CLINICAL REVIEW

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Return to work in patients with head and neck cancer: Systematic review and meta-analysis

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Abstract

Background: The aim of this review was to determine the prevalence of return to work (RTW) amongst head and neck cancer (HNC) survivors and to determine its impact on quality of life (QoL).

Methods: A literature search was conducted in PubMed, Scopus, Embase and CINAHL in March 2021. Articles were included if they reported the number of patients with HNC receiving definitive treatment who were working at the time of diagnosis and returned to work.

Results: There were 21 articles deemed eligible for inclusion. Meta-analysis suggested that 67% of patients with HNC who were employed at diagnosis RTW (95% CI 62%–73%, $I^2 = 97.53\%$). Patients who RTW were demonstrated to have lower levels of anxiety and depressive symptoms on the Hospital Anxiety and Depression Scale.

Conclusions: Return to work is an important clinical outcome which must be considered in the survivorship care of patients with HNC.

KEYWORDS

head and neck, head and neck cancer, otorhinolaryngology, Quality of life, return to work

1 | INTRODUCTION

Head and neck squamous cell carcinoma (HNSCC) is the sixth most common cancer worldwide and encompasses tumors of the oral cavity, larynx, pharynx and sinonasal tract. The incidence of HNSCC is expected to further increase due to the rising rates of HPV (human papillomavirus) related oropharyngeal cancers, especially in developed countries where rates of tobacco use are declining. While the median age of diagnosis of HNSCC is 66, the median age of patients with HPV related HNSCC is much lower at 53.[1] Patients with HNC frequently require treatment with a multimodal approach, consisting of various combinations of surgery, radiotherapy, or chemotherapy.[2,3] Procedures such as laryngectomies, neck dissections and reconstructive procedures contribute to the morbidity burden in HNC patients.[4] Treatment-related adverse effects for these patients can include swallowing difficulties, xerostomia, and impeded speech.[5] Previous research has suggested that patients with HNC may have more difficulties returning to work than those with other solid tumors. This is thought to be due to factors such as impacts upon speaking and swallowing, receipt of multi-modal therapy

and possible disfigurement from treatment.[6] Returning to work creates a sense of return to normalcy and appreciation through mechanisms such as social participation.[7] Conversely, the inability to RTW for cancer survivors has been suggested to result in financial loss, social isolation, and reduction of self-esteem.[8] Failure to RTW post-cancer treatment has been shown to be a factor that contributes towards financial toxicity, which leads to a number of negative outcomes such as reduced quality of life, distress and anxiety.[9] Concerningly, a review investigating interventions to improve RTW for cancer survivors found limited studies investigating this topic and no improvement RTW rate amongst the randomized controlled studies.[10]

While there have been previous studies investigating RTW rates for all cancer types, no review exists specifically focusing on the head and neck cancer population. Given the unique challenges faced by this cohort of patients, specific attention is required to identify the RTW rate in this population, as well as to consider the number of people that are required to either reduce their work hours or change their type of work. Therefore, the aim of this systematic review and meta-analysis was to define the prevalence of RTW amongst HNC survivors and compare QoL between those who RTW and those who do not.

2 | METHODS

This study was performed following the PRISMA guidelines for systematic reviews.

2.1 | Eligibility criteria

Studies were included if they met the following inclusion and exclusion criteria. There were no limits on the year of publication.

2.1.1 | Inclusion criteria

- Included patients with HNC (oral cavity, nasopharynx, oropharynx, hypopharynx larynx, salivary glands, or paranasal sinuses) receiving any form of definitive treatment (surgery, chemotherapy, or radiotherapy).
- Reported number of patients who were working at time of diagnosis that returned to any form of work after completion of HNC treatment
- All types of research designs were considered eligible for inclusion (e.g., retrospective or prospective)

2.1.2 | Exclusion criteria

- Studies that did not report number of patients who returned to work
- Studies that included all tumor types and not HNC alone
- Published in a language other than English
- Conference abstracts and other gray literature (e.g., book chapters)

2.1.3 | Information sources and search strategy

The databases PubMed, Scopus, Embase and CINAHL were searched on the 3rd of March 2021. Searches were limited to studies published in English and those that were published up until the date of study search. The search strategy for PubMed is presented below, with appropriate alterations made for use in each individual database.

(("head and neck" OR "oral" OR nasopharyngeal OR nasopharynx OR laryngeal OR larynx OR hypopharyngeal OR hypopharynx OR oropharyngeal OR glottic OR nasopharynx OR nasopharyngeal OR "upper aerodigestive tract" OR "UADT" OR Trachea OR Tracheal or otorhinolaryngologic OR otorhinolaryngological OR "Salivary Gland" OR Salivary OR Palatal OR Mouth OR Gingival OR Neck OR Head) AND ("cancer" OR "carcinoma" OR "neoplasm" OR "neoplasms" OR "malignancy" OR "squamous cell")) AND ("return to work" OR "work engagement" OR "employment" OR "back to work" OR "occupation" OR "work market" OR "workforce")

2.1.4 | Study selection process

The articles were screened based on their titles and abstracts by the first author who created a list of articles for full text review. These articles were then screened independently in full text by the first and second authors to assess for eligibility.

2.2 | Data collection

A single reviewer (JY) extracted the data from the primary text, tables and supplementary appendices into the data extraction form. The data was then checked for accuracy by a second reviewer (JS) and third reviewer (RM).

2.3 | Data items

Extracted data included information on study methodology, participant characteristics and study outcomes. The

extracted data items for each study are demonstrated in Table 1. This included country of publication, study design, sample size, age exclusion criteria, age, sex, tumor location and stage, treatment received, RTW rate, percentage of people that had reduced work hours or changed employment and the quality of life assessment tools used. Instruments that measured symptoms of anxiety or depression were also included as part of the quality of life section.

2.4 | Risk of bias assessment

Studies deemed eligible for inclusion were assessed for quality using the Joanna Briggs Institute Critical Appraisal Checklist for Analytical Cross-Sectional Studies.[11] This critical appraisal checklist includes eight items, which are scored as Yes, No, or Unclear. A score of eight indicates that all criteria were addressed in the study. The quality assessment was completed independently by two authors, and disagreements were discussed to reach a final quality appraisal score.

2.5 | Synthesis methods

A meta-analysis was performed for the outcomes: RTW and quality of life (QoL). A pooled prevalence of the prevalence of RTW, reduced hours and changed work was calculated with 95% confidence intervals. These variables were all coded as a dichotomous variable (either yes or no). To compare differences in QoL for those that returned to work and those that did not, a meta-analysis of mean differences in QoL scores was performed. Meta-analysis was performed using Stata V16 and a random effects model was used given expected heterogeneity across studies. Statistical significance was defined as $p < 0.05$ and 95% confidence intervals were reported. Study heterogeneity was evaluated through examination of I^2 values. Possible causes of heterogeneity in results were examined using sub-group analysis to determine if any patient, tumor, or geographical characteristics were causing variations in the results. Analyses were conducted with the subgroup variables coded as follows: oropharyngeal only versus other tumor subsites, age ≥ 55 versus age < 55 and age ≥ 60 versus age < 60, age exclusion criteria versus no age exclusion criteria, advanced stage (stages III and IV) >50% versus less than 50% and region (America, Europe, Asia, or Australia).

2.6 | Risk of bias across studies

Funnel plots were created and examined to assess for the presence of publication bias.

3 | RESULTS

3.1 | Study selection

The initial search identified 4344 studies, with 1625 duplicates removed to leave a total of 2719 studies for abstract and title screening (Figure 1). There were 56 articles deemed suitable for full-text analysis, from which 21 studies were eligible for inclusion.

3.2 | Study characteristics

A summary of included study characteristics is demonstrated in Table 1. There was a total of 15 878 patients included across the 21 studies. There were two studies that involved prospective follow-up (Buckwalter et al.[12] and Isaksson et al.[13]), while the rest were retrospective or cross-sectional. Studies were conducted in a variety of geographical locations such as North America, Asia, Europe and Australia. There were only 10 studies that had an upper age limit as part of their exclusion criteria for study eligibility. Most studies included patients with varying head and neck cancer subsites, but two included patients with only oral cavity tumors,[14,15] while three studies including only oropharyngeal tumors.[16–18] There was one study by So et al.[19] that included only patients with nasopharyngeal tumors. Most studies had a minimum follow-up period of at least 6 months post treatment as part of their eligibility criteria. Some studies had longer follow-up periods, with the study by So et al.[19] having a minimum follow-up period of 4 years post treatment, and studies by Chen et al.[20] and Rangabashyam et al.[21] having median follow-ups of 63.6 and 50.9 (RTW group) months, respectively.

