Prevalence of locoregional recurrence and survival post-treatment of head and neck cancers in Africa: a systematic review and meta-analysis

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Summary

Background Recurrent cancers of the head and neck are associated with poor survival outcome. Yet, their burden in Africa is not reliably known. We therefore aimed to estimate the prevalence of recurrence and the 5-year overall survival among patients treated for head and neck cancers (HNC) in Africa.

Method In this systematic review and meta-analysis, we searched four electronic databases (Pubmed, CINAHL, MEDLINE, and Web of Science) and the grey literature for studies reporting the prevalence of HNC recurrence and 5-year overall survival post treatment, published between January 1, 2002, and December 31, 2022. We contacted corresponding authors of relevant studies. Searches were extended to reference lists of review articles and other relevant sources for potentially eligible studies. Each record was assessed for inclusion or exclusion by two independent reviewers. Records with individual-level data on recurrence and survival conducted in Africa were included while exclusion was based on the study design and availability of relevant data. Data were independently extracted by three reviewers from eligible studies, and summary estimates were sought. Our primary outcomes were recurrence and 5-year overall survival of patients who have been treated for HNC, and our secondary outcomes included risk factors, tumor site, squamous cell histology, clinical stage of tumor, and treatment options received. Only records selected for primary outcomes were assessed for secondary outcome data extraction. Random-effects meta-analysis was conducted for each outcome. Meta-regression models were used in addressing sample heterogeneity among the studies. Protocol for this study was registered with PROSPERO, CRD42022372307.

Findings This systematic review and meta-analysis returned 3998 records, yielding 28 included studies after exclusion. Eighteen studies reported on the prevalence of HNC recurrence while 24 articles reported on the 5-year overall survival. Of the pooled total study population, 7199 (70.5%) of 10,218 patients were males while 2603 (25.5%) were females. We found that the prevalence of HNC recurrence was 15.4% (I^2 = 96.2%; 95% CI: 9.5–22.3; n = 3214; k = 18), and the 5-year overall survival was 54.4% (I^2 = 99.5%; 95% CI: 40.1–68.4; n = 9798; k = 24). We also found that the prevalence of smoking and alcohol consumption as risk factors for HNC were 42.6% (I^2 = 98.8%; 95% CI: 25.2–61.0; n = 4374; k = 15) and 35.8% (I^2 = 98.9%; 95% CI: 21.7–51.4; n = 4110; k = 11) respectively. The pooled current prevalence for advanced HNC (clinical stages III-IV) was 80.0% (I^2 = 99.2%; 95% CI: 68.6–89.5; n = 7624; k = 18) compared to 12.2% (I^2 = 96.4%; 95% CI: 6.2–19.8; n = 7624; k = 18) in early disease (clinical stages I-II).

Interpretation The results showed significantly high prevalence of cancer recurrence, poor 5-year overall survival and very high prevalence of advanced cancers at time of diagnosis. This study provides robust evidence for strategies towards prompt diagnosis and appropriate management of HNC to improve patients' outcome in the African continent.

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Keywords: Head and neck cancers; Recurrence; Survival; Risk factors; Clinical stage

Research in context

Evidence before this study

Locoregional recurrence is an essential form of treatment failure that poses profound challenge in the management of patients with HNC, and adversely affects their survival. However, the burden of HNC recurrence and their 5-year overall survival in Africa remains uncertain. In this study, four academic databases (Pubmed, CINAHL, MEDLINE, and Web of Science) were searched for studies on HNC recurrence and 5-year overall survival. Our systematic review contains evidence from 28 studies on recurrence and survival of HNC conducted in Africa between 2002 and 2022.

Added value of this study

To our knowledge, this systematic review and meta-analysis presents the most comprehensive evidence on HNC recurrence and 5-year overall survival, having pooled available primary data in the region within the study period. The study has presented effect size estimates from 10 African countries highlighting their recurrence and 5-year survival alongside their risk factors and prevalence. This systematic review is an important effort towards prognosticating HNC in Africa and guiding patients' management.

Implications of all the available evidence

Findings from this study highlights the need for improved strategies towards reducing or eliminating smoking and alcohol consumption in Africa. Diagnosis and appropriate management of HNC in its early stage, as well as increasing the number of HNC surgeons in Africa are also emphasized. Our study further revealed a disproportionately fewer studies on HNC recurrence and survival conducted in Africa, hence providing robust evidence to mobilize and encourage further research on primary data on HNC in the continent.

Introduction

Head and neck cancers (HNC) arising from the oral cavity, oropharynx, nasopharynx, hypopharynx and the larynx are the most common malignancies of the head and neck.[1] Worldwide, HNC is the sixth leading cancer by incidence.[2,3] The global burden of these malignancies has been linked with human exposure to tobacco-derived carcinogen, excess consumption of alcohol or a combination of both.[4,5] An increasing number of cancers originating in the oropharynx have been correlated to previous infection with oncogenic Human Papilloma virus (HPV) strains, especially the HPV-16, and less frequently by the HPV-18 subtype and other subtypes.[6–8] While some oral premalignant lesions of the HNC presenting as leukoplakia or erythroplakia progressively advance to invasive cancers, most patients only present with an advanced disease devoid of the premalignant phase.[1,9] Depending on the stage of disease, majority of the HNC of the oral cavity is treated by surgical resection which in turn is followed by adjuvant chemotherapy and radiation or primary concomitant chemoradiotherapy (CRT).[10]

Twenty percent of patients who received treatment for early stage disease and 50% of patients with locally advanced disease have been reported to having local recurrence.[2,11] Regardless of treatment, HNC patients who are HPV positive have lower chances of experiencing recurrence or disease progression relative to HPV negative patients.[11] Prognosis for locally recurrent or metastatic HNC is poor with an overall median duration survival of about one year.[12]

HNC patients in Africa may be at greater risk of recurrence and poor survival due to limited diagnostics and treatment options.[13] Further to these factors, HNC patients in Africa are more likely to suffer from socio-economic deprivation, greater levels of poverty, and worse sociocultural factors such as poorer levels of education.[14] Consistent prevalence estimates from Africa are crucial to understanding the burden of local recurrence and survival after treatment of patients in this region and highlighting the necessity for clinical attention. Systematic reviews on the local recurrence of the HNC exist at the global level,[15,16] however, we are not aware of any review conducted on the recurrence and 5-year overall survival for Africa. This study is aimed at systematically reviewing and synthesizing the evidence on the prevalence of local recurrence and survival of HNC in Africa post treatment. This review included the large body of evidence that emerged in this field between 2002 and 2022.

Methods

Search strategy and selection criteria

In this systematic review and meta-analysis, studies were considered eligible if they included patients with confirmed cancers involving any or combination of the oral cavity, oropharynx, nasopharynx, larynx, and/or the hypopharynx and conducted in Africa. In addition, studies were considered eligible if patients received any or a combination of surgical resection, adjuvant chemotherapy and radiation (chemoradiation) or

chemotherapy. Included studies were eligible articles published in any language between 2002 and 2022. Only primary outcome data were included in this review to estimate real-world 'prevalence of local recurrence and/or survival' results that would reflect actual treatment values and could guide decision-making by policy-makers, clinicians, and researchers.

We searched four electronic databases including Pubmed, CINAHL, MEDLINE, and Web of Science on 21 November 2022 and updated it on 20 February 2023 (Supplementary file S1). Search was extended to the grey literature for studies relevant to this review at any stage of completion. Reference lists of review articles and other relevant sources identified during this search and the final included articles were equally checked to identify additional potentially eligible studies. Excluded studies included case reports, observational research studies, qualitative research, and reviews.

Two independent reviewers (HM and PEM) screened identified abstracts and full texts using pre-defined inclusion and exclusion criteria. In the event of conflicts over inclusion, a third reviewer (TE) was involved for resolution. Summary-level data were independently extracted by three reviewers (HM, TKS, and KTB) to Excel sheets using a predetermined protocol, with the extracted data containing information on each study's authors, year and country of study, primary site of tumor, tumor stage, treatment variables, and duration of follow up. Extracted data were further verified by two authors (PEM and TE).

The search strategy involved use of keywords and Medical Subject Headings search terms related to treatment, head and neck cancers, and outcome. The search strategy further contained terms related to Africa. Search terms were adapted to each database. All abstracts were imported to Mendeley, and duplicates were removed. After considering the inclusion criteria, satisfactory full texts were retrieved. Search was also conducted in the trial registries to identify unpublished studies. For unconcluded studies or those with unclear recruitment status, authors were contacted to provide clarity and results which are relevant to the outcomes of interest to this systematic review. Fig. 1 shows the study selection as per the Preferred Reporting Items for Systematic Reviews and Meta-analysis (PRISMA) guidelines.

Statistical analysis

Our primary outcome variables were the locoregional recurrence and 5-year overall survival rates, while the secondary outcome variables included the risk factors for HNC, squamous cell carcinoma histological type, tumor location, clinical stage of the disease and treatment options. Studies were excluded if they were devoid of adequate information to establish its methodological rigor. In the event that a particular article had missing or unclear data, or (some) procedural details were not established in the report, the corresponding author(s) of such article were contacted through email for clarity. Two studies were eliminated by this process as the corresponding authors of these studies could not be reached. Covidence was used to prevent data duplication. When results from a study have been published in two different media, such as a peer reviewed journal and a report, evidence from the peer reviewed journal article was chosen in preference. Furthermore, three reviewers (HM, OO, and PEM) conducted the quality appraisal using the Joanna Briggs Institute (JBI)[17] Critical Appraisal Checklist appraisal tool for Systematic Reviews and Research Syntheses. Consensus was reached through discussions; the internal and external validity as well as the risk of bias of the included studies was evaluated using the JBI tool (see Supplementary file S4).

