression at baseline, measured between diagnosis and start of RT, and some of the patients received neoadjuvant CT (n = 47) [27]. They found no significant differences in depression assessed at start of RT between those who received neoadjuvant CT or those who did not (p = 0.613) [27]. Self-reported pre-existing depression at baseline in the Australian study showed that 17 (12%) of HPV+ OPC patient had DS, 116 (85%) of HPV+ OPC patients had no DS, and 3 (2%) did not know [29] (Tab. III).

Depression following treatment

In the UK study, at 12-month follow-up and after treatment start, 567 (58%) OPC patients completed HADS, with 302 (53.3%) never having experienced DS in the study period, 138 (24.3%) having experienced DS at 0 or 4 months from inclusion but recovered at 12-month follow-up, and 127 (22.4%) having persistent, recurrent, or late DS [26]. The US/SEER study found a cumulative probability of 14% and 19% of being diagnosed with depression by one or 5 years, respectively, following OPC diagnosis and treatment start within 6 months [28]. For matched controls without OPC the probability was 6% and 14%, respectively [28].

In the Australian study, mild depression was reported in 12 patients (9%), moderate depression in 5 (4%), and severe depression in one patient (1%) at 12 months or more after treatment completion [29]. They observed an association between higher PROMIS scores and lower global QoL, lower functioning (all 5 European Organization for Research and Treatment of Cancer Quality of Life Questionnaire [EORTC QLQ-C30] domains), higher head and neck cancer (HNC) symptom burden, and symptom interference with

Age	Male (M) vs. female (F) in number	Follow-up	Measurement of depression
No details about age but included 3 pts. 16 years old	NS	4- and 12-month follow-up	HADS
Mean age: 56 years Min: 28.4 years Max: 79.5 years	M: 108 (83%) F: 22 (17%)	Median of 4.9 years Min: 0.1 years Max: 6 years	PHQ-9
Average age: 61 years Min: 42 years Max: 87 years	M: 114 (84%) F: 22 (16%)	An inclusion criterion was ≥ 12 months following treatment completion Years from RT to follow-up assessment: Mean (SD): 3.0 (1.3) Median (range): 2.8 (1.0-5.5) 1-2 years: 38 (28%) 2-3 years: 34 (25%) 3-4 years: 24 (18%) > 4 years: 40 (29%)	PROMIS - Emotional distress
Median age: 72 years Min: 69 Max: 77	M: 1,864 (74.6%) F: 633 (25.4%)	The median follow-up was 5.4 years and 5.7 years, respectively, for cases and controls	Information regarding depression was extracted from SEER–Medicare-linked database based on ICD-9 coding

daily living [29]. No significant association was seen between self-reported depression and anxiety prior to diagnosis and worse emotional distress post-diagnosis [29] (Tab. III).

Depression and prognosis

The US/Texas study showed a significant association between depression measured with PHQ-9 at baseline and overall survival with a hazard ratio (HR) of 3.6 ($p = 0.022$) when adjusted for comorbidities [27]. Furthermore, they found that per unit increase of PHQ-9 the risk of death ($p = 0.040$) and recurrence ($p = 0.017$) increased by a factor 1.1 (10%) [27]. The US/SEER study also reported that depression was associated with decreased overall survival (HR = 1.63, 95% CI: 1.41-1.88) [28]. However, the survival was lower in the matched non-cancer controls with depression (HR = 3.39, 95% CI: 2.93-3.93) compared to OPC patients with depression (HR = 1.63, 95% CI: 1.41-1.88) [28]. In the UK study pretreatment DS were significantly associated with reduced survival in head and neck cancer patients (HR = 1.65, $p < 0.001$) [26]. This remained significant when adjusting for age, gender, marital status, education level, income, Index of Multiple Deprivation (IMD) score (a score that measures deprivation across areas by combining various indicators into single scores), tumour location and stage, intended treatment, and comorbidity (HR = 1.29, $p = 0.025$), but when additionally adjusting for tobacco usage and alcohol consumption, it was not significant (HR = 1.21, $p = 0.094$) [26].

HPV status and depression

The UK study did not specify the proportions of HPV+ and HPV- OPC patients with DS at follow-up, but they did find an association between pretreatment DS and decreased mean survival for HPV-OPC patients (HR = 1.8, $p = 0.031$) [26]. However, this was not significant when adjusting for age, gender, marital status, education level, income, IMD score, tumour location and stage, intended treatment, comorbidity, tobacco usage, and alcohol consumption (HR = 1.22, $p = 0.514$) [26]. No significant association was found, either before or after adjustment for HPV+ OPC patients [26]. No difference in depression was observed between patients with HPV- and HPV+OPC in the US/Texas study [27]. The Australian study only included HPV+ OPC patients [29] (see Table III).

