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Incidence and risk factors for colorectal cancer in Africa: a systematic review and meta-analysis

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Abstract

Introduction Colorectal cancer (CRC) is the second leading cause of cancer-related death worldwide. There is a significant burden of mortality from colorectal cancer in Africa. Due to the heterogeneity of dietary and lifestyle practices throughout Africa, our work sought to define risk factors for the development of CRC in the African continent.

Methods We systematically searched PubMed, Embase, Global Health, CINAHL, Cochrane CENTRAL, and African Index Medicus for studies written in English, examining the incidence and risk factors of CRC in Africa. A systematic analysis was done to compare different risk factors in constituent studies. A meta-analysis random effects model was fitted to estimate the pooled incidence of CRC.

Results Of 2471 studies screened, 26 were included for the quantitative analysis; 20 in the incidence analysis, and six in the risk factor analysis. The overall ASIR per 100,000 person-years of CRC for males and females was 7.51 and 6.22, respectively. The highest incidence rates were observed between 2012 and 2021. Risk factors for CRC in Africa include tobacco smoking, and consumption of red meat, butter, and alcohol. Protective factors included, regular consumption of fruits and regular physical activity.

Conclusion The incidence of CRC in Africa is higher than that suggested by previous studies. Our study shows that nonmodifiable and modifiable factors contribute to CRC in Africa. High-quality studies conducted on generalizable populations that examine risk factors in a comprehensive fashion are required to inform primary and secondary prevention initiatives for CRC in Africa.

Keywords Colon, Rectum, Cancer, Risk factors, Africa, Incidence, Prevention

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Introduction

Colorectal cancer (CRC) is the third most common cancer and the second leading cause of cancer-related death worldwide. [1] In 2020, there were an estimated 1.93 million newly diagnosed CRC cases and 0.94 million associated deaths, representing 10% of global cancer incidence and 9.4% of cancer-related deaths. [2, 3] Although the incidence rate of CRC is higher in developed countries, it is also rapidly increasing in middle and low-income countries. Within the African continent, there is regional variation in the incidence of CRC, with higher rates reported in the Northern and Eastern African regions compared with Western and Southern regions. [4] Although colorectal cancer was previously thought to be associated with aging, recent studies in Africa have reported an increasing incidence among the younger population. [5–7] This increasing trend of early-onset colorectal cancer has been similar to the rest of the globe including Western Europe, Australia, Brazil, Canada, Korea, and the United Kingdom. [8] Estimates of colorectal cancer incidence in Africa are still not representative of the actual burden of the disease, mainly due to a lack of adequate infrastructure to diagnose patients with CRC, and a lack of population-based cancer registries. [4, 5] While the majority of colorectal cancers are sporadic, studies have suggested that hereditary factors may be predominant in Africa due to approximately 25% of affected individuals being diagnosed under the age of 40 years. [9, 10] Due to conflicting data published on CRC incidence and risk factors in Africa we conducted a systematic review and meta-analysis, aimed at estimating the true incidence and identifying risk factors associated with colorectal cancer in Africa.

Materials and methods

Literature search, eligibility criteria, and screening

This systematic review is reported in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) standard. [11]

We systematically searched PubMed, Embase, Global Health, CINAHL, Cochrane CENTRAL, and African Index Medicus databases from inception to August 31, 2021 with a search strategy that was developed by K.S, a research librarian at Brown University. The search strategy was inclusive of controlled subject headings (MeSH, Emtree) and text words in title/abstract fields. The full search strategy is provided in the Supplementary Table 1. All studies identified from the search were de-duplicated using EndNote and later uploaded into Covidence for screening. Dual-blind screening was conducted using Covidence, by NNT, EFP, ADA, KB, ESC, SCE, and CA. Conflicts were resolved by MM, MFM, and AWA.

To be eligible for inclusion, studies had to be reported in English, conducted on humans, and reported quantitative estimates of the incidence and risk factors of CRC in Africa. Review articles, meta-analyses, commentaries, case reports, abstracts, and letters to editors were excluded. Reference lists of the included articles and studies that cited the included articles were examined for potential inclusion by N.N.T.