Random effect meta-analysis technique was used to analyze the extracted data. For the primary outcome data, two separate a priori primary meta-analysis were conducted—one for the prevalence of recurrence of HNC and the other for the 5-year overall survival of HNC in Africa. In addition, individual sample proportion estimates with their 95% confidence intervals (CIs) were calculated, with stabilized variances via the Freeman-Tukey double arcsine transformation to approximate normal distribution. Random-effects models were fitted via the restricted maximum-likelihood estimation method to estimate variance heterogeneity and the 95% CIs of summary measures were calculated with the Knapp-Hartung variance estimator. Inconsistency was quantified with the I^2 statistic to describe the percentage of variation attributed to between-sample heterogeneity, with values higher than 75% indicating considerable heterogeneity. Funnel plots, together with the Kendall's tau rank correlation and Egger's regression tests for funnel plot asymmetry were performed to assess the potential publication bias in the conducted meta-analyses in this study.

All statistical analyses for this review were conducted using the R software (version 4.2.2) and the *meta* and *metafor* packages. This systematic review and meta-analysis adhered to the Preferred Reporting Items for Systematic Reviews and Meta-analysis (PRISMA) guidelines. This study was a systematic review and thus did not require ethics approval. Protocol for this study was registered in PROSPERO, CRD42022372307.

Role of the funding source

There was no funding source for this study. All authors had access to all data used in this study and accepted the responsibility for the decision to submit the manuscript for publication. All data extraction sheets are available immediately after publication and are published as Supplementary material.

Results

The literature search yielded a total of 3998 records (3963 from databases and 35 from other sources). After

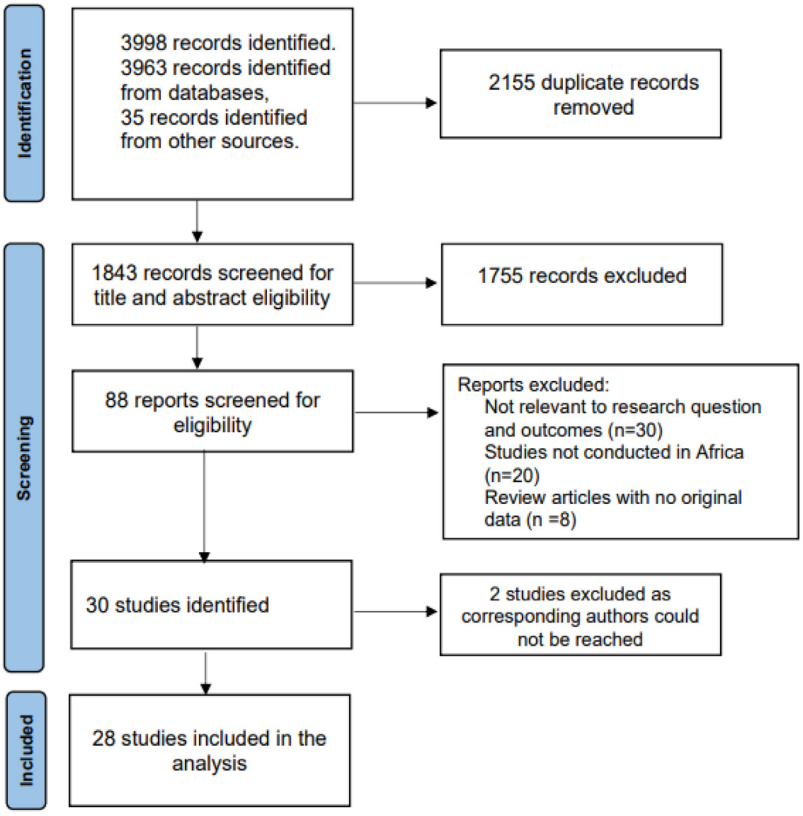

Fig. 1: Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) flow diagram of selected studies.

2155 duplicates were removed, 1843 articles were screened for title and/or abstract eligibility of which 1755 articles were excluded. Eighty-eight full texts articles were assessed, and twenty-eight articles met the set criteria for inclusion in the analysis (Fig. 1). Overall, the included studies reported on a total of 10,218 participants from 10 countries (Nigeria,[18–24] Ghana,[25] Egypt,[26–31] Morocco,[32–34] Tunisia,[35–39] Uganda,[40] Sudan[41] South Africa,[42,43] Tanzania,[44] and Cameroon[45]). One study from Sudan[41] was a Doctoral thesis and was included in our analysis.

Of the 28 studies included in the meta-analysis, 18 reported on the prevalence of recurrence of HNC and 24 studies reported on the 5-year overall survival of HNC. Supplementary file S2 shows the information distribution of the identified 28 HNC studies considered in this study. Of the pooled total study population, 7199 (70.5%) of the 10,218 patients were males while 2603 (25.5%) were females, with 2 studies not specifying the gender distribution of their reported cases. Table 1 shows a summary of prevalence findings in this study.

Recurrence

Prevalence of recurrence of HNC was reported in 18 studies.[18,19,21,23,25,27–30,32,33,35,37–39,42–44] Information distribution of the identified studies for recurrence are shown in Supplementary file S2. Fig. 2 presents the forest plot showing the results of both fixed effect and random effects meta-analysis of the recurrent cases. As expected, the 95% CI for the summary estimate from the random effects model of the recurrent cases was wider compared with the one from the fixed effect model, although differing only slightly in terms of magnitude. For both models, the diamonds representing the estimated prevalence and confidence limits did not cross the line of no recurrence (at origin 0), suggesting that the effect of recurrence prevalence was significant. In addition, the test of heterogeneity ($p < 0.01$) suggested the presence of heterogeneous results, with the heterogeneity statistic (I^2 = 96.2%) indicating a high between-sample heterogeneity and its 95% CI (95.0%–97.1%) indicative of a potentially important to substantial heterogeneity in the effect sizes. The pooled current prevalence of HNC recurrence in this study was estimated at 15.4% (95% CI: 9.5–22.3; n = 3214; number of included estimates [k] = 18) of the patient populations (Fig. 2). The mean age range for HNC recurrence was 14–65 years.

Survival

A 5-year overall survival of HNC was reported in 24 studies.[20–24,26–40,43–46] Fig. 3 shows the forest plot of both

Items	N	n	Prevalence	95% CI	p-value
Recurrence	3214	686	15.4%	9.5–22.3	p < 0.01
5-year overall Survival	9798	4558	54.4%	40.1–68.4	p < 0.01
Risk factors					
Smoking	4374	1874	42.6%	25.2–61.0	p < 0.01
Alcohol	4110	1118	35.8%	21.7–51.4	p < 0.01
Histology type					
Squamous cell Ca	9254	8052	86.1%	71.9–96.0	p < 0.01
Tumor site					
Oral cavity	4322	3417	84.3% (59.1%)[a]	61.5–98.2	p < 0.01
Oropharynx	1227	117	7.1% (2.0%)[a]	2.7–13.4	p < 0.01
Larynx	1612	804	84.8% (13.9%)[a]	53.5–99.9	p < 0.01
Nasopharynx	2017	1360	86.0% (23.5%)[a]	56.4–99.9	p < 0.01
Hypopharynx	1014	80	9.1% (1.4%)[a]	1.2–22.8	p < 0.01
Clinical stage					
Ca stages I & II	7624	1040	12.2% (19.0%)[a]	6.2–19.8	p < 0.01
Ca stages III & IV	7624	4444	80.0% (81.0%)[a]	68.6–89.5	p < 0.01
Treatment options					
Surgery alone	8245	1902	24.9%	12.6–39.7	p < 0.01
Chemotherapy alone	3839	409	12.6%	6.0–21.1	p < 0.01
Surgery and radiotherapy	7270	1783	26.4%	15.6–38.8	p < 0.01
Surgery and chemotherapy	2520	106	3.7%	0.4–9.8	p < 0.01
Surgery, chemotherapy, and radiotherapy	8116	3409	24.7%	12.4–39.5	p < 0.01
Radiotherapy alone	3696	1069	26.9%	13.0–43.5	p < 0.01
Chemotherapy and radiotherapy	3479	1456	49.2%	26.9–71.6	p < 0.01

Abbreviation: N, sample size; n, number of cases; CI, confidence interval. i.e., n/Σn where Σn, sum of n per item being considered. [a]Expressed as a fraction of 100%.

Table 1: **Summary prevalence of characteristic dimensions of head and neck cancers in Africa.**

fixed effect and random effects meta-analysis of the 5-year survival. The 95% CI for the summary estimate from the random effects model of the survival cases was wider compared with the one from the fixed effect model, however, the two results differ only slightly in terms of magnitude. For both models, the diamonds representing the estimated 5-year survival and confidence limits did not cross the line of no survival, suggesting that the effect of survival was significant. The test of heterogeneity ($p < 0.01$) suggested the presence of heterogeneous results, with the heterogeneity statistic ($I^2 = 99.5\%$) indicating a high between-sample heterogeneity and its 95% CI (99.4%–99.8%) indicative of a potentially important to substantial heterogeneity in the effect sizes. The pooled current 5-year overall survival was estimated at 54.4% (95% CI: 40.1–68.4; n = 9798; k = 24) of the patient populations (Fig. 3).

Risk factors

A total of 26 HNC risk factor studies done in Africa were identified as per the study selection of this study, with 15 studies reporting on the prevalence of smoking and 11 studies reporting on the prevalence of alcohol as risk factors of HNC as shown in Supplementary file S2.

