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Systematic Review Article

Socioeconomic Determinants of Esophageal Cancer Incidence in the East African Corridor: A Systematic Review with Meta-Analysis

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ABSTRACT

Background and aim of the work: In the East African corridor, environmental exposures such as alcohol and tobacco are comparatively lower than in many other regions globally. Despite this, more than 40% of global esophageal cancer cases are concentrated in this area. This raises the hypothesis that individual factors, specifically socioeconomic status [SES] indicators such as income, occupation, and education, may contribute to the high incidence of esophageal cancer in this region. Given the limited existing information and lack of meta-analyses on this subject, our study aimed to establish the relationship between SES and the rising prevalence of esophageal cancer in the East African Corridor.

Materials and Methods: We conducted a comprehensive search for observational studies reporting SES in individuals with esophageal cancer, published up to December 2023, using databases including PubMed/Medline, Web of Science, Scopus, Cochrane Library, and African Journal Online. The data extraction and analysis were performed following the PRISMA guidelines. Quality assessment and evaluation of publication bias were conducted using standard tools. To estimate summary effects, meta-analyses were performed with RevMan and Stata software, utilizing random-effects models.

Results: Our study encompassed 18,602 participants from 19 selected studies. The results strongly indicate a significant correlation between education level and esophageal cancer incidence. Individuals with no formal education exhibited a notably higher risk [OR=2.32 [95% CI, 1.89-2.85]], followed by those with only primary education [OR=1.68 [95% CI, 1.48-1.91]], compared to individuals with secondary and higher education. Furthermore, our findings revealed that the risk of esophageal cancer is highest among individuals employed in farming [OR=1.53 [95% CI, 1.24-1.90]] compared to office workers. Additionally, individuals with low family income faced a significantly higher risk [OR=2.82 [95% CI, 1.93-4.12]] compared to those with high family income.

Conclusion: Our study strongly supports the assertion that socioeconomic status is closely correlated with the escalating incidence of esophageal cancer in the East African Corridor.

Keywords: Socio-Economic Status; Esophageal cancer; Africa; Meta-Analysis.

INTRODUCTION

The incidence of esophageal cancer [EC] has undergone a significant surge in Africa in recent decades, particularly in South and East Africa, posing a formidable public health challenge [1, 2]. Esophageal Squamous Cell Carcinoma stands out as the most prevalent subtype in this region [3]. This illness manifests through an array of distressing symptoms, encompassing dysphagia, unintentional weight loss, heartburn, esophageal erosion, ulceration, stricture, and the potential development of Barrett's esophagus [4]. In severe instances, it can lead to life-threatening complications such as esophageal hemorrhage, perforation, and respiratory damage [5]. Men are more vulnerable than women, with an average diagnostic age of 55 years [6].

The global burden of esophageal cancer is substantial, with approximately 60,400 new cases and 54,076 deaths reported annually, according to the latest GLOBOCAN estimates [7]. Notably, Africa alone contributes nearly 49% of these global cases [8], presenting an enduring challenge for health authorities, particularly in sub-Saharan Africa.

Numerous studies have implicated lifestyle as a contributing factor to the development of esophageal cancer in Africa [9, 10]. While often overshadowed, individual factors such as socio-economic status [SES] play a pivotal role in the prognosis and incidence of diseases, including cancer [11]. Systematic reviews have consistently identified socioeconomic differences as a risk factor for various cancer types, including breast cancer [12-14], lung cancer [15], stomach cancer [16], colorectal cancer [17], and prostate cancer [18]. However, a comprehensive synthesis of results about socio-economic disparities and esophageal cancer risk is notably lacking, especially in the highly endemic region of Africa. Existing studies are limited to individual observations, reporting frequencies without statistically examining the relationship between SES and EC incidence.

This underscores the urgent need to investigate the influence of SES on the etiology of esophageal cancer in the populations of the East African corridor.

A comprehensive approach is essential to raise awareness, involving an assessment of socioeconomic factors such as education level, occupation, and income, which may predispose African populations to esophageal cancer.

MATERIALS AND METHODS

The Preferred Reporting Items for Systematic Reviews and Meta-Analyses [PRISMA] guidelines served as the basis for the conduct of this systematic review and meta-analysis [19]. Under the number CRD42024510004, the review protocol is listed in the International Prospective Register of Systematic Reviews [PROSPERO].