3.3 | Risk of bias in studies

The quality assessment results using the Joanna Briggs Institute Critical Appraisal Checklist for Analytical Cross-Sectional Studies is demonstrated in Table 2. Overall, the quality of included studies was relatively high, with 11 studies meeting all the assessed criteria. There were two studies that only met 4 of the 8 criteria[6,22] and one that met 5 of the 8 criteria.[23]

3.4 | Return to work

The meta-analysis demonstrated that the pooled prevalence of RTW in HNC survivors was 67% (95% CI 62%–73%, $I^2 = 97.53\%$, Figure 2). There was high

TABLE 1 Characteristics of included studies

Author (Year)	Country	Study design	Sample size	Follow-up time	Age exclusion criteria	Age (years)	Male (%)	Occupation (%)	Tumor location (%)	Tumor clinical stage (%)	Treatment (%)	RTW (%)	Reduced hours (%)	Changed work (%)	Notes
Vartanian et al. (2006)[27]	Brazil	Cross-sectional	301	Minimum of 2 years disease free	–	52 (median)	78.4	–	Oral cavity—52.5 Oropharynx—18.3 Larynx—25.9 Hypopharynx—3.3	I—17.3 II—23.9 III—31.2 IV—27.6	Surgery—52.8 RT—11.4 Surgery + RT—32.8 Surgery + Chemo RT—3	67.1	–	–	Included only patients that were employed at time of diagnosis
Buckwalter et al. (2007)[12]	United States	Prospective observational	211	Followed up to 12 months post diagnosis	–	52.7 (mean)	76.2	–	Oral cavity—33.5 Oropharynx—30.1 Hypopharynx—4.2 Larynx—19.2 Other/Unknown—13	I–II—33.9 III–IV—60.7 Unknown—5.4	Surgery—31 RT—12.6 Surgery + RT—33 Chemo RT—15 Surgery + Chemo RT—4.6 Other—1.7 Unknown—2.1	57.8	–	–	Patients completed surveys at 3, 6, 9 and 12 months post diagnosis RTW rate reported within 1 year of diagnosis
Verdonck-de Leeuw et al. (2010)[26]	Netherlands	Cross-sectional	53	Minimum of 2 years post curative treatment	≥65	59 (median)	64	–	Oral cavity/oropharynx—37 larynx—34 nasopharynx—18 other—12	I—38 II—17 III—19 IV—27	Surgery—21 Radiotherapy—32 Surgery and Radiotherapy—27 Chemo RT—20	83	–	30.2	
Kjaer et al. (2013)[36]	Denmark	Population based cohort study	1808	–	>60	52 (median)	80	–	Oral cavity—22.1 Oropharynx—37.1 Larynx—32.2 Hypopharynx—8.6	I—18.8 II—19.8 III—20.1 IV—41.3	RT—92.9 Surgery + RT—5.9 Chemo RT—1.2	84.6	–	–	RTW measured 1 year after diagnosis
Handschel et al. (2013)[22]	Germany	Cross-sectional	755	–	–	–	–	Blue Collar—51 White Collar—49	–	–	–	51	–	50.2	Demonstrated that white collar workers had a higher RTW rate (59%) compared to blue collar workers (37%) Changed employment defined as changing profession from before diagnosis

(Continues)

TABLE 1 (Continued)

Author (Year)	Country	Study design	Sample size	Follow-up time	Age exclusion criteria	Age (years)	Male (%)	Occupation (%)	Tumor location (%)	Tumor clinical stage (%)	Treatment (%)	RTW (%)	Reduced hours (%)	Changed work (%)	Notes
Koch et al. (2014)[30]	Germany	Cross-sectional	42	Minimum of 2 years posttreatment	>60	Diagnosis-47.3 (mean) Survey-53 (mean)	80	Blue Collar—50 White Collar—50	Oral cavity—15 Oropharynx—27 Larynx—22 Hypopharynx—9 Nasopharynx—13 Paranasal sinus—6 Salivary glands—9	I—18 II—24 III—26 IV—33 Staged using UICC	Surgery—94.5 RT—67.3 Chemotherapy—21.8	42.9	–	–	Demographics reported for whole cohort, not for those only employed at diagnosis
Gallagher et al. (2015)[37]	Canada	Cross-sectional	98	Minimum 1 year post treatment	–	57.4 (mean)	76	–	–	I-II—34 III-IV—59	Surgery—25 Surgery + RT—75	68.4	–	–	Demographics reported for whole cohort, not for those only employed at diagnosis
Pearce et al. (2015)[24]	Ireland	Cross-sectional	264	Minimum 8 months post diagnosis	–	52 (mean)	71.2	Professional—30.3 Service—15.5 Manual—39.8 Unknown—14.4	Pharynx—22.7 Larynx—31.8 Other—45.5	I—29.5 II—17.4 III—14 IV—22 Unknown—17	Surgery—68.6 RT—65.5 Chemotherapy—25	62.9	52	–	
Baxi et al. (2016)[6]	United States	Cross-sectional	102	Minimum 12 months post diagnosis Median—23 months	–	57 (median)	94.1	Professional—52 Officer and Manager—8.8 Executive or Senior Officer—7.8 Sales Worker—7.8 Craft Worker—5.8 Other—9.8 Not provided—7.8	Oropharynx (HPV +ve)—100	III—14.7 IVA/IVB—85.3	Chemo RT—96.1 Surgery + Chemo RT—3.9	85.3	–	–	
Isaksson et al. (2016)[13]	Sweden	Prospective	57	All patients followed up for 24 months	–	54.6 (mean)	76	–	Oral cavity—20 Oropharynx—42 Larynx—11 Hypopharynx—2 Nasopharynx—6 Sinuses—3 Salivary Glands—9 Unknown Primary - 8	77	Surgery—2 RT—32 Surgery + RT—50 Chemo RT ± Surgery—17	61.4	–	–	RTW rate at 24 months used (also reported at 6 and 12 months) Demographics reported for whole cohort, not for those only employed at diagnosis

TABLE 1 (Continued)

| Author (Year) Country	Study design	Sample size	Follow-up time	Age exclusion criteria	Age (years)	Male (%)	Occupation (%)	Tumor location (%)	Tumor clinical stage (%)	Treatment (%)	RTW (%)	Reduced hours (%)	Changed work (%)	Notes
Argawal et al. (2017)[25] India	Cross-sectional	250	Minimum 6 months post treatment Median—19 months	≥60	48 (median)	87.6	–	Oral cavity—65.2 Oropharynx—10.8 Larynx—7.2 Hypopharynx—8.8 Other—8	I-II—11.2 III—19.6 IV—69.2	Surgery + RT—42.8 Chemo RT—24.4 Surgery + Chemo RT—32.8	81.2	44.8	24.1	
Costa et al. (2018)[31] Spain	Cross-sectional	62	Minimum 2 years post treatment	–	53 (mean)	89	High/Intermediate Qualifications—41 Manual workers—59	Larynx/Hypopharynx—100	–	–	53.2	–	–	All patients that had total laryngectomy
Guiliani et al. (2018)[5] Canada	Cross-sectional	64	No minimum follow-up period	>65	56.5 (median)	63.5		Oral cavity—28.1 Oropharynx—21.9 Larynx/Hypopharynx—14 Others—35.9	–	Surgery—14.1 RT—7.8 Surgery + RT—50 Chemo RT—23.4 Unknown—4.7	67.2	48.4	–	71.2% of patients completed treatment for greater than 6 months
Chen et al. (2019)[14] Taiwan	Cross-sectional	174	Minimum 6 months post treatment Median—33 months	>64.5	53.4 (mean)	–	Unskilled/semiskilled—69.5 Skilled—25.9 Clerk, shop, farm owner—2.3 Semi-profession—2.3 Profession—0	Oral cavity—100	I—34.5 II—21.8 III—14.9 IV—28.7	Surgery—52.9 Surgery + RT—11.5 Surgery + Chemo—8 Surgery + Chemo RT—27.6	55.2	–	22.9	Patients at least 6 months post completion of treatment
Check et al. (2019)[16] United States	Cross-sectional	675	Minimum 12 months post treatment Median—72 months	–	Diagnosis-53.2 (mean) Survey-60.3 (mean)	88.1	–	Oropharynx—100	I-II—5.3 III-IV—94.7	Surgery—0.6 RT—29.9 Surgery + RT—1 Chemo RT—67.1 Surgery + Chemo RT—1.3	67.7	–	–	Patients at least 12 months post completion of treatment
Morales et al. (2019)[17] Australia	Cross-sectional	68	Minimum 4 months post treatment Mean—31.2 months	>65	Diagnosis-54.1 (mean) Survey-57 (mean)	89.7	Blue Collar—32.4 White Collar—67.6	Oropharynx (HPV +ve)—100	I—7.4 II—67.6 III—25	RT—7.4 Surgery + RT—1.5 Chemo RT—85.3 Surgery + Chemo RT—5.9	85.3	39.7	19.6	
Chen et al. (2020)[20] Taiwan	Cross-sectional	150	No minimum follow-up Mean—63.6 months	–	63 0.1 (mean)	94	–	Oral cavity—82 Oropharynx, Hypopharynx and Larynx—18	I—18.7 II—28 III—17.3 IV—36	–	38.7	–	–	