For both the random effects and fixed effect models, the diamonds representing the estimated prevalence and 95% confidence limits in Figs. 4 and 5 did not cross the line of no prevalence, suggesting that the effect of prevalence was significant. For smoking and alcohol, the test of heterogeneity (both $p < 0.01$) suggested the presence of heterogeneous results, with the heterogeneity statistic ($I^2 = 98.8\%$, 98.9%) indicating a high between-sample heterogeneity and its 95% CI (98.5%–99.0%, 98.6%–99.1%) indicative of a potentially important to substantial heterogeneity in the effect sizes. The pooled current prevalence of smoking and alcohol in HNC were estimated at 42.6% (95% CI: 25.2–61.0; n = 4374; k = 15) and 35.8% (95% CI: 21.7–51.4; n = 4110; k = 11) of the patient populations respectively. The mean range age of patients with smoking habit was 14–64 years and 42–64 years for alcohol.

Squamous cell carcinoma histology

Twenty-one out of 28 studies assessed the prevalence of squamous cell carcinoma histology subtype of HNC. Of the pooled total study population, a prevalence rate of 87.0% (8052 of 9254 patients) were recorded across nine countries. For both the random effects and fixed effect models, the diamonds representing the estimated prevalence and 95% confidence limits in Fig. 6 did not cross the line of no prevalence, suggesting that the effect of prevalence was significant. The test of heterogeneity

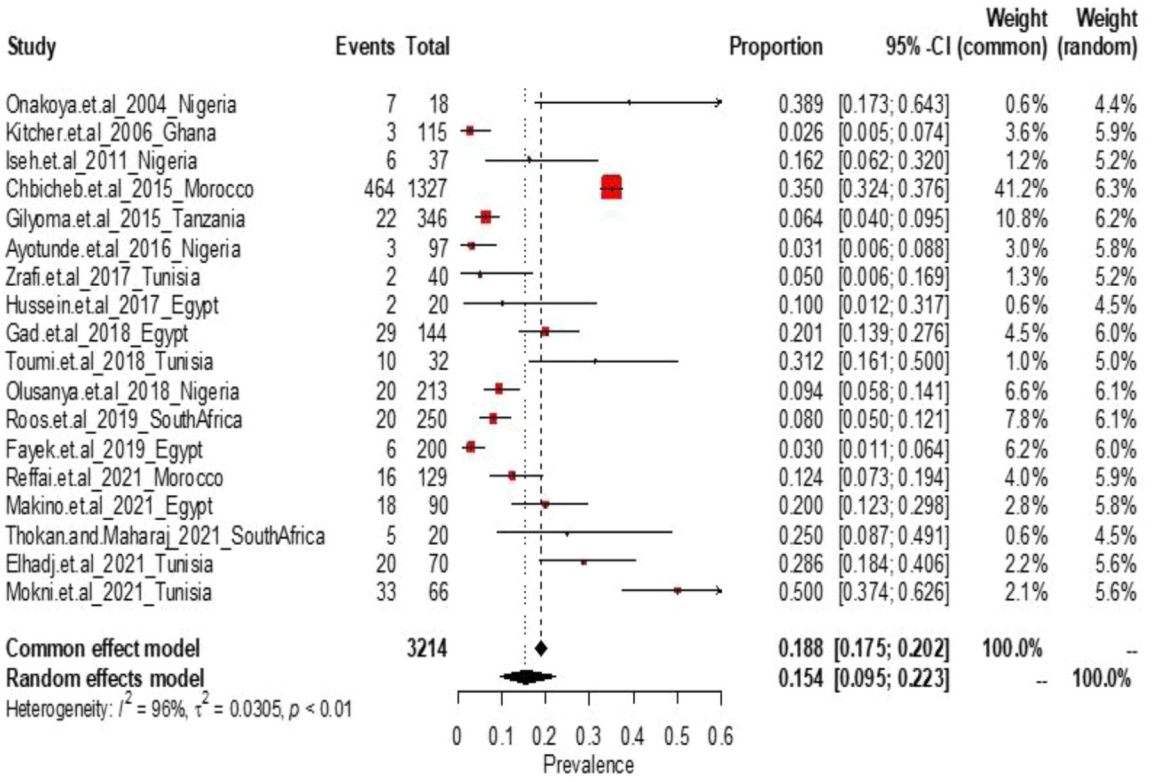

Fig. 2: Prevalence of head and neck cancer recurrence after treatment in Africa. Abbreviation: CI, Confidence interval.

($p < 0.01$) suggested the presence of heterogeneous results, with the heterogeneity statistic (I^2 = 99.5%) indicating a high between-sample heterogeneity and its 95% CI (99.4%–99.6%) indicative of a potentially important to substantial heterogeneity in the effect sizes. The pooled current prevalence of head and neck squamous cell carcinoma (HNSCC) was estimated at 86.1% (95% CI: 71.9–96.0; n = 9254; k = 21) of the patient populations.

Tumor site

A total of 41 HNC tumor site studies done in Africa were identified as per the study selection of this study, with 13 studies reporting on the prevalence of tumors in oral cavity, 5 studies on tumors in the oropharynx, 10 studies on tumors in the larynx, 9 studies on tumors in the nasopharynx and 4 studies on tumors in the hypopharynx (Supplementary file S2). Of the pooled total study population, a prevalence rate of 79.1% (3417 of 4322 patients) for tumors in oral cavity were recorded across 7 countries, 9.5% (117 of 1227 patients) for tumors in oropharynx were recorded across 3 countries, 49.9% (804 of 1612 patients) for tumors in larynx were recorded across 5 countries, 67.4% (1360 of 2017 patients) for tumors in nasopharynx were recorded across 5 countries and 7.9% (80 of 1014 patients) for tumors in hypopharynx were recorded across 3 countries. Moreover, the mean range age of patients with tumors in oral cavity was 42–65 years, 42–65 years for tumors in the oropharynx, 42–63 years for tumors in the larynx, 14–50 years for tumors in the nasopharynx and 42–65 years for tumors in the hypopharynx. Of the pooled total tumor sites, the highest prevalence rate of 59.1% was recorded for the oral cavity tumor, followed by 23.5% for nasopharynx tumor and 13.9% for larynx tumor, while the lowest rate of 1.4% was recorded for the hypopharynx tumor, followed by 2.0% for oropharynx tumor as shown in Table 1.

For both the random effects and fixed effect models, the diamonds representing the estimated prevalence and 95% confidence limits in Supplementary file S6 did not cross the line of no prevalence, suggesting that the effect of prevalence was significant. For the tumor sites (oral cavity, oropharynx, larynx, nasopharynx, and hypopharynx), the test of heterogeneity (all $p < 0.01$) suggested the presence of heterogeneous results, with the heterogeneity statistic (I^2 = 99.7%, 91.5%, 99.6%, 99.6%, 95.3%) indicating a high between-sample heterogeneity and its 95% CI (99.6%–99.7%, 83.2%–95.7%, 99.5%–99.6%, 99.5%–99.7%, 90.8%–97.6%) indicative of a potentially important to substantial heterogeneity in the effect sizes. The pooled current prevalence of HNC was

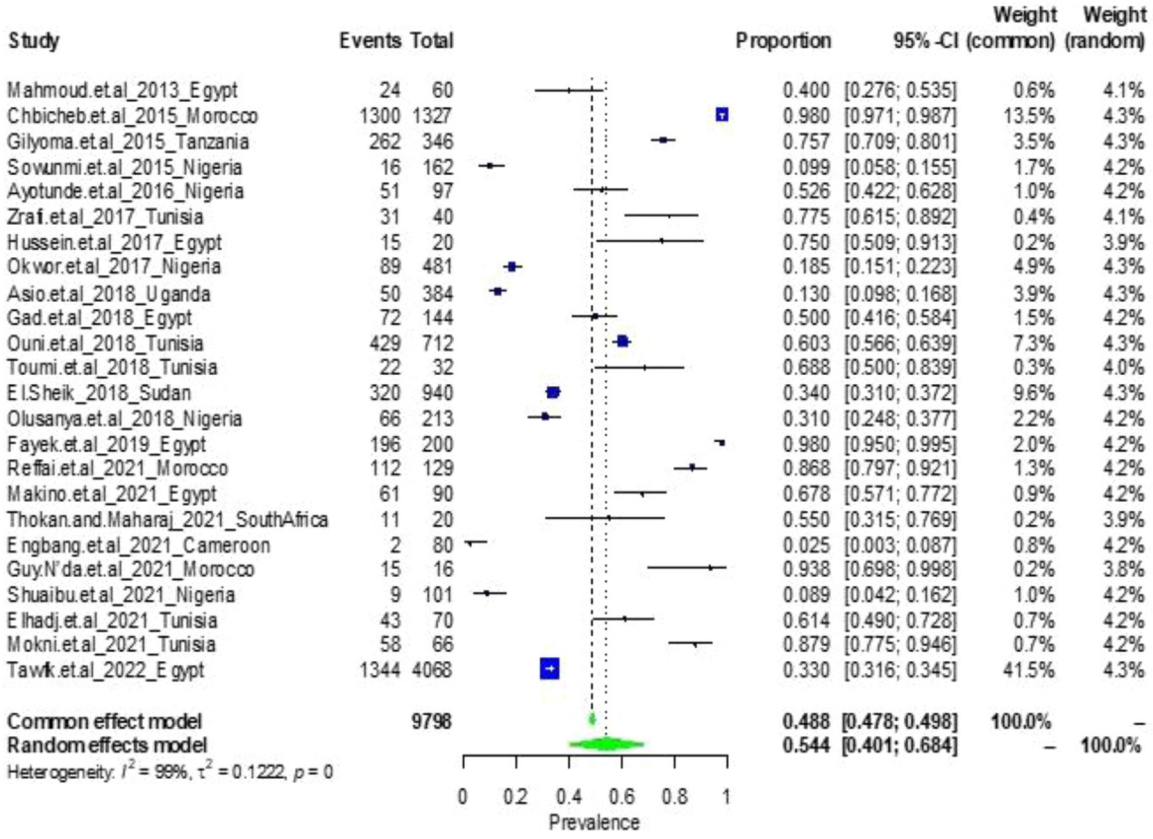

Fig. 3: Current 5-year overall survival of head and neck cancer in Africa. Abbreviation: CI, Confidence interval.