Discussion

This is, to our knowledge, the first systematic review investigating depression in patients with OPC. The proportion

Table II. Overview of anatomical location, histology, HPV status, treatment modalities, and tumour staging.

Author, publication year, country of the study	Anatomical subsite of oropharynx					
	Other oropharyngeal subsite	Palatine tonsils	Base of tongue	Histology	HPV status	
Jansen et al., 2018, the United Kingdom [26]	NS	NS	NS	NS	HPV+: 603 (62%) HPV-: 238 (24%) NS: 132 (14%)	
Shinn et al., 2016, the United States, Texas [27]	NS	NS	NS	SCC	HPV+: 15 (12%) HPV-: 7 (5%) NS: 108 (83%)	
McDowell et al., 2021, Australia [29]	Lateral pharyngeal wall: 1 (1%) Other: 1 (1%)	84 (62%)	50 (36%)	NS	HPV+: 136 (100%) HPV-: 0 (0%)	
Bigelow et al., 2020, the United States [28]	257 (10%)	952 (38%)	1,265 (51%) Lingual tonsils: 23 (1%)	SCC	NS	

NS: not specified; HADS: Hospital Anxiety and Depression Scale; PHQ-9: Physicians Health Questionnaire; CES-D: Center for Epidemiologic Studies Depression Scale; PROMIS: Patient-Reported Outcomes Measurement Information System, Emotional Distress Depression Short Form 8a; HPV+: HPV-positive; HPV-: HPV-negative; ELISA: Enzyme-linked immunosorbent assay; SCC: squamous cell cancer; AJCC: American Joint Committee on Cancer; UICC: Union for International Cancer Control; TNM: tumour, node, and metastasis.

of OPC patients with depression and DS varied from 14% having depression [26,29] to 47% recovering from DS or having persistent, recurrent or late DS [26]. However, the included cohorts were old (2004-2019), and the study designs were heterogeneous in depression screening methods, varying follow-up and data on HPV.

The most widely used treatment regimen was CRT [27-29]. The U.S./Texas study specified the development of depression stratified by treatment regimen and found no significant differences [27]. It might be important for future studies to stratify by treatment regimen since some cancer treatments have been associated with depression through biological mechanisms [34]. Various staging systems were used: AJCC tumour stage, unspecified version [27], AJCC 6th version [28] and the tumour, node and metastasis (TNM) 8th staging system [29]. The Australian study found no impact of stage on the risk of depression [29]. Nonetheless, patients with more advanced disease might be at higher risk of developing depression, with more extensive treatment potentially leading to more severe and long-term side effects negatively impacting QoL.

Most patients had unknown HPV status (2,737, 73%), but among those with known status, most were HPV+ OPC (754, 75%). In the UK study more HPV- OPC patients had DS than HPV+ OPC patients at baseline [26], but no difference was shown in the U.S/Texas study [27]. In general HPV- OPC patients have more risk factors for depression including tobacco and alcohol use, higher age and more comorbidities, which could explain the observed differences observed in the UK study [35-39]. However, the UK study did not report HPV+ and HPV- OPC patient proportions with DS at follow up. The Australian study only included HPV+ OPC patients, and 18 (14%) OPC patients had either mild, moderate or severe depression at follow-up [29]. It should be

	Treatment					
	HPV definition	Chemoradiotherapy (CRT)	Radiotherapy (RT)	Surgery (S)	Surgery + concurrent RT/ CRT	Stage at diagnosis, UICC/AJCC staging system
	Based on ELISA	NS	NS	NS	NS	NS
	NS	Neoadjuvant chemotherapy + radiation: 47 (36%) Concurrent chemotherapy + radiation: 51 (39%)	Radiation only: 32 (25%) Median radiation dose was 70 Gy	NS	NS	AJCC tumor stage: I-II: 10 (7.8%) III-IV: 119 (91.5%) Missing: 1 (0.7%)
	Based on p16 status	Chemotherapy + radiation: High dose cisplatin: 55 (41%) Weekly cisplatin: 33 (24%) Cetuximab: 22 (16%) Other concurrent: 10 (6%) Missing: 1	Radiation only: 16 (12%)	No surgery: 108 (82%) Diagnostic tonsillectomy: 18 (14%) Pre-CRT/RT excisional lymph node biopsy: 6 (5%) Post-treatment neck dissection: 1 (1%) Debulking of the primary: 1 (1%) Missing: 5	NS	UICC/TNM 7: II: 3(2%) III: 20 (15%) IVA: 100 (74%) IVB: 13 (10%) UICC/TNM 8: Stage I: 74 (54%) Stage II: 22 (16%) Stage III: 40 (29%)
	NS	Chemotherapy + radiation: 1,341 (53.7%)	Radiation only: 470 (18.8%)	Surgery only: 159 (6.4%)	Surgery plus radiation: 165 (6.6%) Surgery plus chemotherapy with or without radiation: 362 (14.5%)	AJCC 6th tumour stage: 0: 18 (0.8%) I: 119 (5.5%) II: 185 (8.7%) III: 433 (20.2%) IV: 1,392 (64.8%) Unknown: 350