(Continues)

TABLE 1 (Continued)

Author (Year)	Country	Study design	Sample size	Follow-up time	Age exclusion criteria	Age (years)	Male (%)	Occupation (%)	Tumor location (%)	Tumor clinical stage (%)	Treatment (%)	RTW (%)	Reduced hours (%)	Changed work (%)	Notes
Chen et al (2020)[15]	Taiwan	Retrospective cohort	10 342	5 years	–	49.1 (mean)	91.6	–	Oral cavity—100	–	Surgery—55.8 RT—35.1 Chemo—22.2	85	–	–	1 year RTW rate used (also reported 2, 3, 4 and 5 year RTW)
Granstrom et al. (2020)[18]	Sweden	Cross-sectional	249	All patients completed survey 15 months post diagnosis	≥62	55 (median)	72	–	Oropharynx—100	87	RT—35.9 Chemo RT—42 Surgery + RT—13.6 Surgery + Chemo RT—8.5	83.9	–	–	Demographics reported for whole cohort, not for those only employed at diagnosis
So et al. (2020)[19]	Canada	Cross-sectional	73	Minimum 4 years post treatment Median— 87.6 months	≥65	52 (mean)	71	Manager or Professional—38 Operator, laborer—25 Sales, technical or administrative— 19 Service—15 Other—3	Nasopharynx— 100	I—5 II—15 III—48 IVA—18 IVB—14	RT ± Chemo—100	61.6	31.1	–	Included only patients greater than 4 years disease free
Rangabashyam et al. (2021)[21]	Singapore	Cross-sectional mixed methods	80	Minimum 6 months post treatment Median— 50.9 months (RTW) Median— 31.3 months (no RTW)	>65	50.1 (mean)	70	Blue Collar—45 White Collar—38.8 Pink Collar—16.3	Oral cavity—48.8 Nasopharynx— 33.8 Others—17.5	I–II—58.8 III–IV— 41.3	Surgery—68.8 RT—71.25 Chemo—42.5	56.3	–	–	

aNumber of patients working at time of diagnosis.

FIGURE 1 PRISMA flow diagram [Color figure can be viewed at wileyonlinelibrary.com]
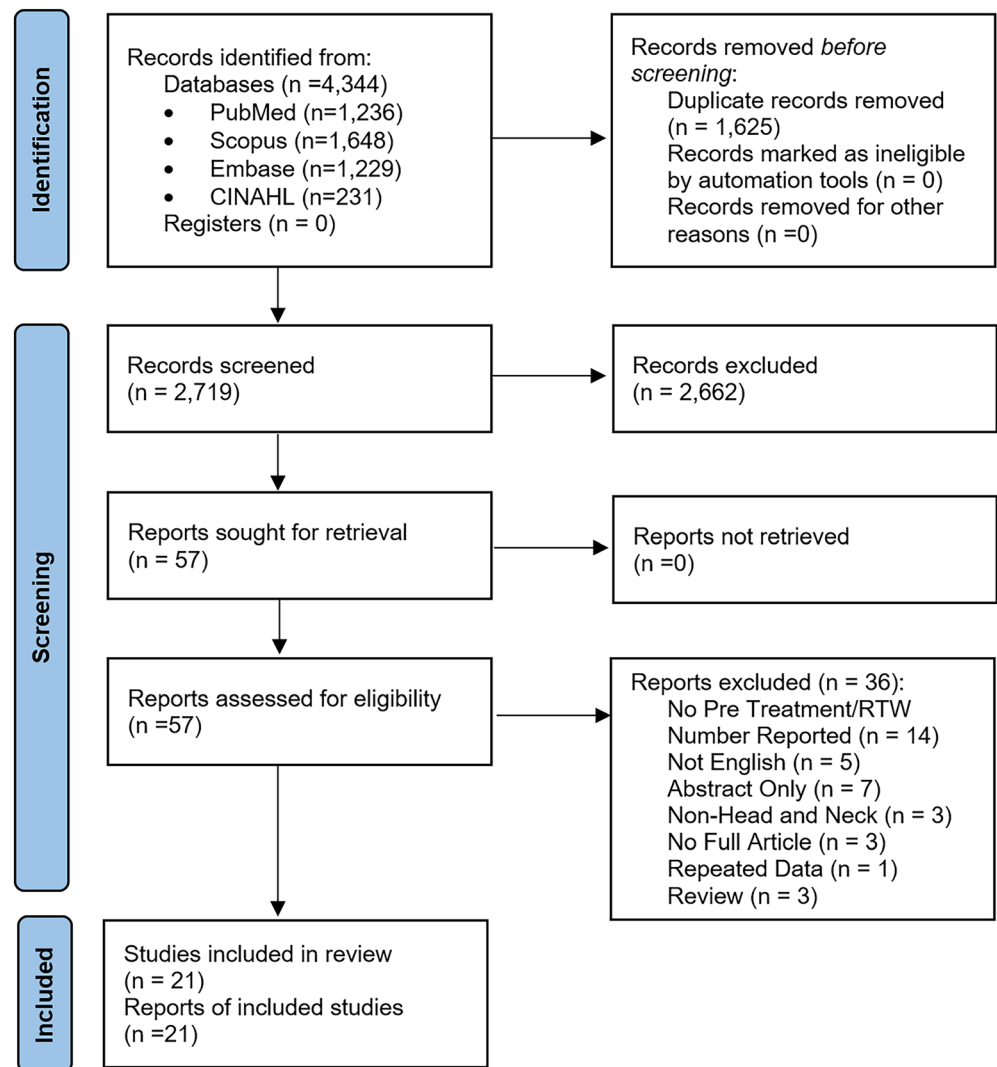
heterogeneity in the reported rate of RTW between studies, as evident by the I^2 value of 97.53%. There were five studies which reported data on number of people who returned to work but had reduced hours.[5,17,19,24,25] A meta-analysis of these studies demonstrated that 44% of HNC survivors worked a reduced number of hours (95% CI 38%–51%, $I^2 = 49.62$%, Figure 3). There were also five studies that reported the number of people who returned to work but had changed occupations.[14,17,22,25,26] The meta-analysis found that 30% of HNC survivors had to change work after completion of their treatment (95% CI 15%–45%, $I^2 = 95.64$%, Figure 4), although there was significant heterogeneity in this finding.

3.5 | Quality of life

As demonstrated in Table 3 there were nine studies that reported QoL outcomes for a RTW and non-RTW groups, with a wide variation in tools used. A meta-analysis was only able to be performed for the Hospital Anxiety and Depression Scale (HADS) using three studies, which showed that patients who RTW had lower anxiety symptoms compared to patients who did not RTW with a mean difference of 1.84 (95% CI −2.89 to −0.79, $p < 0.01$, $I^2 = 0$%, Figure 5). There was also a lower level of depressive symptoms amongst patients who RTW, with a mean difference in HADS of 1.94 (95% CI −2.95 to −0.92, $p < 0.01$, $I^2 = 0$%, Figure 6). All studies reporting HADS scores had long follow-up periods, with the study by Chen et al.[20] having a median follow-up of 63.6 months, the study by So et al.[19] having a median follow-up of 87.6 months and the study by Verdonck et al.[26] only included patients that were at least 2 years post treatment. The two studies reporting outcomes for UW-QoL[14,27] both reported improved QoL for the RTW group. The study by Chen et al.[14] demonstrated that the RTW group had an improved physical function and social–emotional function when compared to the non-RTW group. Studies reporting EORTC had mixed results with the RTW group found to have improved scores in various sub-scales across different studies. For example,