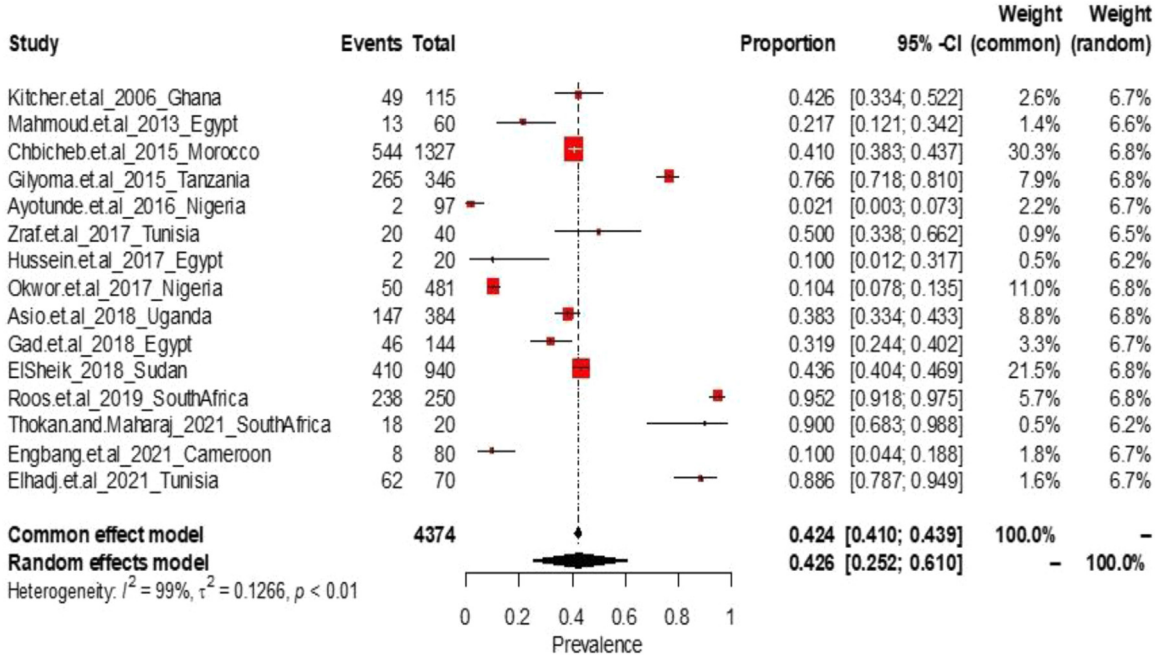

Fig. 4: Current prevalence of smoking in the patient populations. Abbreviation: CI, Confidence interval.

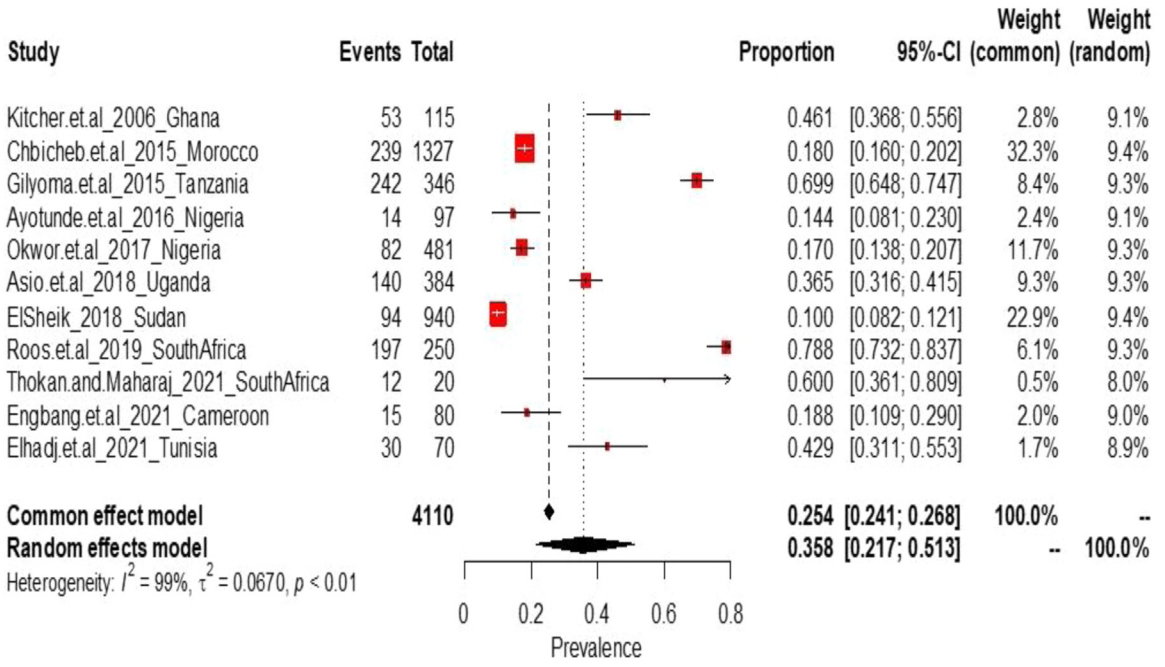

Fig. 5: Current prevalence of alcohol in the patient populations. Abbreviation: CI, Confidence interval.

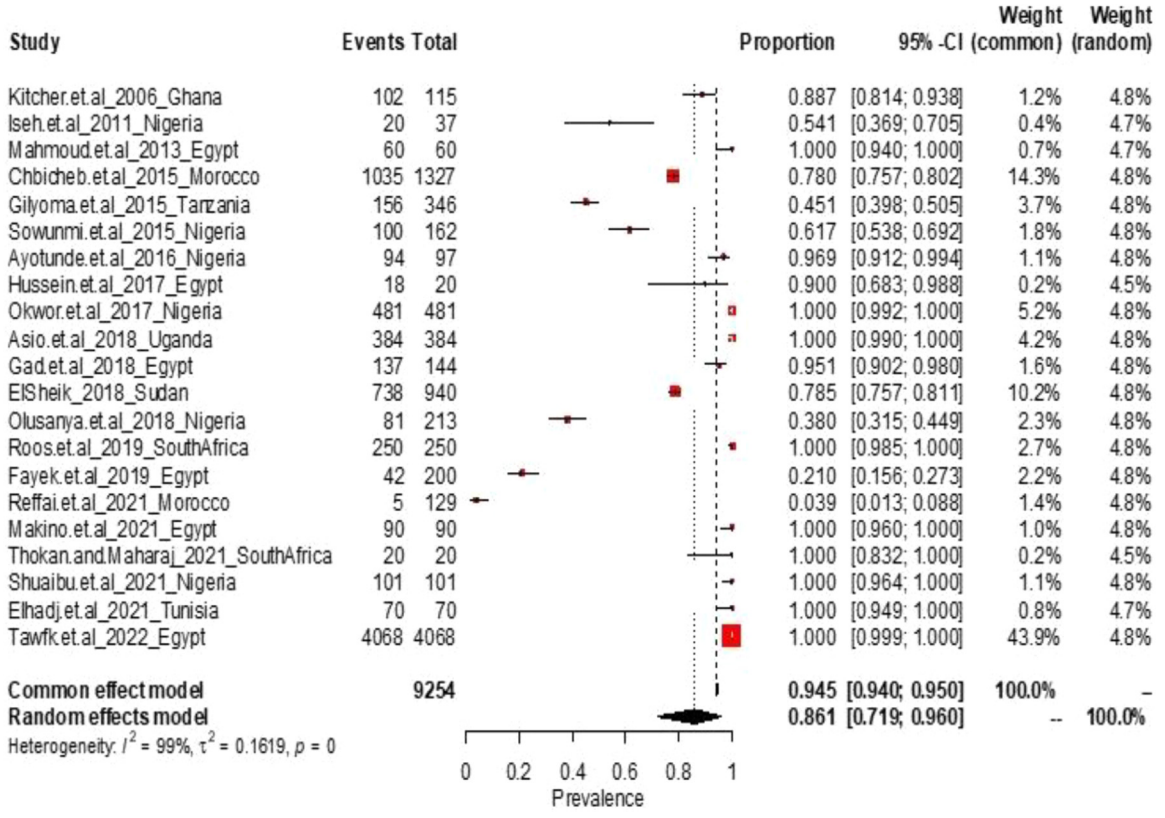

Fig. 6: Current prevalence of head and neck squamous cell carcinoma (HNSCC) histology in the patient populations. Abbreviation: CI, Confidence interval.

estimated at 84.3% (95% CI: 61.5–98.2; n = 4322; k = 13), 7.1% (95% CI: 2.7–13.4; n = 1227; k = 5), 84.8% (95% CI: 53.5–99.9; n = 1612; k = 10), 86.0% (95% CI: 56.4–99.9%; n = 2017; k = 9) and 9.1% (95% CI: 1.2–22.8; n = 1014; k = 4) of the patient populations respectively.

Clinical stage

A total of 10 HNC clinical stage studies done in Africa were identified as per the study selection of this study (Supplementary file S2). Of the pooled total study population, a prevalence rate of 13.6% (1040/7624 patients) for stages I-II were recorded and 58.3% (4444/7624 patients) for stages III-IV were recorded across 9 countries. The mean range age of patients was 42–65 years.