noted that all patients were disease-free at the time of evaluation for depression, and the cohort was small (n = 135) [29]. Due to limited and heterogeneous HPV data, drawing firm conclusions remains challenging. This underscores the importance of including p16 and/or HPV in future studies.

DS have been associated with worse survival in HNC patients [40], which was also reported in the UK study [26]. The U.S./SEER and U.S./Texas studies identified a significant association between development of depression in OPC patients and decreased overall survival [27,28]. However, it is likely that patients with advanced cancer and poor prognosis experience more depression.

The depression questionnaires used [26,27,29] included questions on tiredness, dry mouth, etc. which are also well-known treatment related side effects and might inappropriately classify as DS in OPC patients [13-18]. PHQ-9 and PROMIS have a high sensitivity and specificity to detect clinical depression [30-33], while HADS is recommended as a screening tool[41]. Furthermore, the UK study used a cut off at 7 [26], although the official HADS classify scores from 8-10 as borderline abnormal, and scores above 10 as abnormal [41]. This might overestimate OPC patients with DS in the UK study; incorporating all 3 questionnaires in future research could offer a clearer understanding of the correlation between these instruments in OPC patients. The US/SEEER study used the outdated ICD-9 codes that does not comply with current diagnostics. This highlights the need for more standardised methods for diagnosing and monitoring depression in OPC patients as a preferred final goal.

Since epidemiological data varies regarding to study methods, study populations and depression measurements, it is difficult to compare and generalise the risk of depression in patients with OPC. Studies have reported that the prevalence of major depression among the elderly ranges from 0.9-42% [42-46]. In this review, only the U.S./SEER study

Table III. Overview of depression outcome.

Author, publication year, country of the study	Measurement of depression	Range of scale
Jansen et al., 2018, the United Kingdom [26]	HADS	HADS score > 7 was used as a cut-off for identifying persons with DS
Shinn et al., 2016, the United States, Texas [27]	PHQ-9	From 0 to 27. A cutoff score of 10 has a high positive predictive value for diagnosing major depression
McDowell et al., 2021, Australia [29]	PROMIS (Emotional Distress-Anxiety Short Form 7a [7 items] and Emotional Distress-Depression Short Form 8a)	Scores are converted to t-scores: 60-69.9 indicates moderate levels of depression, ≥ 70 indicates severe levels of depression Range for mild depression NS
Bigelow et al., 2020, the United States [28]	Information regarding depression is extracted from SEER-Medicare-linked database based on ICD-9 coding	NS

HADS: Hospital Anxiety and Depression Scale; PHQ-9: Physician Health Questionnaire; CES-D: Centers for Epidemiological Studies-Depression Scale; PROMIS: Patient-Reported Outcomes Measu
[a] HADS below threshold at all measurements; [b] HADS above threshold at baseline and/or 4-month follow-up, but recovered at 12-month follow-up; [c] HADS above threshold at 12-month follow-up, vation score, tumour location, tumour stage, intended treatment, and comorbidity; and for potential confounding/mediation by tobacco usage and alcohol consumption.