TABLE 2 Quality assessment of included studies

Author (year)	Were the criteria for inclusion in the sample clearly defined?	Were the study subject and the setting described in detail?	Was the exposure measured in a valid and reliable way?	Were objective, standard criteria used for measurement of the condition?	Were confounding factors identified?	Were strategies to deal with confounding factors stated?	Were the outcomes measured in a valid and reliable way?	Was appropriate statistical analysis used?	No. criteria met
Vartanian et al. (2006)[27]	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	8
Buckwalter et al. (2007)[12]	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	8
Liu et al. (2008)[23]	Yes	No	Yes	Yes	No	No	Yes	Yes	5
Verdonck-de Leeuw et al. (2010)[26]	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	8
Kjær et al. (2013)[36]	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	8
Handshcel et al. (2013)[22]	Unclear	Yes	Yes	Yes	No	No	Yes	Unclear	4
Koch et al. (2014)[30]	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	8
Gallagher et al. (2015)[37]	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	8
Pearce et al. (2015)[24]	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	8
Baxi et al. (2016)[6]	Yes	No	Yes	Yes	Unclear	No	Yes	Unclear	4
Isaksson et al. (2016)[13]	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	8
Argawal et al. (2017)[25]	Yes	Yes	Yes	Yes	Unclear	No	Yes	Yes	6
Costa et al. (2018)[31]	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	7
Guiliani et al. (2018)[5]	Yes	Yes	Yes	Yes	No	No	Yes	Yes	6
Chen et al. (2019)[14]	Yes	Unclear	Yes	Yes	Yes	Yes	Yes	Yes	7
Check et al. (2019)[16]	Yes	Yes	Yes	Yes	Unclear	Unclear	Yes	Yes	7
Morales et al. (2019)[16]	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	8
Chen et al. (2020)[20]	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	7
Chen et al. (2020)[15]	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	8
So et al. (2020)[19]	Yes	Unclear	Yes	Yes	Yes	Yes	Yes	Yes	7
Granstrom et al. (2020)[31]	Yes	Yes	Yes	Yes	Unclear	Unclear	Yes	Yes	6
Rangabashyam et al. (2021)[21]	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	8

FIGURE 2 Forest plot for RTW in HNC survivors [Color figure can be viewed at wileyonlinelibrary.com]
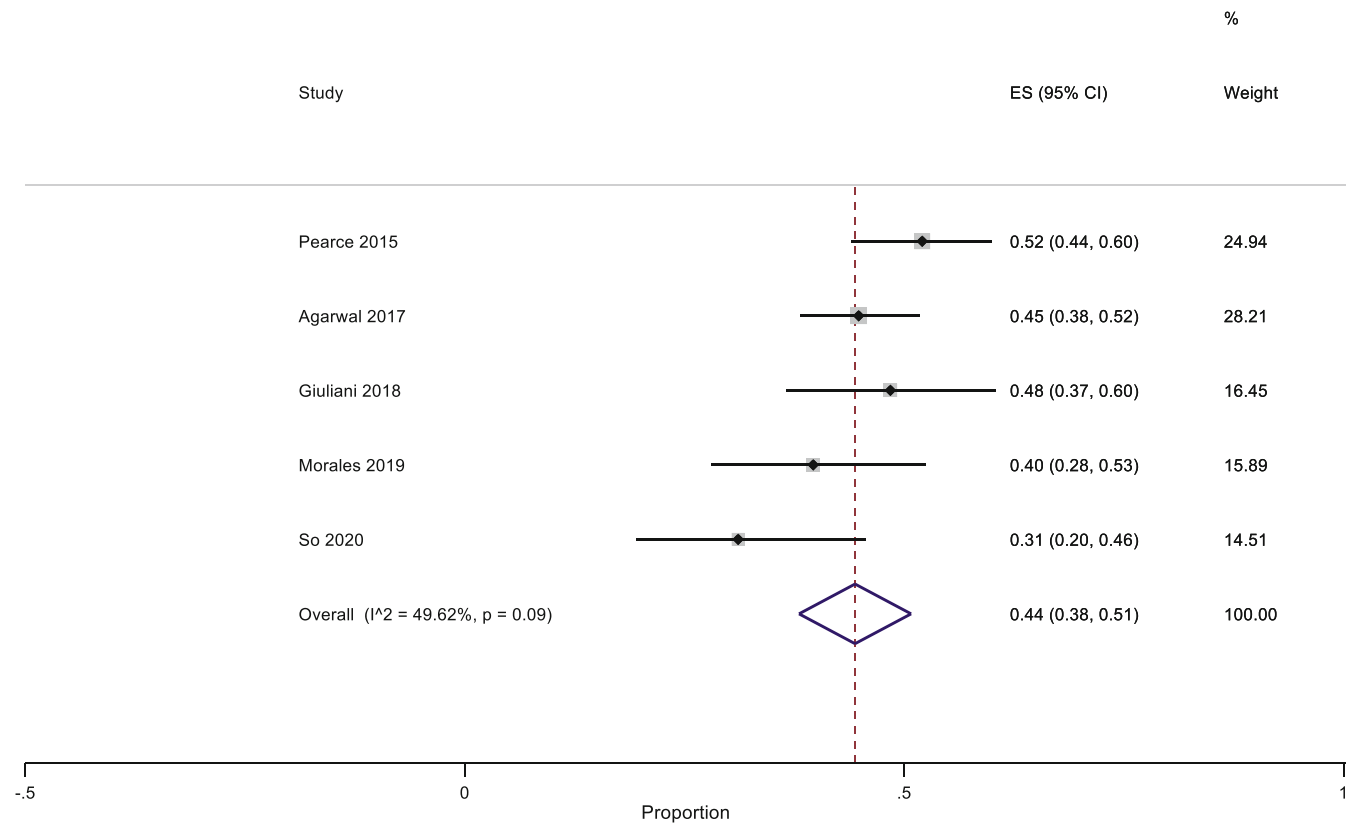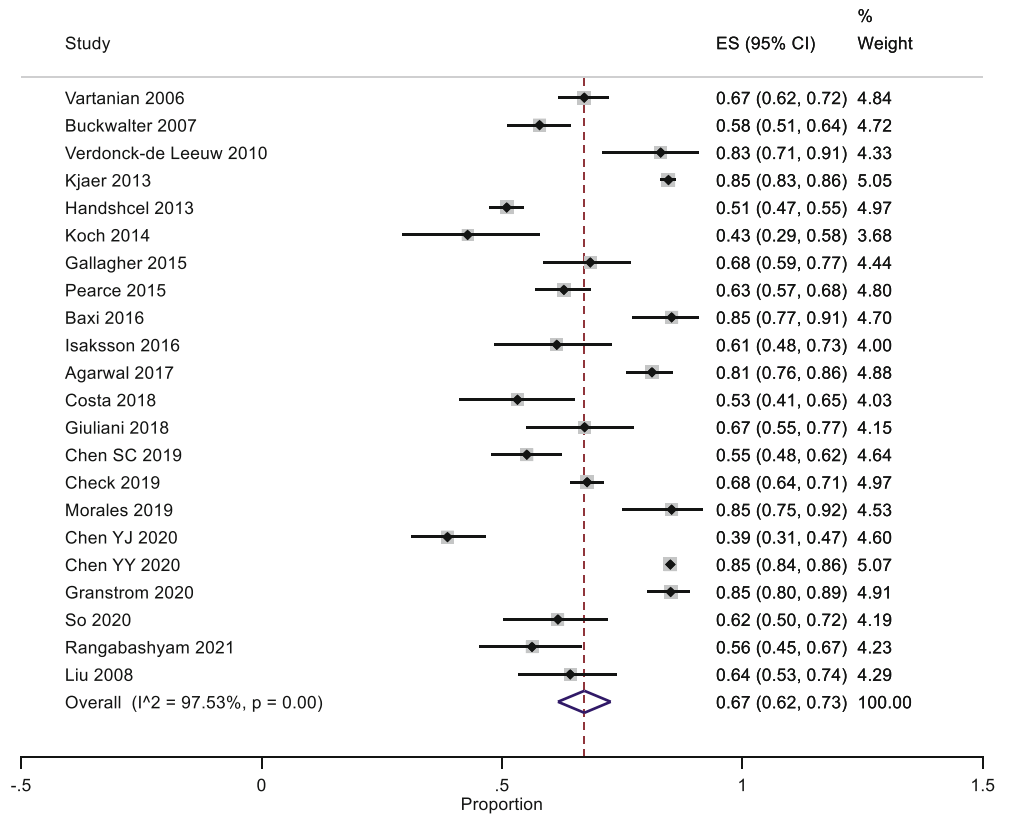