1. Eligibility criteria

The studies were found using the eligibility criteria listed below. **Inclusion criteria**: [1] Empirical studies evaluating the effect of socioeconomic status on the etiology of esophageal cancer in the East African Corridor. Education, income, and occupation were considered as SES measures. [2] Studies had to address the same socioeconomic measure comparably so that results could be combined in a meta-analysis. [3] To distinguish between low- and high-SES groups, socioeconomic measures were to be presented as categorical variables. [4] Studies were to present data that could be used to calculate risk ratios and their corresponding 95% confidence intervals. [5] Studies were required to have obtained ethical clearance and a Newcastle-Ottawa quality score of at least 4 stars out of 8. [6] Studies need to be done on the African continent using adult human subjects. **Disqualified criteria**: [1] The following study types will not be accepted: unpublished work; anonymous reports; nonhuman research; editorials, letters, reviews, and commentary. [2] Research whose data do not permit the computation of odds ratios will likewise be disqualified. [3] Research whose data cannot be accessed, even upon request to the authors, shall likewise be disqualified. [4] Sample size limits will be disregarded.

2. Data sources and search strategy

African Journals Online [AJO], Scopus, Cochrane Library, Web of Science, and Medline/PubMed Databases were queried to identify pertinent electronic studies demonstrating the relationship between esophageal cancer and SES in endemic areas of Africa up to December 2023. The search terms used in these five databases were "socio-economic status" OR "socioeconomic position" OR "economic index" OR "occupational category" OR "occupational classification" OR "educational level" OR "income" "education level" OR "employment" OR "job" OR "economic stability" AND "esophageal neoplasm" OR "esophageal tumor" OR "esophageal cancer" OR "esophageal malignancy" OR "esophageal squamous cell carcinoma" OR "esophageal adenocarcinoma". The operator and symbol usage in these searches were then modified to comply with the specifications of each unique database. After that, a manual search on Google Scholar was done, followed by a cross-search of the references listed in the studies that were found. Regarding the publication date and language, there were no restrictions.

3. Study selection

The identified studies were first exported to EndNote, where duplicates were removed, and then to Rayyan software to better organize the selection and review process [20]. The selection process is reported and structured according to PRISMA flow diagram [21]. The selection process was started by assessing the abstracts and titles of previously found studies. The full texts of the articles whose abstracts and titles satisfied the first eligibility requirements were meticulously examined during the second independent selection process. Lastly, the two authors carefully cross-referenced each individual selection's results to determine which should be included in the study. Any disagreements were discussed and resolved by consensus.

4. Data collection

First author's last name, year of publication, nation, study design, sample size, diagnostic criteria, participant age, number of esophageal cancer cases, number of controls, a measure of SES [education, income, occupation], collection period, data collection methods were all extracted from the included studies. Multi-country studies are dissociated by country as follows: the name of the main author, followed by the year of publication, and the initial of the country name [e.g. **Masukume *et al.***, 2022-M / **Masukume *et al.***, 2022-T; where M= Malawi and T= Tanzania] [22-24]. Results for both measures were extracted from studies that used two distinct SES measurements independently.

5. Quality assessment

The Newcastle-Ottawa Scale [NOS] was used independently by the authors to assess the quality of the different studies included. This assessment was based on the NOS's three dimensions: [I] selection of study groups; [II] group comparison; and [III] assessment of outcomes [25]. The study quality classification system outlined by Stang was utilized for this study. As per this system, the highest possible NOS score is 9 points, with studies scoring 7 to 9 points being classified as high quality; those scoring 4 to 6 as moderate quality; and those scoring 0 to 3 as low quality [25]. Any disagreements between authors were resolved through consensus.

6. Publication bias assessment

The authors proceeded to independently assess possible publication bias was assessed by visual scrutiny of the funnel plot. Subsequently, the Egger regression test [26] was employed to statistically assess any asymmetry detected in the funnel plot. Publication bias was acknowledged when the P-value falls below 0.10 [26]. Then, the Trim and Fill test was used to confirm that the asymmetry of the funnel diagram is not linked to the publication bias of the studies [27]. Risk of bias assessment was performed using STATA version 17.0 [StataCorp LP, Texas] software for Windows.

7. Certainty of Evidence

The reliability of evidence for dietary patterns associated with esophageal cancer recurrence was assessed using GRADE approach [28]. The risk of within-study bias, inconsistency, between-study indirectness and imprecision, publication bias, effect size, and dose-response can all be considered using the GRADE approach. Authors independently assessed the strength of the evidence, and any disagreements between authors were resolved through consensus.

8. Data synthesis and analysis

According to the WHO, SES mainly covers life characteristics, such as employment, insurance status, education, and income or wages, which directly and indirectly influence the risk of developing a disease [29, 14]. In the present work, the level of education has been grouped into 4 categories: no formal education, those who have completed primary education, those who have completed secondary education, and those who have completed tertiary education. Occupations were grouped into farmers, self-employed [shopkeepers, housekeepers, other], and office workers. Incomes were grouped into low and high.