Data extraction and analysis

The eligible studies had data extracted for the country, year of publication, mean age of study participants, sex, age-standardized incidence rate (ASIR), risk factors, odds ratios, study design, and sample size. We also collected data on the demographic, dietary, lifestyle, and behavioral risk factors for colorectal cancer. These variables were reviewed by the authors, prior to developing a data extraction template in Covidence. Meta-analysis was performed using a random effects model with the DerSimonian Laird method to measure raw proportions to estimate a pooled ASIR and their respective 95% confidence interval (CI). We also used DerSimonian and Laird random-effect models to calculate pooled ORs for risk factors that were examined in at least 3 studies. Our preference for a random effects model was informed by the model's ability to incorporate both within-study and between-study variability arising due to differences in study sizes, settings, and methods used over time to diagnose CRC. Data analysis was implemented in STATA 17. Studies not suitable for the meta-analysis (i.e. risk factor reported in less than three studies) were analyzed through a systematic review.

To understand possible causes of heterogeneity, we further stratified the data by period of study (i.e., 1976–1988, 1990–2000, 2001–2010, and 2012–2021) and Africa subregion (i.e., North, West, East, Central and Southern) to produce period and regional-specific estimates. Heterogeneity between studies was assessed using Higgins' index - a measure with ranges between 0% and 100%, and quantifies the proportion of inter-study variability that can be attributed to heterogeneity rather than chance ($I2 > 50\%$ was considered high heterogeneity). The Cochran's Q test was used to determine whether there were differences between primary studies or if the variation seen was due to chance [12]. Publication bias was assessed using the Rosenthal approach to the Fail-safe N (file draw analysis), with Egger's regression asymmetry test (ERAT), and Kendall's Tau test (KTT) for rank correlation test for funnel plot asymmetry [13].

Study quality was measured using the Newcastle-Ottawa Scale (NOS), a validated tool for assessing quantitative cross-sectional, case-control, and cohort studies. Scores of 7 to the maximum score of 9 were defined as high quality, scores of 4–6 as intermediate quality, and scores of 1–3 as low quality [14, 15].

Results

Study characteristics

Of the 26 studies retained after screening and full-text review (Fig. 1, Supplementary Table 1), 20 studies had ASIR reported but no risk factors whereas, six reported factors associated with colorectal cancer but had no estimates of ASIR. These studies covered a total of 17 African countries −8(30.8%), 7(23.3%), 7(23.3%), and 4(13.3%), from North Africa, Southern, East Africa, and West Africa, respectively.

Incidence

Twenty studies reported the incidence of colorectal cancer [16–34] (Supplementary Table 2). The overall ASIR of CRC was 7.51 cases (95% CI: 5.90–9.12) per 100,000 population in males (Figs. 2) and 6.22 cases (95% CI: 4.87–7.58) per 100,000 population in females (Fig. 3).

By African subregions, the highest pooled ASIRs of CRC in men were reported in Northern Africa [9.66 (95% CI: 4.99–14.33) per 100,000 population] and Southern Africa [8.44 (95% CI: 4.80–12.09) per 100,000]. The lowest was reported in Eastern Africa [6.24 (95% CI: 4.38–8.10) per 100,000 population] and West Africa [3.78 (95% CI: 1.64–5.91) per 100,000] (Fig. 2). Similarly, in females, the highest pooled ASIRs of CRC were reported in Northern Africa [8.40 (95% CI: 4.62–12.18) per 100,000] and in Southern Africa [7.00 (95% CI: 3.96–10.03) per 100,000], and the lowest were in Eastern Africa [5.29 (95% CI: 3.84–6.73) per 100,000], and West Africa [2.08 (95% CI: 0.41–3.74) per 100,000 person-years] (Fig. 3).

Stratification on time period of study revealed that the male-specific ASIR was highest for studies conducted during 2012–2021 and lowest for studies conducted during 2000–2010 (Fig. 4). Similarly, ASIRs in females were highest during 2012–2021 and lowest in 2000–2010 (Fig. 5).

Risk factors

Six studies reported quantitative data estimating the association between several demographic, dietary, and lifestyle factors, and the development of CRC [35–40] (Supplementary Table 3).

Demographics

Two studies examined the association of demographic factors with the development of CRC in Africa [35, 36]. Both studies were case-control studies. In one study in Tunisia, the authors revealed a significant association between female gender and colorectal cancer (OR=2.20; 95% CI: 1.16–4.2) [35]. *Negrechi and Taleb* in Algeria found significant associations between CRC and a history of any cancer in first-degree relatives (OR=2.46; 95% CI: 1.50–4.05) and second-degree or third-degree relatives