FIGURE 3 Forest plot for reduced work hours in HNC survivors [Color figure can be viewed at wileyonlinelibrary.com]
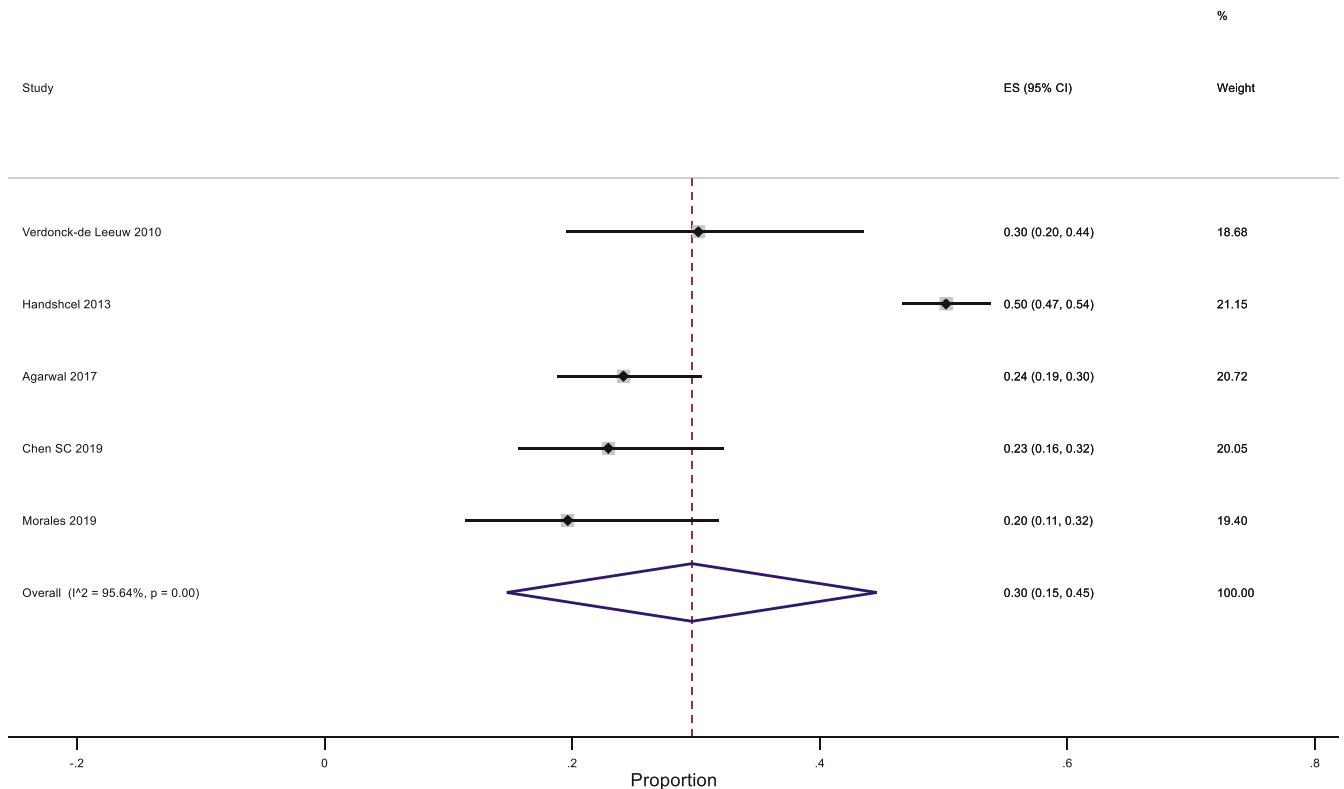
FIGURE 4 Forest plot for changed work in HNC survivors [Color figure can be viewed at wileyonlinelibrary.com]

the study by Verdonck et al.[26] found that the RTW group had an improvement in loss of appetite, social eating, social contact, teeth, opening mouth, dry mouth and sticky saliva compared to the non RTW group. The study by Agarwal et al.[25] found a higher global QoL for the RTW group (77.5 vs. 72.3, $p = 0.014$), as well as a reduced symptom burden from coughing but more problems with sticky saliva. Granstrom et al.[18] reported that local pain, swallowing, appearance and trouble talking on the phone were all associated with RTW. Both studies that reported data for MDASI-HN found that the RTW group had a lower symptom burden, with Check et al.[16] demonstrating lower total symptom, total interference, and total severity. So et al.[19] highlighted that the RTW group had a lower symptom severity score. There were two studies that investigated FACT-HN and both found that the RTW group had a statistically significant increased total score (improved QoL).[17,19]

3.6 | Sub-group analyses

Sub-group analysis (Appendix A) demonstrated that studies consisting of patients with only oropharyngeal tumors had a higher RTW rate than the rest of the studies (80% vs. 64%, $p = 0.01$). There was no difference in RTW rate for studies with a median age greater than 55 compared with those under 55 (72% vs. 66%, $p = 0.26$). Only two studies had a median age over 60[16,20] and these had a lower RTW rate, mostly due to the effect of the Chen et al. study which had a RTW rate of 39%. The sub-group analysis comparing studies with a higher proportion of advanced staged cancers showed a similar RTW rate to studies that had lower proportions of advanced tumors (65% vs. 71%, $p = 0.42$). There was no difference in RTW rate between studies with no age exclusion criteria and those with an age exclusion criteria (64% vs. 71%, $p = 0.25$). Additionally, there was no differences in RTW rates across differing geographical regions.

3.7 | Publication bias

Visual inspect of the funnel plots for mean difference in the HADS anxiety and HADS depression scores demonstrated no evidence of publication bias (Appendix B). This was confirmed with the Egger's test which was non-significant for both HADS anxiety ($p = 0.807$) and HADS depression ($p = 0.988$).

4 | DISCUSSION

This review demonstrated that while most patients with HNC are able to return to some form of work after

TABLE 3 Quality of life assessment tools used in included studies

Study (Year)	Quality of life used	Findings
Vartanian et al. (2006)[27]	UW—QOL	RTW: Composite Score ≥ 75%–71.6% No RTW: Composite Score ≥ 75%–28.4%, $p = 0.007$
Verdonck-de Leeuw et al. (2010)[26]	EORTC QLQ-C30 & EORTC QLQ H&N35	RTW group had statistically significant improved scores for the following domains: loss of appetite (2.38 vs. 16.67), social eating (2.98 vs. 18.4), social contact (3.33 vs. 17.92), teeth (4.76 vs. 41.67), opening mouth (15.48 vs. 58.33), dry mouth (32.14 vs. 70.83) and sticky saliva (17.86 vs. 58.33)
	HADS (total score)	RTW: 7.56 ± 5.48 No RTW: 11.38 ± 8.40
Agarwal et al. (2017)[25]	EORTC-QLQ-C30	RTW group had statistically significant improved scores for global QoL (77.5 vs. 72.3, $p = 0.014$)
	EORTC-QLQ-H&N35	RTW group had statistically significant improved scores for coughing (12.2 vs. 20.6, $p = 0.001$) and worse QoL for sticky saliva (27.8 vs. 16.6, $p = 0.004$)
Chen et al. (2019)[14]	Social support scale (SSS)	RTW group needed less tangible social support (61.85 vs. 69.55, $p = 0.044$) and had more positive social interactions (59.38 vs. 51.28, $p = 0.039$)
	UW-QOL	RTW had statistically significant improvement in scores for physical function (71.58 vs. 59.72, $p = 0.001$) and social–emotional function (73.96 vs. 64.36, $p = 0.001$)
Check et al. (2019)[19]	MDASI-HN	RTW group had lower scores for total symptom (1.2 vs. 1.8, $p < 0.001$), total interference (0.8 vs. 1.5, $p < 0.001$) and total severity (1.2 vs. 1.7, $p < 0.001$)
Morales et al. (2019)[17]	FACT-H&N and subscales	RTW group had higher QoL for total score (117.0 vs. 96.1, $p = 0.002$) and the subscales physical well-being (23.9 vs. 18.4, $p = 0.04$), and functional well-being (22.3 vs. 17.7, $p = 0.01$)
Chen et al. (2020)[20]	HADS	RTW group had lower anxiety (2.7 vs. 4.7, $p = 0.006$) and depression (3.8 vs. 5.7, $p = 0.005$)
	Brief illness perception questionnaire	RTW group had lower scores for cognitive illness representations (25.3 vs. 29.3, $p = 0.001$) and higher scores for illness comprehensibility (6.3 vs. 5.3, $p = 0.017$)
	Mini-mental adjustment to cancer	RTW group had lower scores for hopeless and helpless (3.6 vs. 6.3, $p = 0.001$), anxious preoccupation (7.0 vs. 9.3, $p = 0.04$), fatalism (7.9 vs. 9.0, $p = 0.01$) and higher scores for avoidance (6.4 vs. 5.0, $p = 0.033$)
Granstrom et al. (2020)[18]	EORTC QLQ-H&N35	Following domains were associated with RTW on univariable analysis: local pain (OR 0.97, $p < 0.001$), swallowing (OR 0.96, $p < 0.001$), appearance (OR 0.40, $p < 0.001$) and trouble talking on the phone (OR 0.29, $p < 0.001$)
So et al. (2020)[19]	FACT-H&N	RTW group had higher total score (107.8 vs. 96.1, $p = 0.039$)
	MDASI-HN	RTW group had lower symptom severity—1.9 vs. 2.8 ($p = 0.041$)
	HADS	RTW group had lower anxiety (5.7 vs. 7.4, $p = 0.049$) and depression (4.5 vs. 6.4, $p = 0.05$) scores

completion of treatment (67%), there are a still a significant number of patients who are either unable to RTW or work a reduced number of hours (44% of those that RTW). There were also a proportion of people who changed their type of work after their treatment (30%). Patients who were able to RTW had lower levels of anxiety and depression (HADS score) compared to those that did not RTW.