The qualitative analysis of the data was meticulously extracted from the included studies by GTK and EJN and subjected to systematic analysis. Table 1 displays the condensed results of the systematic review. Statistical analyses were carried out for quantitative synthesis using the Stata software [Version 17.0; StataCorp] for Windows. The pooled effect estimates and their corresponding 95% CI were calculated by the inverse variance method of DerSimonian and Laird [30]. Odds ratios [OR] with matching 95% Confidence Intervals [95% CI] were used to illustrate dichotomous data about SES and esophageal cancer in a forest plot. We used a random-effects model to account for study heterogeneity. The I^2 statistic was employed to assess the heterogeneity among the studies included and the significance was set at $P < 0.05$ [31]. Significant heterogeneity can be observed when the I^2 value is between 75% and 100%. Subgroup analysis considered the different types of SES [education, income, occupation] frequently reported among the populations to identify those with a high incidence of EC. P-values and confidence intervals were visually inspected to assess differences between subgroups.

RESULTS

1. Literature search results

The electronic yielded a total of 327,111 studies and manual searches have not provided any additional research. 200,098 titles and abstracts were thoroughly reviewed after duplicates were removed. Then, 108 studies were chosen for full-text analysis and 134 studies were eliminated for various reasons, including abstracts from conferences, comments, and non-alignment with the study's geographic focus. Ultimately, 19 studies [see Figure 1 and Table 1] that fully satisfied our inclusion criteria were chosen for qualitative and quantitative analysis.

2. Study characteristics and quality assessment

The combined sample of 18,602 people, comprising 7,174 cases and 11,428 controls, was covered by the 19 included studies, all of which were case-control studies. Participants came from the Eastern and Southern African sub-regions, specifically Malawi, Ethiopia, Zambia, Kenya, South Africa, Tanzania, Zimbabwe and Mozambique. The control group consisted of healthy volunteers with no history of cancer, while the cases were patients diagnosed with esophageal cancer by current protocols. Socioeconomic factors across these studies were collected through questionnaires. All the studies included were of high quality for the most part and of moderate quality for some.

3. Education level

Figure 2 shows the effect of education on esophageal cancer incidence in the East African Corridor. Analysis of Figures 2A and 2B shows a highly significant risk of esophageal cancer among those with no formal education A [OR = 2.32 [95% CI, 1.89 - 2.85]; $P < 0.00001$; $I^2 = 68\%$], followed by those with only primary education [OR = 1.68 [95% CI, 1.48 - 1.91]; $P < 0.00001$; $I^2 = 33\%$] compared to those with higher education. However, no significance [OR = 1.58 [95% CI, 1.01 - 2.49]; $P = 0.05$; $I^2 = 31\%$] was observed in those who had completed secondary education compared to those with higher education [Figure 2C]. Egger's test gave a P-value of 0.8243, 0.7023, and 0.5292 respectively for those with no formal education, those who had completed primary and secondary education suggesting the absence of publication bias.

4. Impact of occupation on incidence of esophageal cancer

Figure 3 illustrates the relationship between the risk of developing EC and occupation In the East African corridor. Farmers [Figure 3A] are more likely than office workers to develop esophageal cancer [OR = 1.53 [95%CI, 1.24 - 1.90]; $P < 0.0001$; $I^2 = 71\%$]. The Egger test gave a P value of 0.7311, suggesting the absence of publication bias. Nevertheless, no correlation was found between esophageal cancer and the other occupations [housewives, merchants [business], private workers] in the area [OR = 0.96 [0.45 - 2.02]; $P = 0.91$; $I^2 = 86\%$] [Figure 3B].

5. Effect of family income on etiology of esophageal cancer

Figure 4 presents the results of the influence of income on the risk of esophageal cancer in the East African Corridor. Analysis of this figure shows that people with low incomes have a higher risk of developing esophageal cancer than people with high incomes. The overall pooled OR for low income was 2.82 [95%CI, 1.93 - 4.12], with an overall $p < 0.001$ and high heterogeneity $I^2 = 75\%$. The Egger test yielded a p-value of 0.0969, suggesting the absence of publication bias.