Of the pooled total clinical stages, the highest prevalence rate of 81.0% was recorded for the stages III-IV, while the lowest rate of 19.0% was recorded for the stages I-II as shown in Table 1. For both the random effects and fixed effect models, the diamonds representing the estimated prevalence and 95% confidence limits in Figs. 7 and 8 did not cross the line of no prevalence, suggesting that the effect of prevalence was significant. For the two clinical stages (I-II and III-IV), the test of heterogeneity (both $p < 0.01$) suggested the presence of heterogeneous results, with the heterogeneity statistic (I^2 = 96.4%, 99.2%) indicating a high between-sample heterogeneity and its 95% CI (95.3%–97.2%, 99.0%–99.3%) indicative of a potentially important to substantial heterogeneity in the effect sizes. The pooled current prevalence of HNC for stages I-II and III-IV were estimated at 12.2% (95% CI: 6.2–19.8; n = 7624; k = 18) and 80.0% (95% CI: 68.6–89.5; n = 7624; k = 18) of the patient populations respectively.

Treatment options

Of the 28 studies included in this systematic review and meta-analysis, 14 studies reported on the prevalence of treatment with surgery only, 10 on treatment with chemotherapy only, 15 on treatment with surgery and radiotherapy, and 6 on treatment with surgery and chemotherapy. Sixteen studies assessed treatment with surgery, chemotherapy, and radiotherapy, 11 on treatment with radiotherapy only and 13 studies on treatment with chemotherapy and radiotherapy (Supplementary file S2). Of the pooled total study population, a prevalence rate of 23.1% (1902 of 8245 patients) for treatment with surgery only were recorded across 9 countries, 10.7% (409 of 3839 patients) for treatment with chemotherapy only were recorded across 6 countries, 24.5% (1783 of 7270 patients) for treatment with surgery and radiotherapy were recorded across 8 countries, 4.2% (106 of 2520 patients) for treatment with surgery and chemotherapy were recorded across 5 countries, 42.0% (3409 of 8116 patients) for treatment with surgery, chemotherapy and radiotherapy were recorded across 8 countries, 28.9% (1069 of 3696 patients) for treatment with radiotherapy only were recorded across 7 countries, and 41.9% (1456 of 3479 patients) for treatment with chemotherapy and radiotherapy were recorded across 8 countries.

For both the random effects and fixed effect models, the diamonds representing the estimated prevalence and 95% confidence limits in Supplementary file S6 did not cross the line of no prevalence, suggesting that the effect of prevalence was significant. For the treatment options (surgery only, chemotherapy only, surgery and radiotherapy, surgery and chemotherapy, and surgery, chemotherapy and radiotherapy, radiotherapy only and chemotherapy and radiotherapy), the tests of heterogeneity ($p < 0.01$) suggested the presence of heterogeneous results, with the heterogeneity statistic (I^2 = 98.7%, 97.1%, 96.9%, 97.2%, 99.7%, 98.2%, 99.2%) indicating a high between-sample heterogeneity and its 95% CI (98.4%–98.9%, 96.0%–97.9%, 95.9%–97.6%, 95.6%–98.2%, 99.6%–99.7%, 97.7%–98.7%, 99.0%–99.3%) indicative of a potentially important to substantial heterogeneity in the effect sizes. The pooled current prevalence of HNC treatment options were estimated at 24.9% (95% CI: 12.6–39.7; n = 8245; k = 14), 12.6% (95% CI: 6.0–21.1; n = 3839; k = 10), 26.4% (95% CI: 15.6–38.8; n = 7270; k = 15), 3.7% (95% CI: 0.4–9.8; n = 2520; k = 6), 24.7% (95% CI: 12.4–39.51; n = 8116; k = 16), 26.9% (95% CI: 13.0–43.5; n = 3696; k = 11) and 49.2% (95% CI: 26.9–71.6; n = 3479; k = 13) of the patient populations for the following treatment modalities: surgery only, chemotherapy only, combined surgery and radiotherapy, combined surgery and chemotherapy, combined surgery, chemotherapy and radiotherapy, radiotherapy only and combined chemotherapy and radiotherapy respectively.

Risk of publication bias

Fig. 9 shows the funnel plots for the recurrence cases (top) and the 5-year overall survival (bottom), with the standard error (left side) and sample size (right side) used as the measure of precision on the y-axis. When there is no publication bias, the data points in a funnel plot form a roughly symmetrical upside-down funnel, with results from small studies scattered widely at the bottom of the funnel. In the HNC recurrence, the data points showed an asymmetrical pattern in the funnel plot that might be indicative of publication bias and the presence of small-study effects, although the effect is not very evident. Similar deductions can be observed for the 5-year overall survival. Likewise, in Supplementary file S8, asymmetrical patterns can be seen in the funnel plots for Squamous Cell Carcinoma histology, treatment options, tumor sites, risk factors, and clinical stages.

Rank correlation

Since a funnel plot may give a subjective and wrong impression of publication bias especially when the

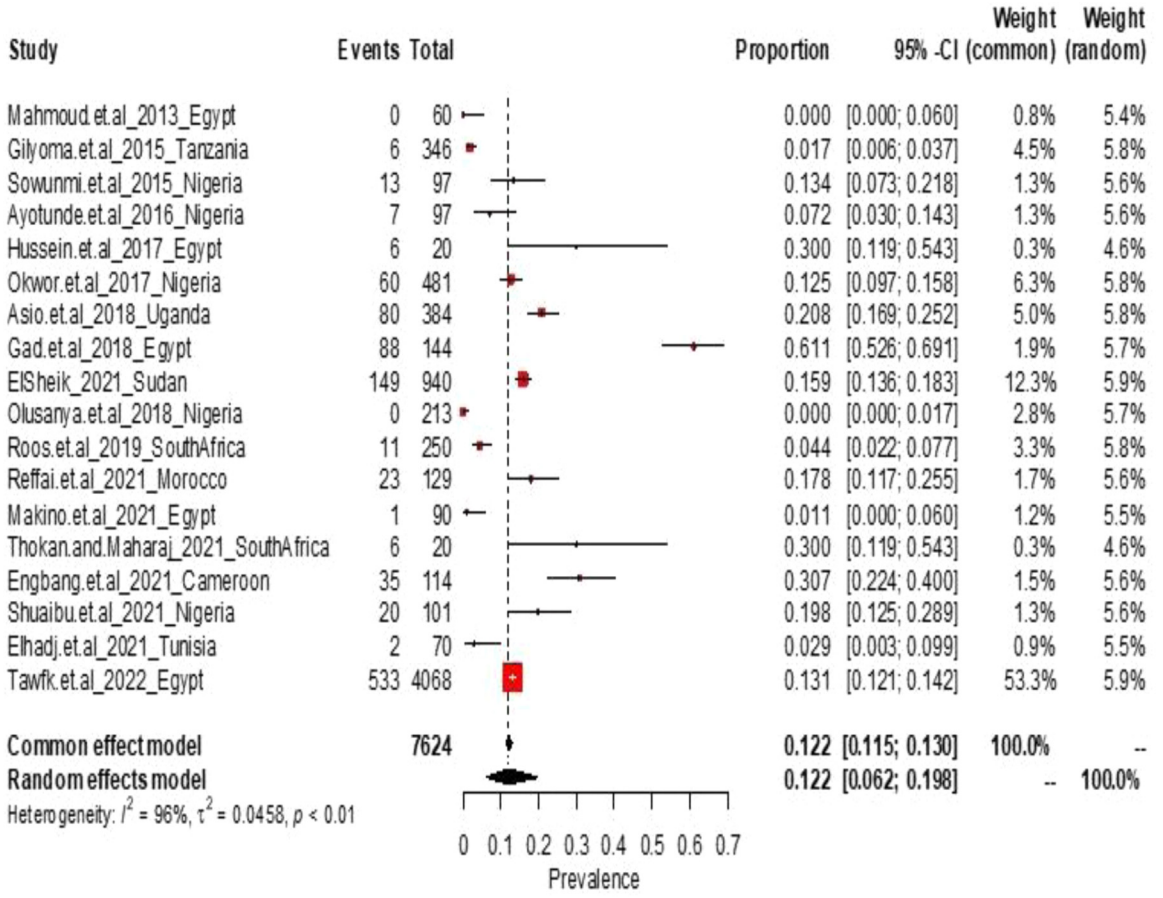

Fig. 7: Current prevalence of stages I-II in the patient populations. Abbreviation: CI, Confidence interval.

appearance of the funnel plot can change quite dramatically depending on the scale on its y-axis, statistical tests such as the rank correlation test and Egger's test were performed to further assess the potential publication bias in the conducted meta-analyses in this study. From the (Kendall's tau [τ]) rank correlation tests for funnel plot asymmetry performed, it can be concluded at a 5% level of significance that there is a significant relationship between the sample size and the observed effect size of each study for the HNC recurrence (τ = 0.43, p = 0.01), 5-year overall survival (τ = 0.64, p < 0.01), Squamous Cell Carcinoma histology (τ = 0.74, p < 0.01), treatment with surgery only (τ = 0.57, p < 0.01), treatment with surgery and radiotherapy (τ = 0.47, p = 0.02), treatment with surgery, chemotherapy and radiotherapy (τ = 0.38, p = 0.04), treatment with radiotherapy only (τ = 0.60, p = 0.01), treatment with chemotherapy and radiotherapy (τ = 0.44, p = 0.04), tumors in oral cavity (τ = 0.66, p < 0.01), tumors in the nasopharynx (τ = 0.72, p = 0.01), smoking (τ = 0.57, p < 0.01), alcohol consumption (τ = 0.53, p = 0.03), clinical stages I-II (τ = 0.71, p < 0.01), and clinical stages III-IV (τ = 0.73, p < 0.01). However, the rank correlation test fails to find a significant relationship between sample size and effect size of each study for treatment with chemotherapy only (τ = 0.33, p = 0.22), treatment with surgery and chemotherapy (τ = 0.60, p = 0.14), tumors in the oropharynx (τ = 0.40, p = 0.48), tumors in the larynx (τ = 0.45, p = 0.07), and tumors in the hypopharynx (τ = –0.33, p = 0.75).