Similar to other meta-analyses on RTW rates in all types of cancers, there was significant variability between studies in the reported RTW rate. For example, meta-analyses on RTW for only European and Japanese studies involving mixed cancer patients reported ranges between 39%–77% and 53.8%–95%, respectively.[28,29] The wide variability in the RTW rate reported in both this meta-analysis and the literature is likely due to a variety of sociodemographic and clinical characteristics, as well as variations in measurement of RTW between studies. Only 10 of the studies in this meta-analysis had an upper age limit exclusion as part of the eligibility criteria, and older patients included in the other studies could have been considering retirement even before diagnosis. Additionally, some studies had long follow-up periods, and this may have meant that patients who were employed at diagnosis could have been unemployed at the time of survey completion simply because they had retired from work. Conversely, some studies had shorter follow-up periods and these patients may have returned to work
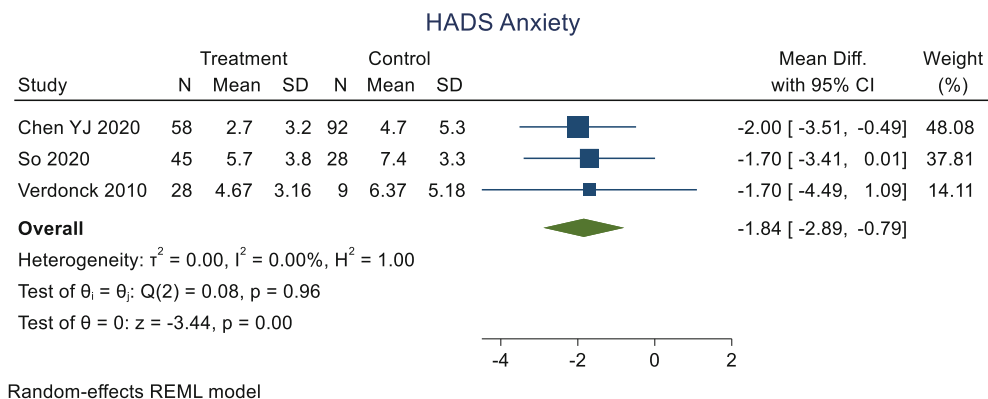
HADS Anxiety

Study	Treatment N	Mean	SD	Control N	Mean	SD	Mean Diff. with 95% CI	Weight (%)
Chen YJ 2020	58	2.7	3.2	92	4.7	5.3	-2.00 [-3.51, -0.49]	48.08
So 2020	45	5.7	3.8	28	7.4	3.3	-1.70 [-3.41, 0.01]	37.81
Verdonck 2010	28	4.67	3.16	9	6.37	5.18	-1.70 [-4.49, 1.09]	14.11
Overall							-1.84 [-2.89, -0.79]	

Heterogeneity: $\tau^2 = 0.00$, $I^2 = 0.00\%$, $H^2 = 1.00$

Test of $\theta_i = \theta_j$: Q(2) = 0.08, p = 0.96

Test of $\theta = 0$: z = -3.44, p = 0.00

Random-effects REML model

FIGURE 5 Forest plot for HADS anxiety [Color figure can be viewed at wileyonlinelibrary.com]

HADS Depression

Study	Treatment N	Mean	SD	Control N	Mean	SD	Mean Diff. with 95% CI	Weight (%)
Chen 2020	58	3.8	3.5	92	5.7	4.6	-1.90 [-3.28, -0.52]	53.71
So 2020	45	4.5	3.7	28	6.4	4.4	-1.90 [-3.78, -0.02]	29.16
Verdonck 2010	28	2.89	3.12	9	5	3.7	-2.11 [-4.56, 0.34]	17.14
Overall							-1.94 [-2.95, -0.92]	

Heterogeneity: $\tau^2 = 0.00$, $I^2 = 0.00\%$, $H^2 = 1.00$

Test of $\theta_i = \theta_j$: Q(2) = 0.02, p = 0.99

Test of $\theta = 0$: z = -3.74, p = 0.00
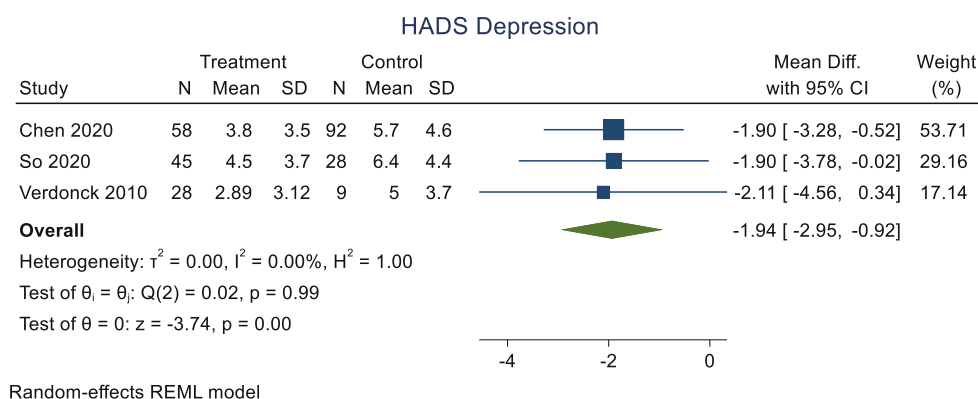
Random-effects REML model

FIGURE 6 Forest plot for HADS depression [Color figure can be viewed at wileyonlinelibrary.com]

later if they were given sufficient time. Future studies investigating RTW in the head and neck cancer population need to consider an upper age limit as part of the inclusion criteria, and exclude patients from the RTW rate if they have retired from work due to reasons unrelated to their cancer treatment, particularly in studies with long follow-up periods. Additionally, adequate follow-up should be allowed for patients to RTW. Prospective longitudinal studies involving regular follow-up would be helpful to further delineate these patterns, rather than cross-sectional studies that currently comprise the majority of the literature.

The differences in patient and clinical characteristics between included studies are another likely explanation for the significant variability in RTW rates. Head and neck cancer is a heterogenous group of cancers with wide variations in treatment dependent on location and stage of tumor, meaning there is more heterogeneity than in other types of tumors. Age is another factor that can influence RTW rate. For example, the study by Chen et al.[20] reported the lowest RTW rate of 39%, which is most likely explained by the older mean age of the patients included in the study (63 years) resulting from the lack of an upper age limit exclusion. As expected, a higher age has previously been associated with reduced RTW rates.[26] Occupation has also been identified as an important factor impacting upon RTW, with people in white collar occupations found to have improved rates of

RTW (amongst Indian patients with HNC).[25] Not all studies reported occupations for participants, making it challenging to determine the effects of this factor on RTW rates in this systematic review.