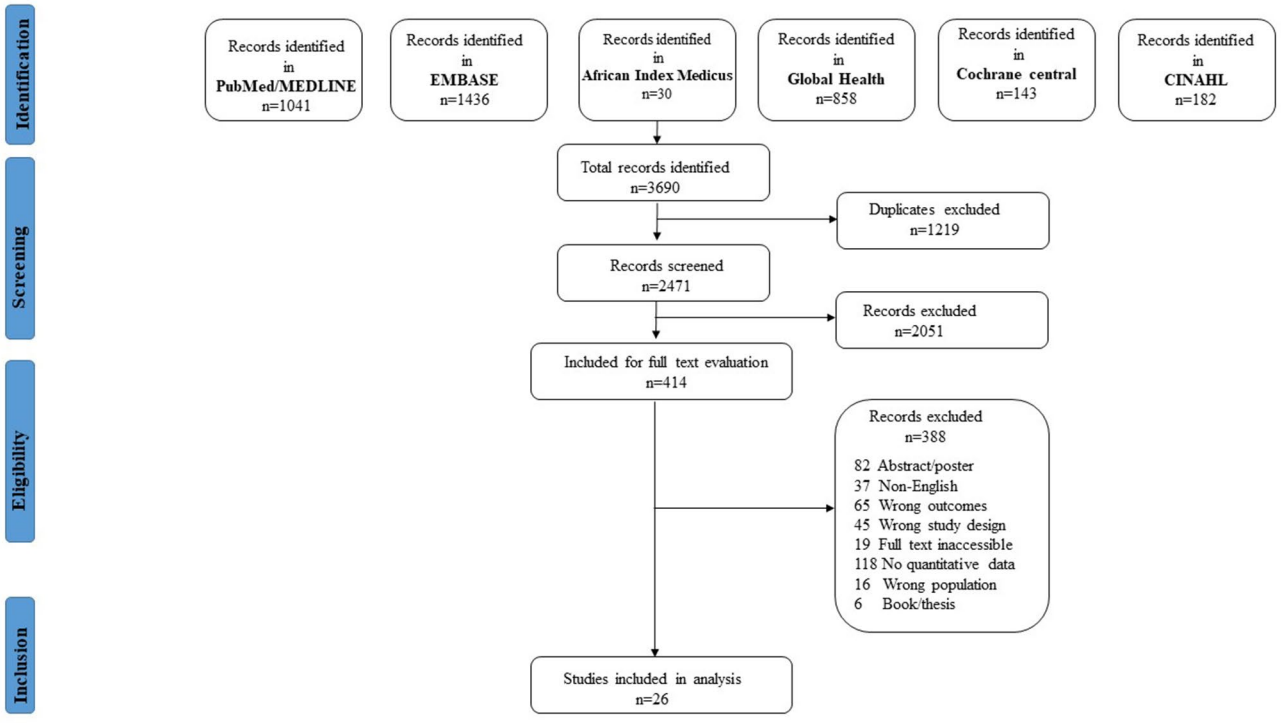

Fig. 1 PRISMA flow diagram for systematic literature review of age-standardized incidence rates (per 100000 population), and association of demographic, comorbidities, dietary, type of lifestyle, and family history risk factors for colorectal cancer in Africa, year 1967–2021. Abbreviations: PRISMA – Preferred Reporting Items for Systematic Reviews and Meta-Analyses