	Depression outcome	HPV+/-
	Baseline prevalence: Population with DS (HADS >7) 173 patients out of 973 (17.8%) Population without DS (HADS ≤ 7): 800 patients out of 973 (82.2%) 12-month follow-up prevalence: At follow-up 567 (58%) completed HADS Prevalence of patients who "never had DS"[a]: 302 patients out of 567 (53.3%) Prevalence of patients who "recovered from DS"[b]: 138 patients out of 567 (24.3%) Prevalence of patients who had "persistent/recurrent/late DS at 12-month follow-up"[c]: 127 patients out of 567 (22.4%) Mean survival: DS were significantly associated with reduced 1,509 days survival in head and neck cancer patients based on HADS (HR = 1.65, p < 0.001) When adjusted[e] no significance was found (HR = 1.21, p = 0.094)	Baseline results: HPV+ DS: 95 (15.7%) No DS: 508 (84.3%) HPV- DS: 53 (22.3%) No DS: 185 (77.7%) Overall survival: Cox regression analyses on the association between pretreatment DS and mean survival: HPV+ OPC: Base case: Reference; No DS vs DS: 0.75 (p = 0.479); Adjusted: Reference; No DS vs DS: 0.65 (p = 0.304) HPV- OPC: Base case: Reference; No DS vs DS: 1.80 (p = 0.031); Adjusted: Reference; No DS vs DS: 1.22 (p = 0.514)
	Baseline: PHQ-9: Prevalence of patients who were above the cutoff: 19 patients out of 130 (15%) Overall survival: Showed a significant association between PHQ-9 depression and the overall survival (HR = 3.6, p = 0.022). For every unit increase of PHQ-9 the risk of death (p = 0.040) and recurrence (p = 0.017) increased by a factor 1.1 (10%)	No difference in depression status was observed between HPV+ and HPV- OPC
	Characteristics: Self-reported pre-existing depression: Yes: 17 (12%) No: 116 (85%) Do not know: 3 (2%) Follow-up: Mild range: 12 patients out of 135 (9%) Moderate range: 5 patients out of 135 (4%) Severe range: 1 patient out of 135 (1%) Mean scores for depression were 45.2 (SD = 7.85, range 38.2-70.7)	Only HPV+ patients included; all results described in Table II regard HPV+ patients
	Baseline prevalence: Depression: 112 patients of 2,497 (4.5%) Cumulative probability: Cumulative probability of being diagnosed with depression by 1 year in cases after treatment is 14% Cumulative probability of being diagnosed with depression by 5 years in cases after treatment is 19% Overall survival: Depression was associated with decreased overall survival (HR = 1.63, 95% CI: 1.41-1.88)	NS

rement Information System; SEER: Surveillance, epidemiology, and end results, DS: depressive symptoms.
regardless of outcome at baseline and 4-month follow-up; [d] The base case analysis is adjusted for age and gender; [e] Adjusted for age, gender, marital status, education level, income, IMD depri-

compared with matched non-cancer controls and found a higher cumulative probability of depression among OPC patients [28]. In a recent Danish study, the prevalence of existing depression among people aged 65-74 years old was 10.2% among men and 15.4% among women [47]. This aligns with the results observed in this review. However, it should be noted that the majority represented in this study were men (4:1) who have a lower risk of depression [45,47].

A limitation to the study is that 3 studies included patients from 2004-2014 [26-28]. Also, this review did not include a formal risk of bias assessment, which limits the ability to fully assess the quality and reliability of the evidence presented. The studies used non-standardised, heterogeneous methods and study designs with differences in depression screening measurements, follow-up, and HPV availability. Only one study used a current tumour staging system [29], making it difficult to make conclusions on the relation between tumour stage and depression. Moreover, for most patients the depression status prior to OPC diagnosis was unknown, making it difficult to accurately assess their baseline psychological condition. Also, there is a potential selection bias, since patients with sufficient mental resources are more likely to participate in clinical trials.

Currently, no specific depression screening is a part of the follow-up regimen for OPC patients in Denmark. Based on our results, systematically screening for depression following OPC should be considered. Collaborations with patient associations could also facilitate increased awareness about the risk of depression in OPC patients. Likewise, screening for depression in patients with oral cancer is also suggested in a recent study [21]. Our results indicate that patients with HPV- OPC are at higher risk of DS [26], highlighting the importance of additional follow-up for this specific group. Future trials should employ standardised methods for evaluation of depression, p16 and HPV status, tumour stage and treatment regimen to better identify OPC patients at risk of developing post-diagnosis depression.

Conclusions

The findings of this systematic review indicate a risk of developing depression among patients with OPC, with 14% to 46.7% of patients having depression or DS. In conclusion, screening for depression among OPC patients should be a part of standard treatment, preferably with a multi-professional staff including psychiatrists, psychotherapists and psychologists to incorporate comprehensive patient care, optimally in collaboration with patient associations, to emphasise patient empowerment.

Conflict of interest statement

The authors declare no conflict of interest.

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Author contributions

IS: conceptualization, visualization, methodology, writing original draft; CJK: conceptualization, visualization, methodology, writing original draft; ALFC: supervision, conceptualization, visualization, methodology, writing - review and editing; ASK: writing - review and editing; KKJ: writing - review and editing; CC: writing - review and editing; CVB: supervision, conceptualization, writing - review and editing.

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