Table [1]: Characteristics of the different studies included for meta-analysis

Author's [Date]	Country	study population	Cases/ controls	Socioeconomic factors evaluate	Period of collect	Data collection methods	NOS
Asombang *et al.* [2016] [32]	Zambia	Adults [≥ 18 years]	27/45	Education [None, primary, secondary, tertiary]; income [low, irregular/unsure, high]	November 2010 and January 2012	Questionnaire	6
Cunha *et al.* [2022] [33]	Mozambique	Adults [≥ 18 years]	143/212	Education level [none, primary, secondary & higher]; Income [high, medium, low]	Between 2006 and 2010	Standardized questionnaire	5
Dessalegn *et al.* [2022] [34]	Ethiopia	Adults [≥ 18 years]	338/338	Educational status [None, primary school, secondary, university]; occupation [government worker, housewife, merchant, private worker, farmer]; Monthly income [high, medium, low]	February 2019 to August 2020	Questionnaire	5
Deybasso *et al.* [2022] [35]	Ethiopia	Adults [≥ 18 years]	104/208	Occupation [Farmer, housewife, government & private employee]; level of education [unable to read and write, able to read and write, Primary, Above]; index [1st, 2nd, 3rd]	From June 1, 2019, to June 30, 2020	Administration of questionnaire	6
Kaimila *et al.* [2022] [36]	Malawi	Adults [≥ 18 years]	300/300	Occupation [Farmer, other]; Education [tertiary, secondary, primary, None]	Between 2017 and 2020	Interviewed using a structured questionnaire	7
Kayamba *et al.* [2015] [37]	Zambia	Adults [≥ 18 years]	50/50	Education [primary, secondary or higher]	October 2013 to May 2014	Simple questionnaire	5
Kayamba *et al.* [2022] [38]	Zambia	Adults [≥ 18 years]	131/235	Education level attained [tertiary, secondary, primary, none] occupation [employed by government, private worker, farmer, None]; income [high, low]	Between October 2018 and May 2021.	Interviewer-administered questionnaires	6
Leon *et al.* [2017] [39]	Ethiopia	Adults [≥ 18 years]	73/133	Education [illiterate, primary, secondary & university]	Between May 2012 and May 2013	Questionnaire	5
Masukume *et al.* [2022] [23]	Malawi, Tanzania	Adults [≥ 18 years]	539/ 593 310/ 313	Formal education [None/partial primary, Completed primary; Secondary and above]; occupation [farming, non-farming]	Malawi [2017-2020] Tanzania [2015-2019]	Administration of questionnaire	7
Menya *et al.* [2019] [40]	Kenya	Adults [≥ 18 years]	422/414	Occupation [Farmer, other]; Education [None/partial primary, Completed primary; Secondary and university]	From 08/2013 to 03/2018	Administration of questionnaire	4
Mlombe *et al.* [2015] [41]	Malawi	Adults [≥ 18 years]	96/180	Economic status [low income, medium income, high income]	From January 2011 to February 2013	Administration of questionnaire	5
Mmbaga *et al.* [2021] [42]	Tanzania	Adults [≥ 18 years]	471/ 471	Occupation [Business, office work, farmer]; International Wealth Index score [High, Medium, low],	Between 2013 and 2015	Administration of questionnaire	6
Narh *et al.* [2021] [22]	Tanzania, Malawi Kenya	Adults [≥ 18 years]	310/313 539/593 95/97	Education [None/partial primary, Completed primary; Secondary and above]; Occupation [Farmer, office worker]	2015-2018 in Kenya, 2015-2020 in Tanzania and 2017-2020 in Malawi	Interviews with questionnaire	5
Pacella-Norman *et al.* [2002] [43]	South Africa	Adults [≥ 18 years]	405/2174	Work category [office worker, others]	Between March 1995 to April 1999	Interviews with questionnaire	5
Sammon [1998] [44]	South Africa	Adults [≥ 18 years]	130/130	Education [None/partial primary, Completed primary; Secondary and High]	Between 1987 - 1988	Interviews	4
Segal *et al.* [1988] [45]	South Africa	Adults [≥ 18 years]	200/391	Education [yrs] [None/partial primary, Completed primary; Secondary and above]	during 1984 and 1985	Interviews with questionnaire	7
Sewram *et al.* [2016] [46]	South Africa	Adults [≥ 18 years]	670/1188	Education [years] [None, Primary, secondary, and more].	Between November 2001 and February 2003	Interviews with questionnaire	5
Simba *et al.* [2023] [24]	Tanzania, Malawi Kenya	Adults [≥ 18 years]	310/313 539/592 430/440	Education [None/partial primary; Completed primary; Secondary and above]	Kenya: August 2013 and March 2018. Tanzania: November 2015 and December 2019. Malawi: June 2017 and May 2020.	Interviews using comprehensive structured questionnaire	7
Vizcaino *et al.* [1995] [47]	Zimbabwe	Adults [≥ 18 years]	542/1705	Occupational status [Medium+ High, low, Farmer, Miner]	during the period 1963-1977.	Interviewed with questionnaire.	6