Egger's test

From the Egger's regression tests for funnel plot asymmetry performed, it can be concluded at a 5% level of significance that small-study effects truly exist in the meta-analysis study for the HNC recurrence (t = 2.82, df = 16, p = 0.01), 5-year overall survival (t = 5.37, df = 22, p < 0.01), Squamous Cell Carcinoma histology (t = 5.40, df = 19, p < 0.01), treatment with surgery only (t = 4.42, df = 12, p < 0.01), treatment with surgery and radiotherapy (t = 3.3, df = 13, p = 0.01), treatment with surgery, chemotherapy and radiotherapy (t = 2.29, df = 14, p = 0.04), treatment with radiotherapy only

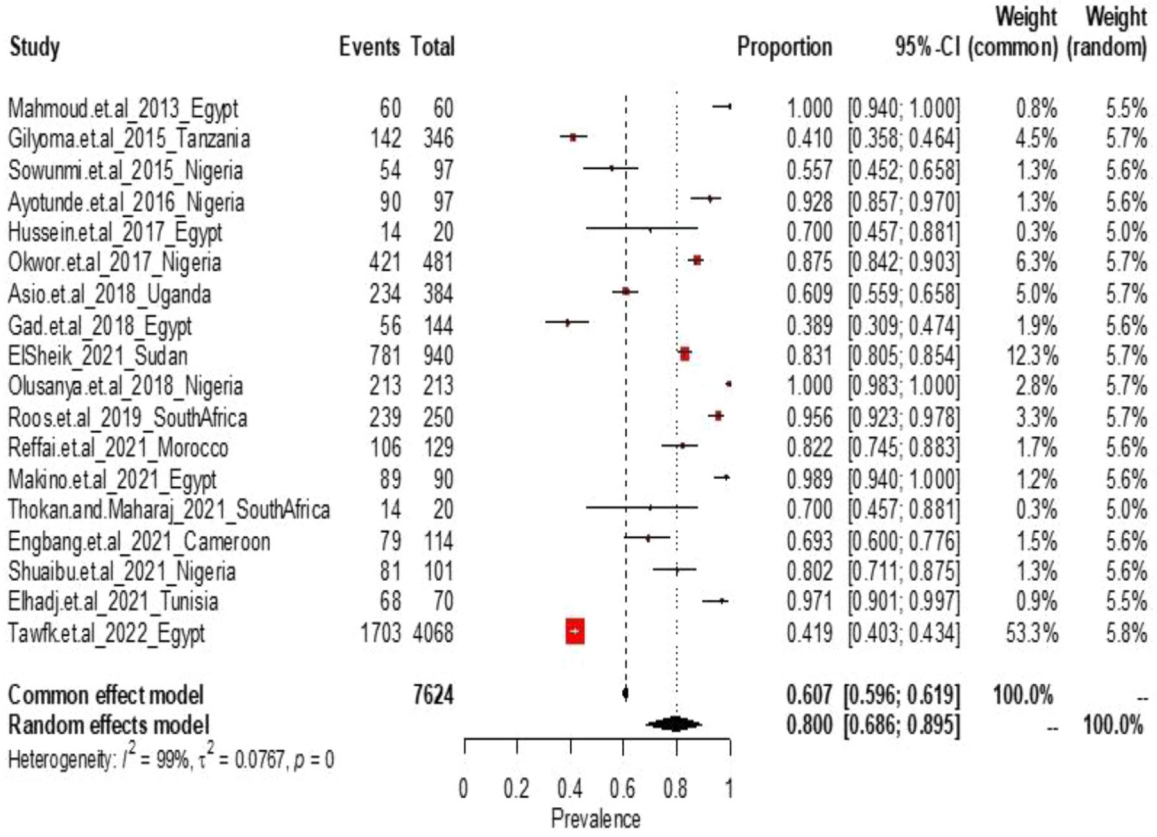

Fig. 8: Current prevalence of stages III-IV in the patient populations. Abbreviation: CI, Confidence interval.

(t = 4.12, df = 9, p < 0.01), treatment with chemotherapy and radiotherapy (t = 3.29, df = 11, p = 0.01), tumors in oral cavity (t = 4.12, df = 11, p < 0.01), tumors in the larynx (t = 2.43, df = 8, p = 0.04), tumors in the nasopharynx (t = 2.87, df = 7, p = 0.02), smoking (t = 5.11, df = 13, p < 0.01), alcohol consumption (t = 3.70, df = 9, p = 0.01), clinical stages I-II (t = 3.75, df = 16, p < 0.01), and clinical stages III-IV (t = 8.71, df = 16, p < 0.01). Thus, their resulting funnel plots are significantly asymmetrical, indicating that the data points in the funnel plot are indeed asymmetrical. Overall, this corroborates with the initial findings from the funnel plots that there were small-study effects. However, the Egger's test was not significant for treatment with chemotherapy only (t = 1.52, df = 8, p = 0.17), treatment with surgery and chemotherapy (t = 0.87, df = 4, p = 0.44), tumors in the oropharynx (t = 2.50, df = 3, p = 0.09), and tumors in the hypopharynx (t = 0.39, df = 2, p = 0.74), possibly indicating no funnel plot asymmetry.

Sensitivity analysis

Using the trim-and-fill method to adjust for the effect estimate for the presence of asymmetry in the funnel plots, this method added eight imputed missing studies to the meta-analysis of HNC recurrence, leading to an adjusted random effects prevalence of 29.41% (95% CI: 19.55–40.32), with a 98.1% heterogeneity statistic (I^2 = 98.1%; 95% CI: 97.7–98.4; k = 26 (with 8 added studies)). Similarly, for the 5-year overall survival, the trim-and-fill method added seven imputed missing studies to the meta-analysis, leading to an adjusted random effects prevalence of 35.77% (95% CI: 20.61–52.50), with a 99.7% heterogeneity statistic (I^2 = 99.7%; 95% CI: 99.3–99.9; k = 31 (with 7 added studies)). Since the difference between the heterogeneity for HNC recurrence before using the trim-and-fill method (96.2%) and after applying it was negligible, the validity of the estimated summary effect size can be said to be robust. Similar deductions can be observed for the 5-year overall survival, with a 99.5% heterogeneous before using the trim-and-fill method. In addition, the heterogeneity results obtained after applying the trim-and-fill method to the meta-analyses were slightly higher (although negligible) compared to the ones obtained before applying the method. This could be as a result of adding imputed missing studies which likely extended the distribution range of the meta-

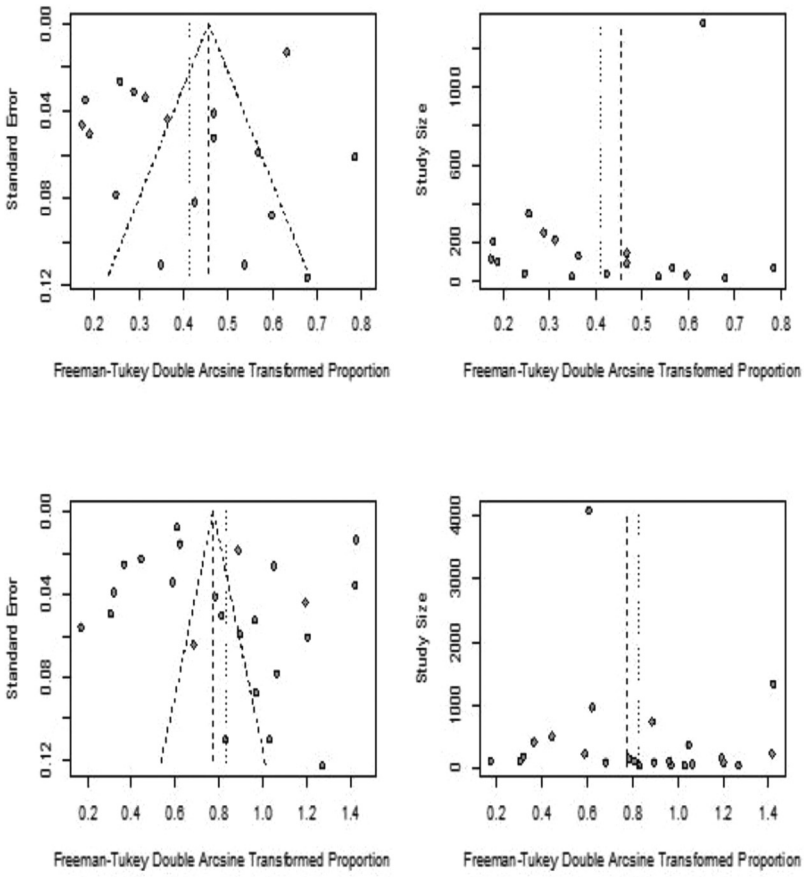

Fig. 9: Funnel plots for HNC recurrence (top) and the 5-year overall survival (bottom).

analyses and thus leading to more heterogeneous bias-adjusted meta-analyses.

Study quality analysis

The JBI critical appraisal toolkit was used in categorizing each of the included studies into three—low, moderate and high quality. Studies were categorized as low-quality if they scored 49% or less. Studies scoring between 50 and 69% were categorized as moderate quality, while those scoring 70% and above were assessed as high quality. Using this toolkit, most of the included studies were categorized as moderate quality studies (see Supplementary file S4).