Clinical factors such as late stage, higher comorbidity scores, increased treatment modalities and surgery as a modality of treatment have been associated with reduced RTW rates in HNC survivors.[12,26,27,30] Cancer-related symptoms such as fatigue and oral dysfunction have also been identified as the most common barriers to RTW.[12,26,27] While all studies included in this analysis were focused on HNCs, some studies focused on specific treatment modalities or forms of HNC. For example, Costa et al.[31] focused exclusively on patients who had laryngectomies,[31] while studies by Handschel et al.[22] and Chen et al.[14] focused exclusively on oral cavity cancer survivors.[14,22] The sub-group analysis suggested that patients with oropharyngeal tumors had a higher rate of RTW compared to the rest of the studies. This is likely due to the high proportion of people with HPV positive oropharyngeal cancer, who are generally younger at diagnosis and of a higher education level. Higher education attainment has been associated with an increased RTW rate in a previous study of patients with various tumor types.[3]

As suggested in the meta-analysis there were reduced depression and anxiety scores for the RTW group. Individual studies used various QoL measurement tools (e.g., FACT-H&N, MDASI-HN, HADS, and EORTC-QLQ-

H&N35) and as such a meta-analysis of QoL was not possible given that there were not three or more studies reporting the same outcome measure. However, based upon review of the results from these individual studies (Table 3) it was apparent that the group of patients who successfully RTW had higher QoL scores when compared to the non-RTW group. The impact of RTW on QOL has also been explored in studies on breast cancer survivors. Consistent with our findings, Schmidt et al. and Zomkowski et al. demonstrated QOL-related functions and symptoms were significantly improved amongst breast cancer survivors who RTW.[32,33] Whether it is the poorer QoL that prevents patients from being able to RTW or that patients not employed have a lower QoL due to factors such as social isolation remains to be elucidated. However, two studies included in this review[16,19] demonstrated a higher symptom burden in patients who did not RTW (measured by the MDASI-HN), suggesting that addressing these symptoms could be an avenue for improving RTW.

Clinicians should be aware that RTW is an integral element of survivorship care for patients with head and neck cancers. This was highlighted in the American Head and Neck Society's "Head and Neck Cancer Survivorship Consensus Statement" which included RTW as a core component of survivorship care.[34] Clinicians involved in the survivorship team are encouraged to counsel patients on their medical disability rights as outlined in national laws.[34] As highlighted in a recent review article, RTW is also influenced by factors outside the healthcare setting, highlighting the importance of support from employers and co-workers.[35] This suggests that interventions aimed to improve RTW amongst HNC survivors must be multifactorial and consider not only addressing symptoms and side effects of cancer treatment but also issues in the workplace.

The main limitation of this systematic review and meta-analysis was the significant heterogeneity in the RTW rates due to variations in study designs and eligibility criteria. Included studies were predominantly conducted in developed, western countries with advanced healthcare systems (mainly North America and Europe). Although most of the studies looked broadly at all HNC survivors, some included studies focused on particular forms of HNC or particular treatment modalities. There were also significant differences in the exclusion criteria for age limits in studies. Similarly, while most studies determined their upper age limit by their national retirement age, many studies did not explicitly state such a cut-off. There were significant differences in the reporting of data which may influence employment status such as HPV status, smoking status and modalities of treatment these patients received. There was also a wide variation in the QoL tools used in studies which limited the ability to perform meta-analyses.

5 | CONCLUSION

This systematic review and meta-analysis highlights that while the majority of HNC survivors are able to RTW, there are a significant proportion that do not RTW, or have to reduce their hours or change work. Patients who are unable to RTW were found to have higher levels of anxiety and depressive symptoms and a lower quality of life. Future studies need to use consistent definitions for RTW and consider confounding factors which may influence RTW rate such as length of follow-up and retirement.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request.

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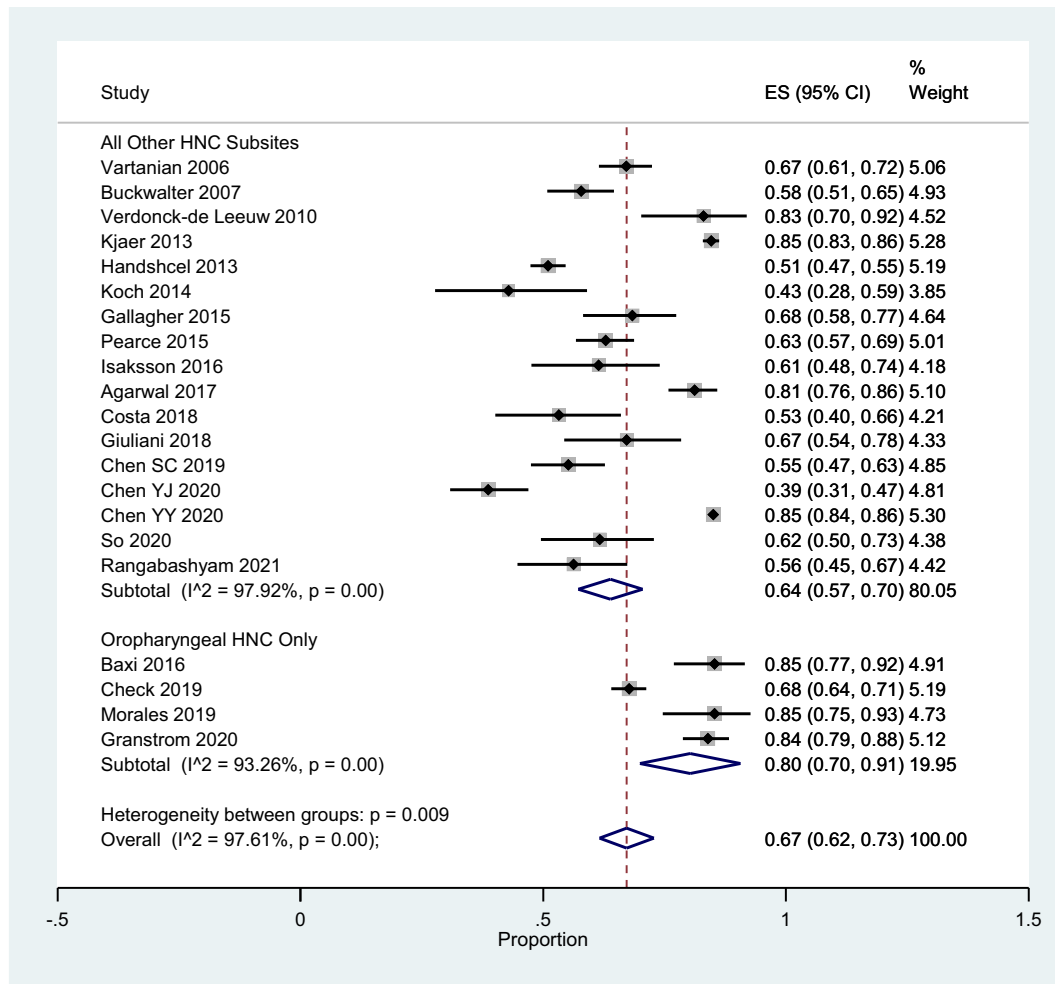
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APPENDIX A: Sub-group analyses

Oropharyngeal tumors only versus other HNC subsites
Age >55 versus <55 (L) and age >60 versus <60 (R)

Oropharyngeal Tumours Only vs Other HNC Subsites

Study	ES (95% CI)	% Weight
All Other HNC Subsites		
Vartanian 2006	0.67 (0.61, 0.72)	5.06
Buckwalter 2007	0.58 (0.51, 0.65)	4.93
Verdonck-de Leeuw 2010	0.83 (0.70, 0.92)	4.52
Kjaer 2013	0.85 (0.83, 0.86)	5.28
Handshcel 2013	0.51 (0.47, 0.55)	5.19
Koch 2014	0.43 (0.28, 0.59)	3.85
Gallagher 2015	0.68 (0.58, 0.77)	4.64
Pearce 2015	0.63 (0.57, 0.69)	5.01
Isaksson 2016	0.61 (0.48, 0.74)	4.18
Agarwal 2017	0.81 (0.76, 0.86)	5.10
Costa 2018	0.53 (0.40, 0.66)	4.21
Giuliani 2018	0.67 (0.54, 0.78)	4.33
Chen SC 2019	0.55 (0.47, 0.63)	4.85
Chen YJ 2020	0.39 (0.31, 0.47)	4.81
Chen YY 2020	0.85 (0.84, 0.86)	5.30
So 2020	0.62 (0.50, 0.73)	4.38
Rangabashyam 2021	0.56 (0.45, 0.67)	4.42
Subtotal (I^2 = 97.92%, p = 0.00)	0.64 (0.57, 0.70)	80.05
Oropharyngeal HNC Only		
Baxi 2016	0.85 (0.77, 0.92)	4.91
Check 2019	0.68 (0.64, 0.71)	5.19
Morales 2019	0.85 (0.75, 0.93)	4.73
Granstrom 2020	0.84 (0.79, 0.88)	5.12
Subtotal (I^2 = 93.26%, p = 0.00)	0.80 (0.70, 0.91)	19.95
Heterogeneity between groups: p = 0.009		
Overall (I^2 = 97.61%, p = 0.00);	0.67 (0.62, 0.73)	100.00