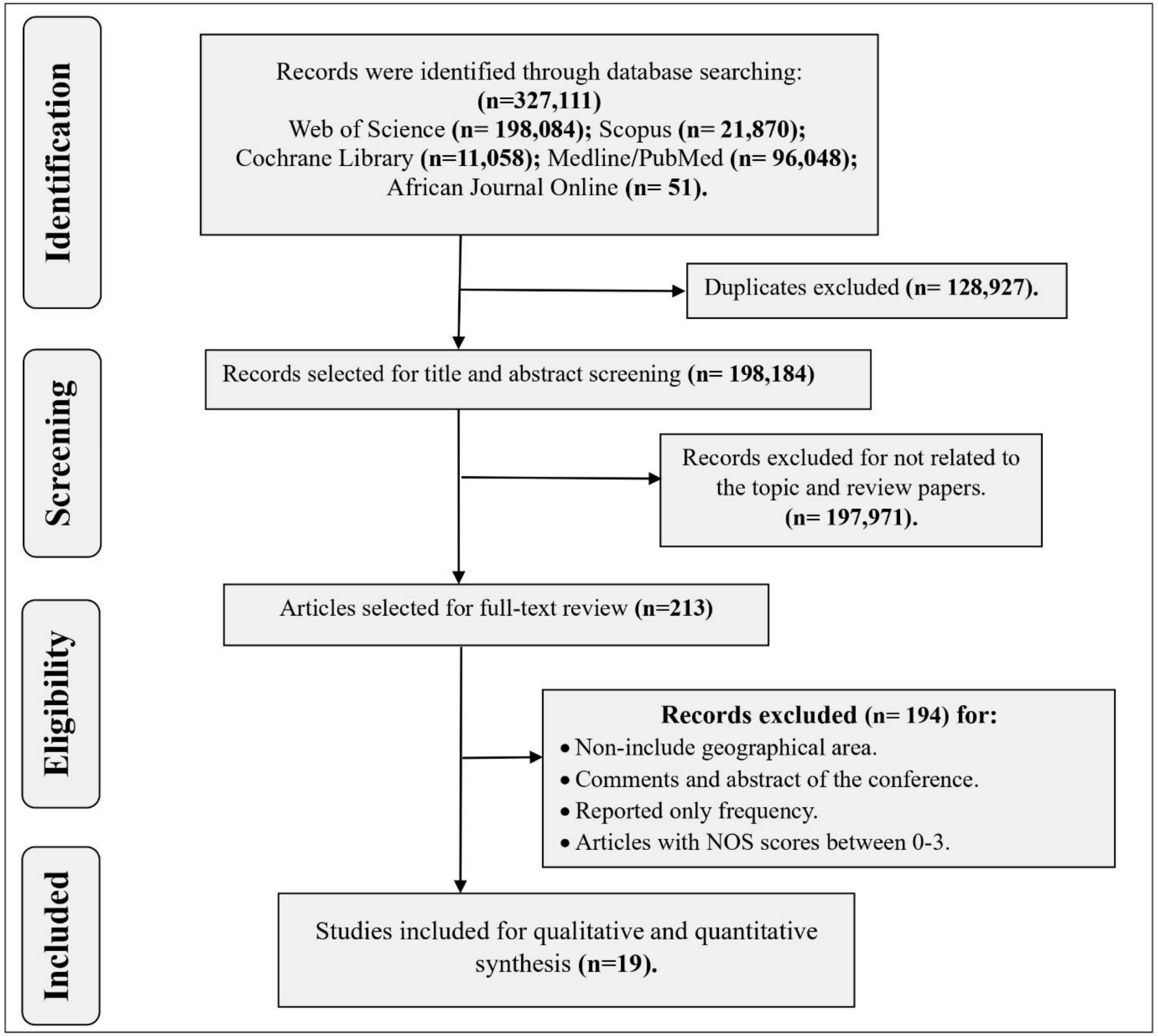


Figure [1]: Schematic flow diagram for the selection of