From the JBI assessment of study quality done for the recurrence, three studies[32,42,44] were identified to be of low quality. After excluding them from the meta-analysis, the prevalence of HNC recurrence stood at 15.57% (I^2 = 90.4%; 95% CI: 85.9–93.5; n = 1291; k = 15). Applying the trim-and-fill method, five imputed missing studies were added to the meta-analysis of HNC recurrence, leading to an adjusted random effects prevalence of 8.43% (I^2 = 92.9%; 95% CI: 90.4–94.8; k = 20 (with 5 added studies)) with a minimal change in the I^2 heterogeneity from 90.4% to 92.9%. Similarly, for the 5-year overall survival, five studies[20,31,32,44,45] were identified to be of low quality. After excluding them from the meta-analysis of HNC survival, the prevalence of HNC 5-year overall survival stood at 57.25% (I^2 = 98.5%; 95% CI: 98.2–98.8; n = 3815; k = 19). Applying the trim-and-fill method, seven imputed missing studies were added to the meta-analysis, leading to an adjusted random effects prevalence of 37.54% (I^2 = 98.8%; 95% CI: 98.6–99.0; k = 26 (with 7 added studies)).

Influence analysis on risk of bias

Recurrence

One study[32] was detected as an outlier and found to be adding more to the heterogeneity of the meta-analysis. After excluding it from the meta-analysis, the prevalence of HNC recurrence stood at 14.2% (I^2 = 90.0%; 95% CI: 85.6–93.1; n = 1887; k = 17) with a slight shrinkage of the I^2 heterogeneity from 96.2% to 90.0%. Using the trim-and-fill method to adjust for the effect estimate for the presence of asymmetry in the funnel plot, this method added five imputed missing studies to

the meta-analysis, leading to an adjusted random effects prevalence of 7.98% (I^2 = 92.6%; 95% CI: 90.1–94.5; k = 22 (with 5 added studies)) with a slight shrinkage of the I^2 heterogeneity from 98.1% to 92.6%.

Survival

Two studies[31,32] under survival were detected as outliers and found to be adding more to the heterogeneity of the meta-analysis. After excluding them from the meta-analysis, the prevalence of HNC 5-year overall survival stood at 52.6% (I^2 = 98.6%; 95% CI: 98.4–98.9; n = 4403; k = 22) with minimal shrinkage of the I^2 heterogeneity from 99.5% to 98.6%. The trim-and-fill method added six imputed missing studies to the meta-analysis, leading to an adjusted random effects prevalence of 36.28% (I^2 = 99.0%; 95% CI: 98.9–99.2; k = 28 (with 6 added studies)) with a negligible shrinkage of the I^2 heterogeneity from 99.7% to 99.0%.

Squamous cell carcinoma histology

One study[31] in the SCC histology was detected as an outlier and found to be adding more to the heterogeneity of the meta-analysis. After excluding it from the meta-analysis, the prevalence of Squamous Cell Carcinoma histology stood at 84.7% (I^2 = 99.2%; 95% CI: 99.0–99.3; n = 5186; k = 20) with no meaningful shrinkage of the I^2 heterogeneity from 99.5% to 99.2%.

Treatment options

We elicited one study[31] in the treatment by surgery only category as an outlier and found to be adding more to the heterogeneity of the meta-analysis. After excluding it from the meta-analysis, the prevalence of HNC treatment with surgery only stood at 25.5% (I^2 = 98.7%; 95% CI: 98.4–99.0; n = 4177; k = 13) with no shrinkage of the I^2 heterogeneity from 98.7% to 98.7%. For the treatment with chemotherapy only, one study[42] was detected as an outlier and found to be adding more to the heterogeneity of the meta-analysis. After excluding it from the meta-analysis, the prevalence stood at 10.4% (I^2 = 95.6%; 95% CI: 93.5–97.1; n = 3589; k = 9) with a slight shrinkage of the I^2 heterogeneity from 97.1% to 95.6%. For treatment with surgery and radiotherapy, one study[31] was detected as an outlier and found to be adding more to the heterogeneity of the meta-analysis. After excluding it from the meta-analysis, the prevalence stood at 26.5% (I^2 = 97.0%; 95% CI: 96.0–97.7; n = 3202; k = 14) with no shrinkage of the I^2 heterogeneity from 96.9% to 97.0%. Furthermore, for treatment with surgery and chemotherapy, one study[44] was detected as an outlier and found to be adding more to the heterogeneity of the meta-analysis. After excluding it from the meta-analysis, the prevalence stood at 1.6% (I^2 = 65.2%; 95% CI: 8.8–86.7; n = 2174; k = 5) with a considerable shrinkage of the I^2 heterogeneity from 97.2% to 65.2%. For treatment with surgery, chemotherapy and radiotherapy, one study[31] was detected as an outlier and found to be adding more to the heterogeneity of the meta-analysis. After excluding it from the meta-analysis, the prevalence stood at 21.9% (I^2 = 98.5%; 95% CI: 98.2–98.8; n = 4048; k = 15) with a trivial shrinkage of the I^2 heterogeneity from 99.7% to 98.5%. For treatment with chemotherapy and radiotherapy, one study[36] was detected as an outlier and found to be adding more to the heterogeneity of the meta-analysis. After excluding it from the meta-analysis, the prevalence stood at 46.7% (I^2 = 98.9%; 95% CI: 98.6–99.1; n = 2767; k = 12) with a trivial shrinkage of the I^2 heterogeneity from 99.2% to 98.9%. However, for the treatment with radiotherapy only, no studies were found to be adding more to the heterogeneity (98.2%) of the meta-analysis.

Tumor site

For tumors in oral cavity, a study[32] was detected as an outlier and found to be adding more to the heterogeneity of the meta-analysis. After excluding it from the meta-analysis, the prevalence stood at 81.7% (I^2 = 99.7%; 95% CI: 99.6–99.7 n = 2995; k = 12) with no shrinkage of the I^2 heterogeneity from 99.7% to 99.7%. For tumors in the oropharynx, one study[44] was detected as an outlier and found to be adding more to the heterogeneity of the meta-analysis. After excluding it from the meta-analysis, the prevalence stood at 5.3% (I^2 = 86.9%; 95% CI: 68.4–94.6; n = 881; k = 4) with a slight shrinkage of the I^2 heterogeneity from 91.5% to 86.9%. For tumors in the larynx, one study[42] was detected as an outlier and found to be adding more to the heterogeneity of the meta-analysis. After excluding it from the meta-analysis, the prevalence stood at 81.6% (I^2 = 99.5%; 95% CI: 99.4–99.6; n = 1362; k = 9) with no shrinkage of the I^2 heterogeneity from 99.6% to 99.5%. For tumors in the nasopharynx, one study[36] was detected as an outlier and found to be adding more to the heterogeneity of the meta-analysis. After excluding it from the meta-analysis, the prevalence stood at 82.5% (I^2 = 99.4%; 95% CI: 99.2–99.5; n = 1305; k = 8) with no meaningful shrinkage of the I^2 heterogeneity from 99.6% to 99.4%. For tumors in the hypopharynx, one study[20] was detected as an outlier and found to be adding more to the heterogeneity of the meta-analysis. After excluding it from the meta-analysis, the prevalence stood at 12.2% (I^2 = 96.6%; 95% CI: 92.9–98.4; n = 917; k = 3) with very little shrinkage of the I^2 heterogeneity from 95.3% to 96.6%.

Risk factors

For smoking, one study[32] was detected as an outlier and found to be adding more to the heterogeneity of the meta-analysis. After excluding it from the meta-analysis, the prevalence stood at 42.7% (I^2 = 98.9%; 95% CI: 98.6–99.1; n = 3047; k = 14) with no shrinkage of the I^2 heterogeneity from 98.8% to 98.9%. However, for alcohol consumption, no studies were found to be

adding more to the heterogeneity (98.9%) of the meta-analysis.

Clinical stages

For clinical stages I-II, one study[31] was found to be an outlier and observed to be adding more to the heterogeneity of the meta-analysis. After excluding it from the meta-analysis, the prevalence stood at 12.2% (I^2 = 96.6%; 95% CI: 95.6–97.4; n = 3556; k = 17) with no meaningful shrinkage of the I^2 heterogeneity from 96.4% to 96.6%. Likewise, for the clinical stages III-IV, the same study[31] was detected as an outlier and found to be adding more to the heterogeneity of the meta-analysis. After excluding it from the meta-analysis, the prevalence stood at 82.0% (I^2 = 98.0%; 95% CI: 97.5–98.4; n = 3556; k = 17) with a trivial shrinkage of the I^2 heterogeneity from 99.2% to 98.0%.

Discussion

This study provides a comprehensive synthesis of evidence describing the prevalence of recurrence and a 5-year overall survival of head and neck cancers in Africa. The results show a lower recurrence rate, and a lower 5-year overall survival among patients treated for head and neck cancers involving the oral cavity, oropharynx, nasopharynx, larynx and the hypopharynx relative to the general population.[47,48] Similar to the general population,[1] men are at fivefold higher risk than women for developing HNC in Africa. Our analysis showed the mean age range of HNC recurrence to be 14–65 years. Majority of HNC in Africa were oral cavity cancers. This study has aided in pooling together data on the effects of different treatment modalities related to recurrent HNC in Africa as well as in deciding potential predictors of this group of cancers. Although lower than that of the general population, the recurrence prevalence rate of 15.4% from this systematic review and meta-analysis was still appreciable. Supporting evidence showed that the tumor stage, tumor site, and treatment options contribute to prognosticating cancer recurrence.[49]

In the United States, the 5-year survival rate for all races for the period 2004 and 2010 was estimated at 66% for oral cavity and pharyngeal cancers and 63% for laryngeal cancer,[50] which is greater than the survival rate found in this study (54.4%). Advances in treatment increase survival and may delay or prevent cancer deaths.[51] Diagnosis of most HNC cancers are made at advanced stages when both medical and surgical treatment offers less benefit.[52] Furthermore, poor survival outcome of patients in our study relative to studies in the United States may be accounted for by the limited diagnostic and treatment resources in addition to variations in the regional aetiological and pathological patterns of the disease.[53] The link between poor socio-economic status and poor health has been well reported.[54] Poor nutrition is fast growing in Africa,[55] and this does not only impact on the clinical outcomes of patients, but also a modifiable risk factor.[56] Poverty also adversely affects patients' ability to commute a long distance to health facilities where care is accessed. The survival rate from this study on the other hand compares better to other studies where survival rates were estimated between 30% and 40%.[57–60] The better survival observed in this study may be related to poor data capturing of real time cases in Africa[61,62] as compared to the more accurate cancer statistics in the developed world.