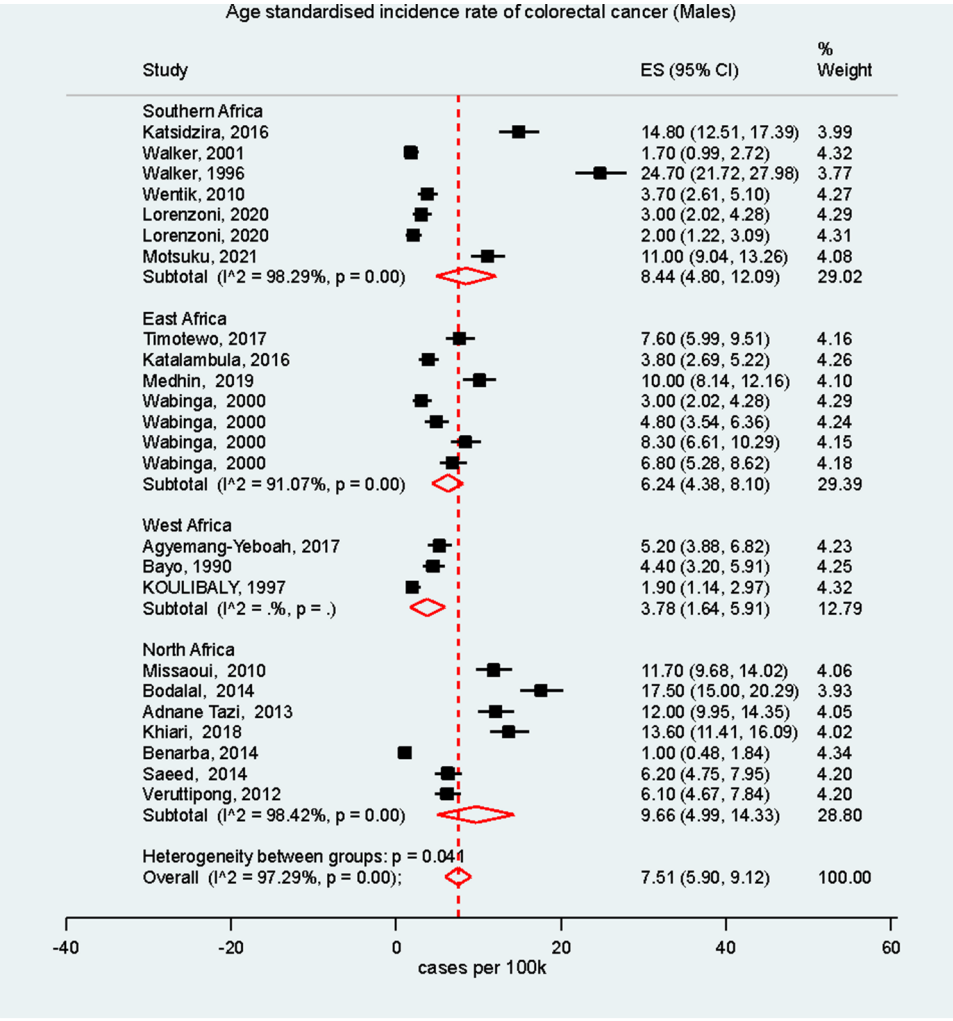

Fig. 2 Age-standardized incidence rates (ASIR) per 100,000 persons of colorectal cancer among males in Africa, year 1990-2021

(OR=2.50; 95% CI: 1.61–3.90), a family history of CRC in first-degree relatives (OR=7.45; 95% CI: 1.67–.

33.23) and second-degree or third-degree relatives (OR=4.94; 95% CI: 1.39–17.47) [36].

Dietary factors

All six included studies examined the association between diet and the development of CRC. The associations with the development of CRC for dietary factors that were examined in at least 3 studies are displayed in Figs. 6 and 7.

Regular intake of fruits was significantly associated with lower odds of developing CRC (pooled OR=0.19 95% CI: 0.04–0.87). On the other hand, high butter intake was associated with higher odds of developing CRC (pooled OR=2.42, 95% CI: 1.22–4.81). Regular intake of red meat (pooled OR=1.87; 95% CI: 0.52–6.72), vegetable (pooled OR=0.44; 95% CI, 0.14–1.42), yogurt (pooled OR=0.73, 95% CI: 0.53-1.00) and fish (pooled OR=0.86; 95% CI, 0.36–2.08) were not significantly associated with the risk of CRC. There was considerable heterogeneity among estimates for frequent red meat, vegetables, fruits, and fish consumption (I>60%), meanwhile, there was minimal heterogeneity among risk estimates for butter and yogurt consumption (<60%). Two studies examined the relationship of processed meat with the development of CRC; one study observed a higher risk [37], and the other reported no difference [38]. Similarly, two studies examined the relationship of regular coffee consumption with the development of CRC; one study observed a lower risk [40], and the other reported no difference [38].

Lifestyle factors

Five studies examined the association of lifestyle or occupational factors with the development of CRC. The associations with CRC for lifestyle factors examined in at least 3 studies are displayed in Fig. 8. Alcohol (pooled OR 2.38; 95% CI, 1.26–4.49) and tobacco consumption (pooled OR 2.27; 95% CI, 1.59–3.42) were significantly associated with higher odds of developing CRC.