study. N= sample size

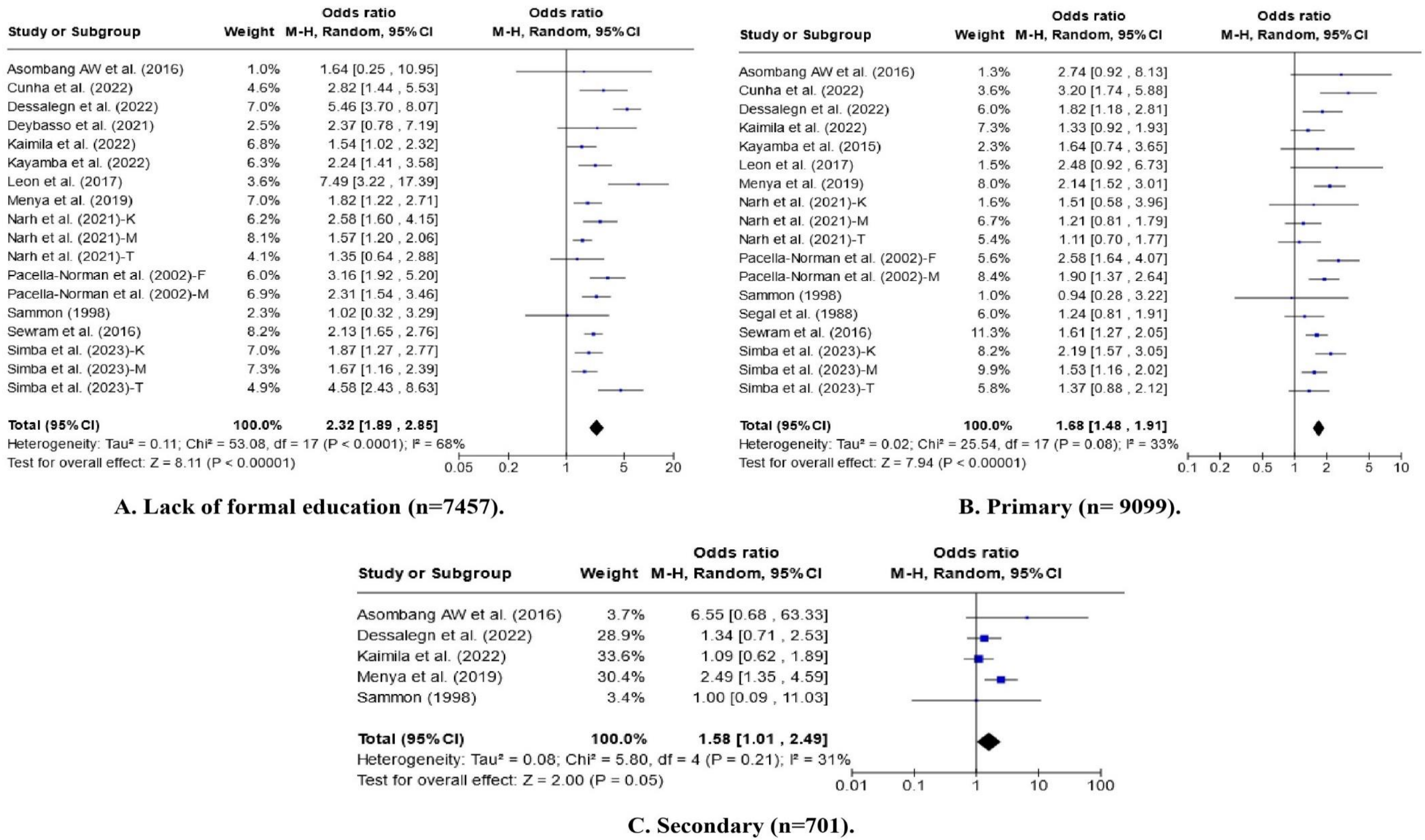
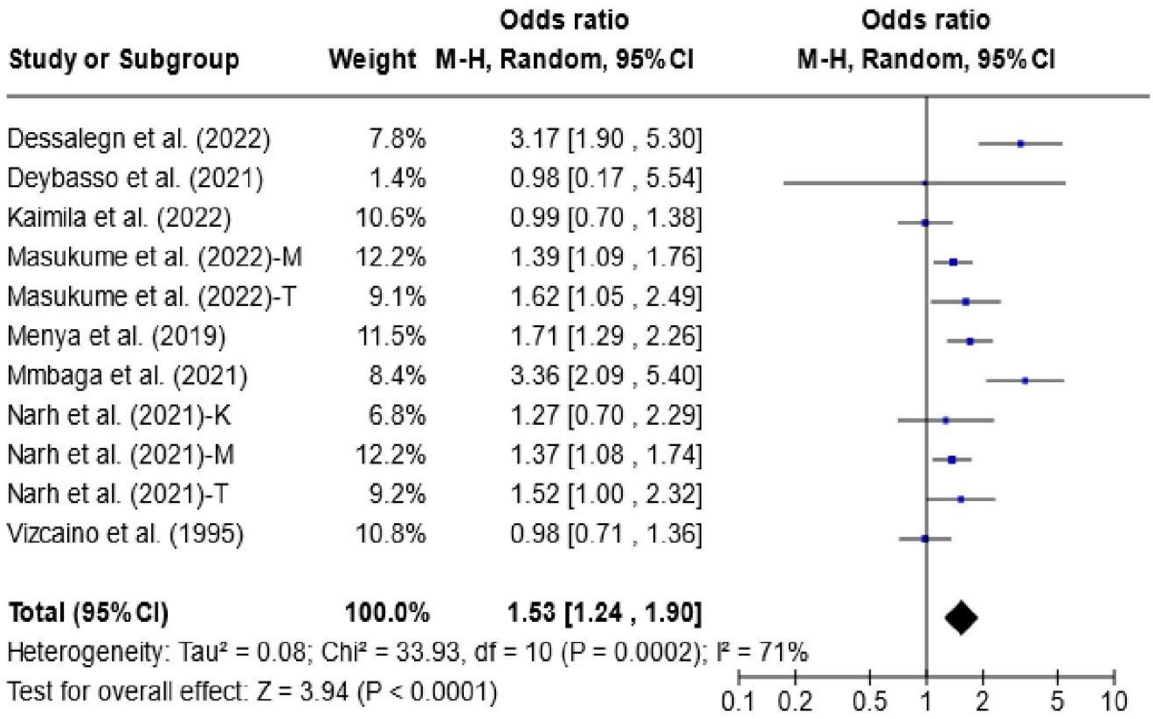