Evidence from our study showed that combination of chemotherapy and radiotherapy is the most prevalent treatment option in Africa. Although chemotherapy and radiotherapy combination has been reported to improve overall survival, progression-free survival, locoregional control, and decreases HNC deaths,[63] this combination in Africa does not eliminate the significant acute toxicity and long-term cardiac and renal morbidity associated with combined chemotherapy and radiation,[64] and the reported benefits may not have been well quantified. The preference of this combination may not be separated from the very low number of trained head and neck surgeons in the region. According to the African Head and Neck Society (AfHNS), the entire Africa had only 14 trained head and neck surgeons in 2018.[65] As at 2021, Africa had 19 head and neck surgeons[66] serving a regional population of 1.4 billion people. The result of this is long waiting time for surgery, preference for radiotherapy instead of surgery, or worse still, patients being operated by less experienced surgeons giving rise to poor outcomes. As evidenced in another study, most patients in Africa with curative disease were treated as palliative due to system failures.[67] As the boundaries of head and neck cancer surgery increase, the risk of surgical complications such as cranial nerve injuries, vascular injuries, as well as damage to swallowing, phonation, and taste also increases.[68] Furthermore, despite the presence of symptoms and visible tumors in HNCs, many of them are diagnosed at advanced stages (III & IV), when surgery offers little or no benefit to the patients.[69]

Though identified as a significant risk factor for HNC in this study as in other studies,[70–75] smoking prevalence among patients with HNC was lower compared to those from the United States, where the prevalence of smokers at diagnosis of HNC was 56.2%,[72] 75.2% in the United Kingdom,[76] and risk of 1.54 (95% CI: 1.14, 2.06) in Nepal.[77] Consistent evidence from several studies have indicated that tobacco smoking in any form carries the risk of increasing oral cancer by two to tenfold in men and women. For example, there is a 10 times higher risk for HNC among smokers, and an association of 70–80% new cases of HNC with a combined smoking and alcohol usage[73] which resonates with findings of this African study. Although our study did not interrogate the impact of quitting smoking prior to

treatment, another study revealed a 3.7 times odds of complete response to first-line treatment among quitters as compared to those who continued smoking.[78] Furthermore, there is a 2.37 odds of developing HNSCC among tobacco only users as compared to 5.7 in combined smokers and alcohol users.[73] The smoking rates in this study compares well with previous studies reporting a range of 26.4%–56%.[75,79] The high smoking rate in Africa may be attributed to adverse life circumstances such as negative life events, difficulties in relationships, educational deprivations, poor emotional and social support, and adverse neighborhood conditions associated with living in areas of deprivation where the odds of quitting smoking is reportedly higher.[80] Likewise, the prevalence of alcohol consumption in this study was lower than that from another study with prevalence of 72.3% among alcohol consumers.[76] While some studies have suggested that the rising prevalence of oral and pharyngeal cancers were primarily due to increases in HPV,[51] this systematic review and meta-analysis did not explore the underlying causes of cancers at the different head and neck sites.

We report the highest prevalence of HNC occurred in the oral cavity followed by the nasopharynx. Dominance of oral cavity cancers have been demonstrated by other studies.[81,82] Although the influence of contributing risk factors varies across diverse population groups, oral cancer is mainly a disease of poor people[83] where high prevalence of tobacco and alcohol use,[83] unhealthy diet and poor oral sex hygiene have been credited.[84] Notably, nasopharyngeal carcinoma (NPC) in this study was predominant in North Africa (Supplementary file S2). This finding correlates with other studies[33,85] where the highest NPC where reported to be more prevalent in North Africa relative to other African countries. Genetic, environmental and viral (EBV) factors have also been attributed to this dominance in the Northern parts of Africa.[86]

In this study, a high prevalence of advanced cancer with a prevalence of 80.0% for clinical stages III and IV was found. As previously indicated, clinical stage at presentation is one of the most significant prognostic factors for HNC outcome.[87] Explanations for diagnosis of most HNC at advanced stages in Africa are often multifactorial and may include patients' and healthcare worker's ignorance of cancer signs and symptoms, poor access to quality healthcare service, and inadequate medical resources emanating from fragmented healthcare system[88] within the region. Advanced stage clinical presentation has also been attributed to delays in initiation of treatment by health professionals.[87,89,90]

Our sensitivity analysis of the JBI study quality revealed that although the low quality studies were excluded from the meta analyses for recurrence and survival, this did not significantly change the heterogeneities obtained before their exclusion. This sensitivity finding goes to emphasize the methodological rigour of our study. We further showed the presence of asymmetry were detected in the funnel plots which might be indicative of publication bias, it is crucial to note that publication bias is just one of many possible reasons for funnel plot asymmetry among others such as social preferences of the authors and source of research funding. In addition, from the rank correlation tests performed, the presence of a significant relationship between sample size and effect size provided evidence of asymmetry in the funnel plot and suggested the possibility of publication bias. However, a non-significant test results should not be taken as evidence of a lack of publication bias when the meta-analysis involves small study sizes, as is the case in this study due to the limited numbers of HNC-related researches done in Africa. Furthermore, following detection of asymmetry in the funnel plots, the trim-and-fill method was used in adjusting for the effect estimate of this bias. The heterogeneity results obtained after applying the trim-and-fill method to the meta-analyses were slightly higher (although negligibly so) compared to the ones obtained before applying the method. However, there are no guarantees that the adjusted random effects obtained will match what would have been observed in the absence of publication bias. In addition, this method does not take into account reasons for the presence of funnel plot asymmetry. Thus, any conclusions regarding the presence of publication bias based on these methods should be drawn with caution.

This systematic review and meta-analysis has potential limitations. Firstly, evidence from this study in which only data from ten countries in Africa were found confirms the longstanding inequities in global research, marked by disproportionately greater number of studies from the developed countries as compared to fewer studies emanating from the middle-income and low-income countries.[91] Secondly, the methodological options used in this study–such as histological type, decision to assess associated risk factors separately, and segregation of treatment options were strongly influenced by evidence provided in the literature. For example, very few studies consistent with our primary outcome variables (recurrence and overall survival) reported on HPV as a risk factor. In addition, too few studies reported on pathological characteristics such as nodal extensions or involved surgical margins despite clear evidence that these features have increased predisposition to recurrence.[92,93] It is noteworthy that prevalence as an epidemiological measure is scaled based on the average life expectancy of the cancer. Moreover, despite efforts to reach two corresponding authors of studies where relevant data were outstanding in the published articles, these authors could not be reached making such information not available. Lastly, the heterogeneity between samples found in this current study were high, which are not unusual in meta-analyses of prevalence-oriented data. In addition,

several sensitivity analyses were conducted via a leave-one-out approach whereby each meta-analysis was re-ran, iteratively removing studies. Little to no changes were observed among the obtained heterogeneity statistics (I^2 values) and they were consistent with the significant levels of heterogeneity of the main findings.

Locoregional recurrence in HNC post-treatment is a clinically important and predominant pattern of failure that presents serious challenges in management and adversely affects survival outcome. This systematic review and meta-analysis show the burden of HNC recurrence as well as 5-year overall survival among treated patients within Africa. Evidence from this study validates the importance of interventions aimed at smoking and alcohol reduction or elimination. Most of such interventions have been proven to be cost effective even for the low- and middle-income countries (LMIC). Knowledge of signs and symptoms of HNC, healthy meal, as well as good oral and sexual hygiene are vital. Effective screening protocols for HNC within the healthcare systems need to be set. In addition, population-based screening warrants strong considerations. Provision of visual screening training by health professionals is strongly advocated. Training and retention of more head and neck surgeons in Africa remains crucial in patients' management. Success in these depends on political will, intersectoral collaborations as well as culturally sensitive health promotion messages disseminated through educational campaigns and mass media to reach both the advantaged and disadvantaged communities. Further prevalence studies in HNC, as well as its risk factors are encouraged to be conducted in the region to provide stronger evidence on the burden of this important group of cancers in the continent. In addition, studies of subgroups based on different treatment options for tumor stage should also be considered using a multivariate analysis.

Contributors

Conceptualization: HM, TE, PEM; Study design: HM, TE, OO, PEM; Literature search: HM, TE, PEM; Risk of bias assessment: HM, OO, PEM; Data extraction: HM, TKS, KTB; Data verification: HM, TE, OO, TKS, KTB, ADF, AM, MM, PEM; Formal analysis: HM, OO; Investigation: HM, TE, OO, TKS, KTB, ADF, AM, MM, PEM; Writing—original draft: HM, OO; Writing—review and editing: HM, TE, OO, TKS, KTB, ADF, AM, MM, PEM.

Data sharing statement

All data collected for this systematic review and meta-analysis, including search strategy, the review protocol, and data extraction sheets, are available immediately after publication and are either published as supplementary material or can be accessed through the corresponding author.

Protocol link: https://www.crd.york.ac.uk/prospero/display_record.php?ID=CRD42022372307.

Declaration of interests

The authors declare no competing interests.

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Appendix A. Supplementary data

Supplementary data related to this article can be found at https://doi.org/10.1016/j.eclinm.2023.101964.

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