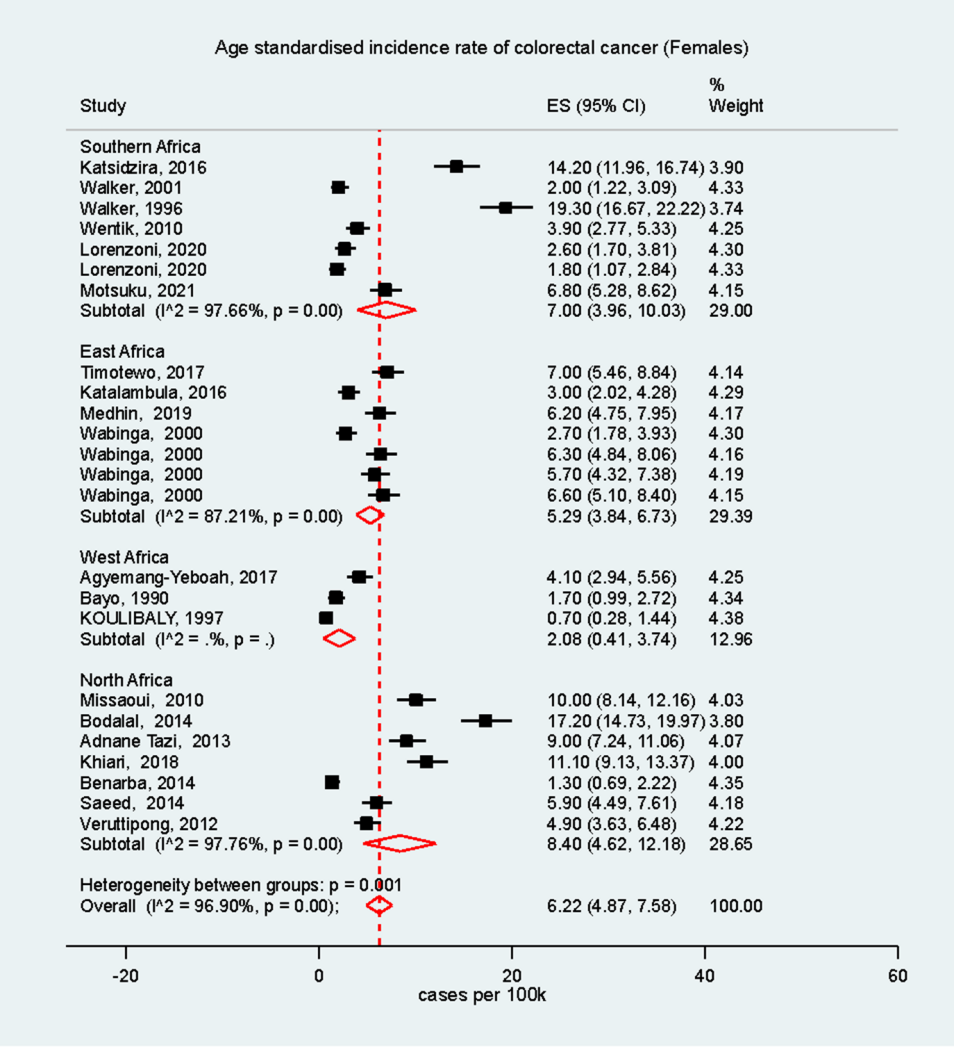

Fig. 3 Age-standardized incidence rates (ASIR) per 100,000 persons of colorectal cancer among females in Africa, year 1990-2021

Regular physical activity was significantly associated with lower odds of developing CRC (pooled OR 0.12; 95% CI: 0.02–0.65). There was considerable heterogeneity among estimates for frequent alcohol, tobacco smoking, and physical activity (I>60%).

Two studies examined the relationship between regular intake of soft drinks and the onset of CRC; both studies observed significantly higher odds of CRC [36, 37].

Assessment of bias

Our analysis showed possible publication bias for estimated pooled ASIR for both males (P-value<0.000q) and females (P-value<0.0001). The ERAT and KTT for rank correlation test for funnel plot asymmetry didn't find any asymmetry due to the publication bias for overall ASIR rate (p-value=0.24083 and 0.82364, respectively), and male ASIR (p-value=0.00952 and 0.09587), Eastern ASIR (p-value=0.30931 and 0.91946).

Discussion

This paper provides a comprehensive analysis of the incidence rate and risk factors of CRC in Africa. According to our analysis, the estimated annual ASIR of CRC was 7.51 per 100,000 person-years in males and 6.22 per 100,000 person-years in females. This is comparable to the GLOBOCAN ASIR of 9.1 per 100,000 person-years in males and 7.5 per 100,000 person-years in females [41]. Our regional analysis of ASIR per 100,000 person-years of CRC in males showed the highest incidence in North Africa (9.66/100,000 person-years), followed by Southern Africa (8.44/100,000 person-years) and East Africa (6.24/100,000 person-years). In females, we observed a similar pattern of ASIRs with the highest rates in Northern and Southern Africa. In this study, West Africa had the lowest pooled ASIRs in both genders. There are significant similarities in our results when compared to GLOBOCAN data which shows the highest rates in Southern and Northern Africa and the