Figure [2]: Forest plot showing the influence of education level on the incidence of esophageal cancer. N= sample size

A. Farmers (n=7442).



B. Self-employed (n= 1034).

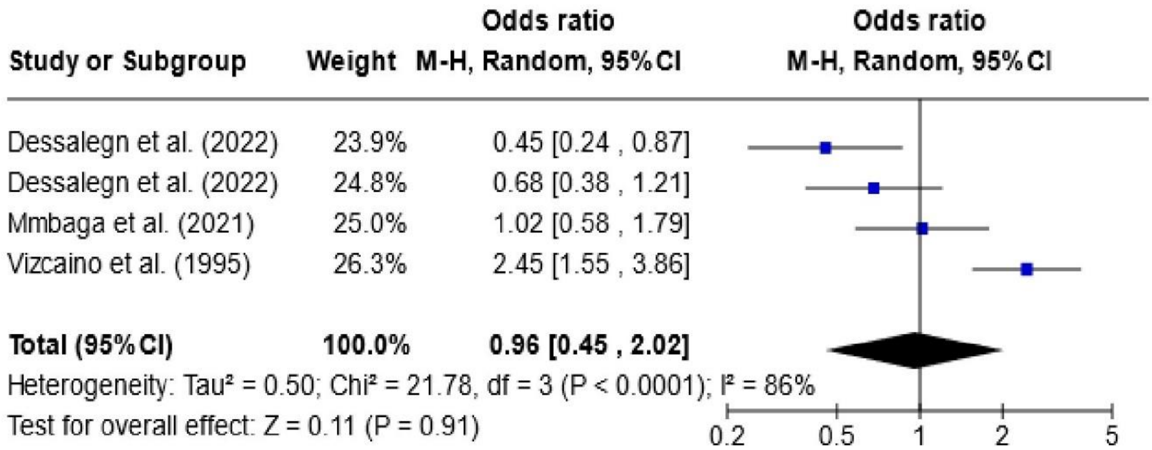


Figure [3]: Forest plot showing the influence of occupation on the incidence of esophageal cancer. N= sample size

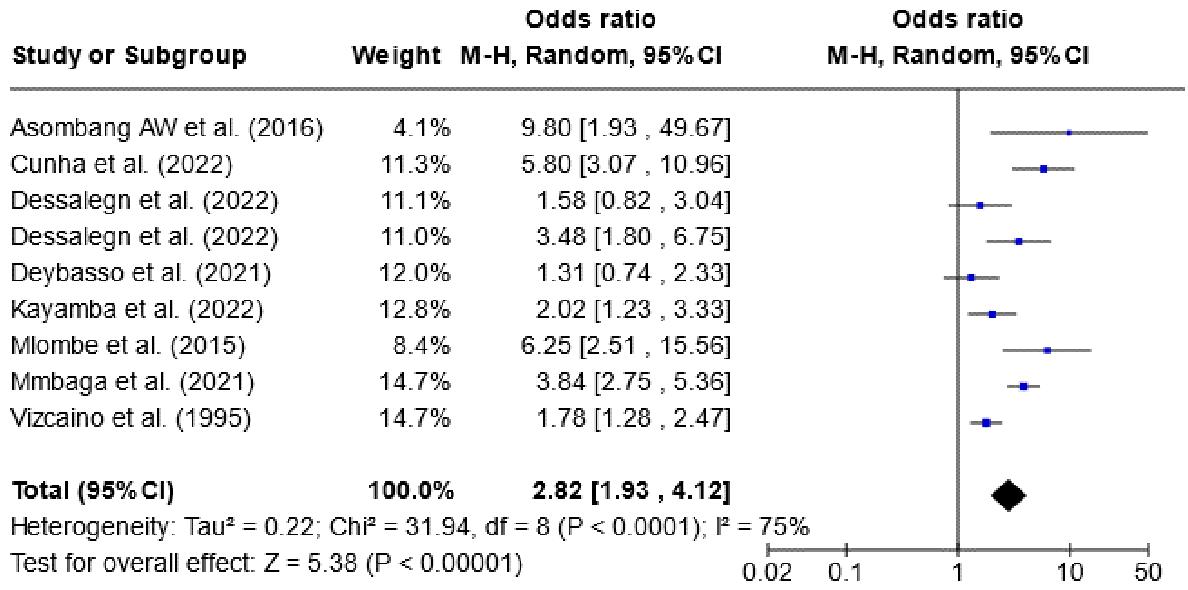


Figure [4]: Forest plot showing the influence of income on the incidence of esophageal cancer. sample size =3169

DISCUSSION

Despite not be often considered as important as environmental factors, individual determinants such as socioeconomic status [SES] play a pivotal role in shaping disease incidence, particularly in the context of cancer [11]. SES is defined by the World Health Organization [WHO] as a composite of life characteristics, encompassing employment, insurance status, education, and income or wages, all of which exert direct and indirect influences on disease development [30, 14]. The East African corridor, housing the world's largest concentration of Esophageal Squamous Cell Carcinoma [ESCC] cases, became the focal point of our work, aiming to elucidate the intricate link between socioeconomic factors and the heightened prevalence of EC in this highly endemic region.