Proportion

Age > 55 vs <55 (L) and Age >60 vs <60 (R)
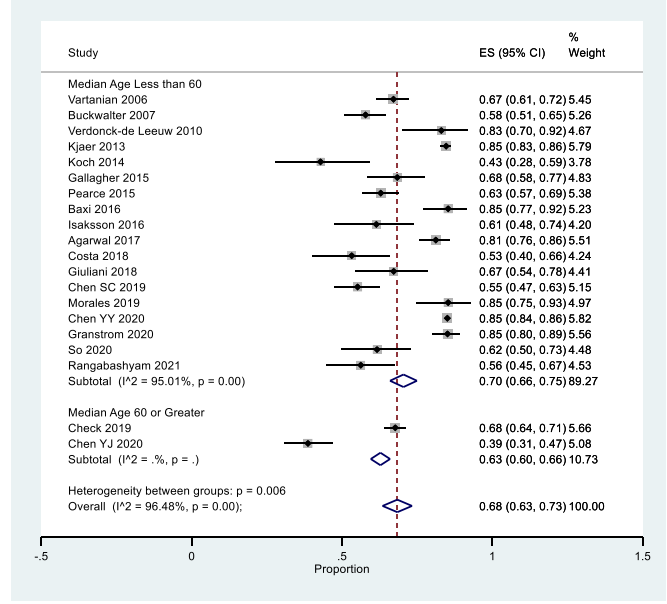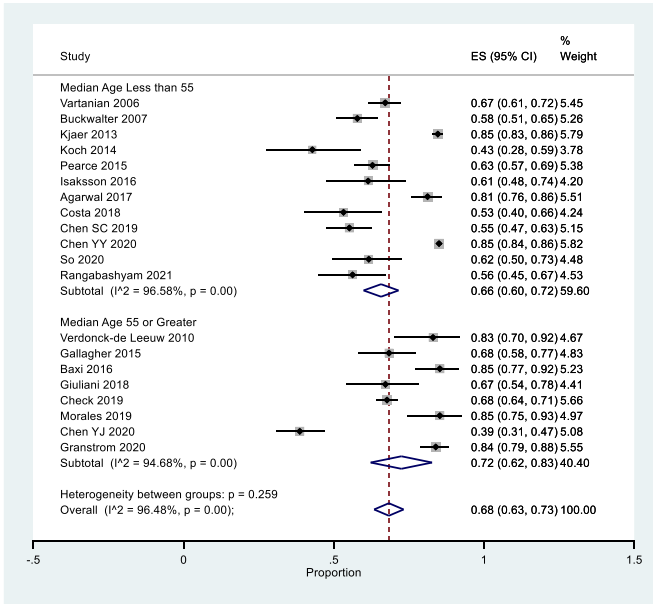
Studies with no age exclusion criteria versus those with an age exclusion criteria

Studies with no age exclusion criteria vs those with an age exclusion criteria

Stage of cancers—greater than 50% of patients with advanced cancers versus less than 50% with advanced cancers

Stage of Cancers – Greater than 50% of Patients with Advanced Cancers vs Less than 50% with Advanced Cancers

Study	ES (95% CI)	% Weight
Greater than 50% of Patients with Advanced Stage Cancers		
Vartanian 2006	0.67 (0.61, 0.72)	5.06
Buckwalter 2007	0.58 (0.51, 0.65)	4.93
Kjaer 2013	0.85 (0.83, 0.86)	5.28
Handshcel 2013	0.51 (0.47, 0.55)	5.19
Koch 2014	0.43 (0.28, 0.59)	3.85
Gallagher 2015	0.68 (0.58, 0.77)	4.64
Baxi 2016	0.85 (0.77, 0.92)	4.91
Isaksson 2016	0.61 (0.48, 0.74)	4.17
Agarwal 2017	0.81 (0.76, 0.86)	5.10
Costa 2018	0.53 (0.40, 0.66)	4.21
Giuliani 2018	0.67 (0.54, 0.78)	4.33
Check 2019	0.68 (0.64, 0.71)	5.19
Chen YJ 2020	0.39 (0.31, 0.47)	4.81
Granstrom 2020	0.85 (0.80, 0.89)	5.13
So 2020	0.62 (0.50, 0.73)	4.38
Subtotal (I^2 = 97.28%, p = 0.00)	0.65 (0.57, 0.73)	71.17
Less than 50% of Patients with Advanced Stage Cancers		
Verdonck-de Leeuw 2010	0.83 (0.70, 0.92)	4.52
Pearce 2015	0.63 (0.57, 0.69)	5.01
Chen SC 2019	0.55 (0.47, 0.63)	4.85
Morales 2019	0.85 (0.75, 0.93)	4.73
Chen YY 2020	0.85 (0.84, 0.86)	5.30
Rangabashyam 2021	0.56 (0.45, 0.67)	4.42
Subtotal (I^2 = 96.47%, p = 0.00)	0.71 (0.59, 0.84)	28.83
Heterogeneity between groups: p = 0.424		
Overall (I^2 = 97.62%, p = 0.00);	0.67 (0.62, 0.73)	100.00

Proportion

RTW by region (America, Europe, Asia and Australia)

RTW by Region (America, Europe, Asia and Australia)

Study	ES (95% CI)	% Weight
Americas		
Vartanian 2006	0.67 (0.61, 0.72)	5.06
Buckwalter 2007	0.58 (0.51, 0.65)	4.93
Gallagher 2015	0.68 (0.58, 0.77)	4.64
Baxi 2016	0.85 (0.77, 0.92)	4.91
Giuliani 2018	0.67 (0.54, 0.78)	4.33
Check 2019	0.68 (0.64, 0.71)	5.19
So 2020	0.62 (0.50, 0.73)	4.38
Subtotal (I^2 = 82.70%, p = 0.00)	0.68 (0.62, 0.74)	33.44
Europe		
Verdonck-de Leeuw 2010	0.83 (0.70, 0.92)	4.52
Kjaer 2013	0.85 (0.83, 0.86)	5.28
Handshcel 2013	0.51 (0.47, 0.55)	5.19
Koch 2014	0.43 (0.28, 0.59)	3.85
Pearce 2015	0.63 (0.57, 0.69)	5.01
Isaksson 2016	0.61 (0.48, 0.74)	4.17
Costa 2018	0.53 (0.40, 0.66)	4.21
Granstrom 2020	0.85 (0.80, 0.89)	5.13
Subtotal (I^2 = 98.06%, p = 0.00)	0.66 (0.53, 0.79)	37.35
Asia		
Agarwal 2017	0.81 (0.76, 0.86)	5.10
Chen SC 2019	0.55 (0.47, 0.63)	4.85
Chen YJ 2020	0.39 (0.31, 0.47)	4.81
Chen YY 2020	0.85 (0.84, 0.86)	5.30
Rangabashyam 2021	0.56 (0.45, 0.67)	4.42
Subtotal (I^2 = 98.20%, p = 0.00)	0.64 (0.47, 0.80)	24.47
Australia		
Morales 2019	0.85 (0.75, 0.93)	4.73
Heterogeneity between groups: p = 0.005		
Overall (I^2 = 97.62%, p = 0.00);	0.67 (0.62, 0.73)	100.00

Proportion

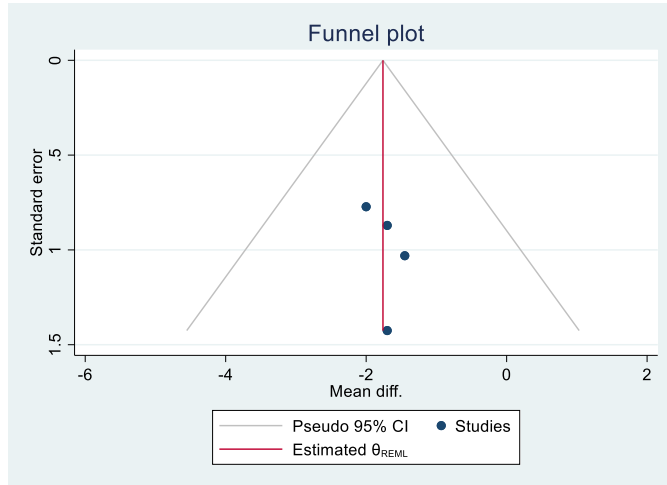-.5   0   .5   1   1.5

APPENDIX B: Funnel plots

HADS anxiety—funnel plot

HADS Anxiety – Funnel Plot

HADS Depression – Funnel Plot