Our meta-analysis underscores a substantial risk of esophageal cancer among individuals with no formal education [OR = 2.32 [95% CI, 1.89 - 2.85]] and those with only primary education [OR = 1.68 [95% CI, 1.48 - 1.91]], compared to their counterparts with secondary and higher education. These findings align with studies on stomach and breast cancers by **Vathesatogkit *et al.*** [48] and **Taheri *et al.*** [14], respectively. The observed association may be attributed to the limited access to decent employment opportunities for individuals with lower education levels, often leading them to engage in occupations such as farming, where exposure to chemical carcinogens is heightened, including pesticides.

Our study also reveals a significant correlation between occupation and the risk of esophageal cancer, with farmers facing a notably elevated risk [OR = 1.53 [95% CI, 1.24 - 1.90]] compared to individuals employed in other sectors. The agricultural environment exposes workers to various carcinogens such as Polycyclic Aromatic Hydrocarbons [PAHs] from organic material combustion, N-nitroso compounds [NNCs] from stomachs of large mammals, and pesticides, all implicated in esophageal cancer [49-51].

Furthermore, our investigation indicates a close association between education, occupation, and income. Individuals with lower incomes face a higher risk of esophageal cancer compared to those with higher incomes. This can be attributed to the tendency, particularly in the African context, for lower-income individuals to opt for locally-produced products with questionable manufacturing processes, including traditional alcoholic beverages and tobacco products. The unknown composition of these products exposes individuals to higher levels of carcinogens compared to commercially manufactured alternatives. Additionally, higher-income individuals tend to seek medical attention promptly, contributing to earlier cancer diagnosis compared to their lower-income counterparts, often diagnosed in advanced stages.

Global comparisons and subgroup analyses reveal significant heterogeneity among the studies. Variances in education, income, and employment status, leading to differing exposures to carcinogens, likely contribute to this heterogeneity. Additionally, variations in population characteristics, cancer stage [38], like comorbidities [52], lifestyles such as alcohol, dietary habits, and others [46, 10], and socioeconomic statuses such as income, education, and occupation [35] and geographical area [24], may also contribute to the observed heterogeneity.

In summary, individuals with higher SES tend to be better informed and equipped to navigate esophageal cancer risks, thereby reducing their vulnerability. This study underscores the imperative for African governments to prioritize the protection of vulnerable populations, emphasizing the promotion of tools that foster common well-being, such as accessible education and decent employment opportunities for all. This call to action aligns with efforts to address health disparities and improve overall societal health outcomes.

Limitations: Several limitations were encountered in the execution of this study. Primarily, the inherent risks of confounding and bias are nearly unavoidable in observational studies. The reliance on observational designs introduces potential sources of bias, limiting the ability to establish causal relationships definitively. Furthermore, despite all the studies addressing the relationship between socioeconomic status [SES] and esophageal cancer [EC] risk originating from East and Southern Africa, the limited number of studies per country impeded a comprehensive stratified assessment by countries. This limitation restricts the broader generalizability of our findings and emphasizes the need for more extensive research coverage in each specific region.

Moreover, the relatively modest size of the study population posed constraints on the precision of our risk assessments. A larger and more diverse population would enhance the robustness of our findings and allow for more nuanced subgroup analyses. Additionally, the absence of a clear correlation between levels of education and employment, as well as between employment and income in the included studies, limits a more nuanced understanding of the strength of the association between SES and the incidence of EC. Future studies with more detailed data on the interplay between these socioeconomic factors would provide a more comprehensive insight into their collective impact on esophageal cancer risk.

Despite these limitations, it is our contention that acknowledging and addressing these challenges represents a critical step toward refining the understanding of SES and its intricate links with esophageal cancer. A more nuanced investigation, considering the complexities of socioeconomic factors, would significantly contribute to the advancement of knowledge in this field.

Conclusions: In summary, this systematic review and meta-analysis illuminate an inverse association between esophageal cancer incidence and educational attainment, income, and occupation in high-endemic areas of Africa. Notably, individuals engaged in farming occupations face a significantly greater risk. While the limitations underline the cautious interpretation of our findings, they also highlight the imperative for further research refinement. The overarching conclusion remains that esophageal cancer is intricately linked to socioeconomic disparities. As health transcends being an option to become a priority, governments must prioritize equitable access to education and decent work for all citizens. Addressing these socioeconomic determinants is paramount to mitigating the incidence of esophageal cancer in the East African corridor. This study provides valuable insights that can inform targeted interventions and policy decisions aimed at reducing health disparities in this vulnerable population.

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