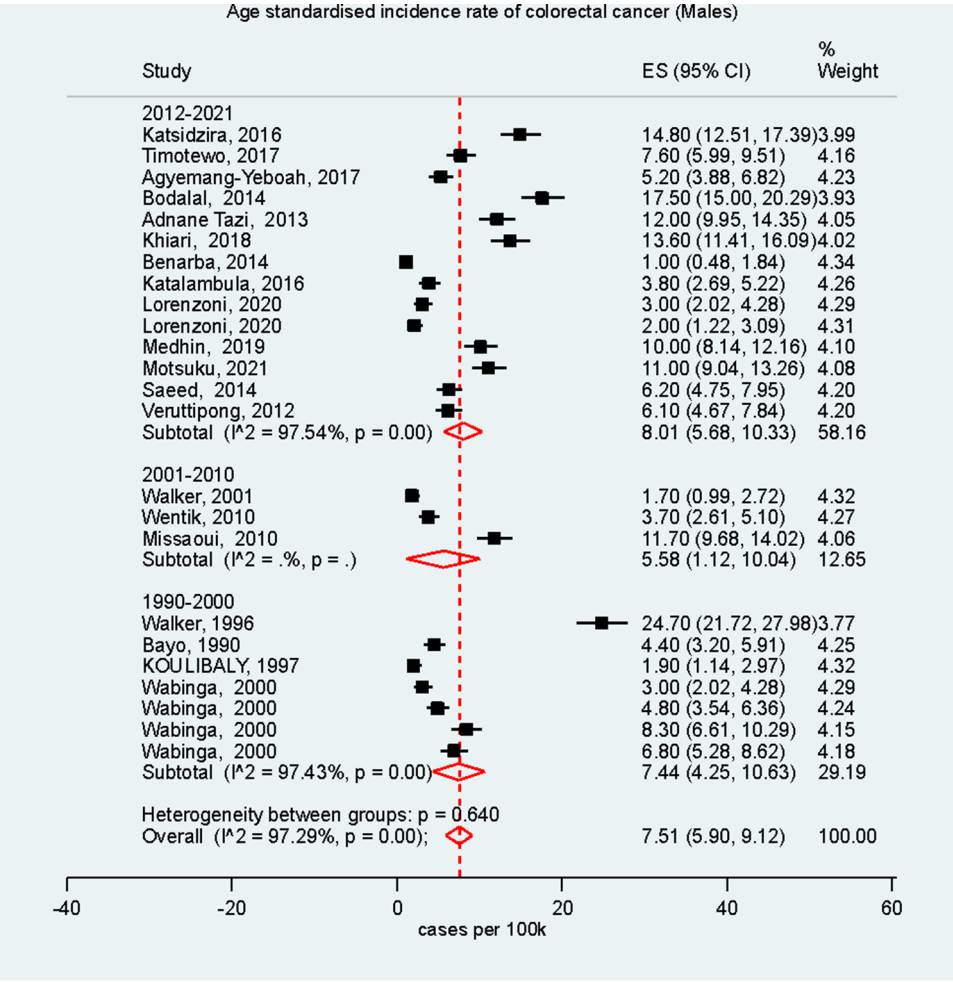

Fig. 4 Age-standardized incidence rates (ASIR) per 100,000 persons of colorectal cancer among males in Africa by decades

lowest ASIRs in Western Africa. Reasons for observed differences in regional ASIR may include the differences in sources of data and the variations in regional publication volume, as our study showed that incidence rates were higher in regions with greater numbers of included studies. On evaluating ASIRs by decades, our finding that incidence rates are highest in the most recent decade adds evidence to the recent studies that suggest a rapidly rising incidence of CRC in Africa [42, 43]. In Africa, the rising incidence of CRC has been attributed to population growth, aging, changing risk factors such as westernization of the African diet, increasing diagnosis, and registration of colorectal cancer cases through population-based cancer registries [44–46]. Despite this, epidemiological measures of colorectal cancer throughout the African continent are still highly heterogeneous and non-representative, and less than 30% of African nations have functional national cancer-based registries [10, 47]. In the absence of CRC screening programs in most African countries, most of the currently available data on CRC incidence come from patients with advanced disease. The direct relationship between regional publication volume and incidence of CRC in Africa further suggests that countries with more diagnostic capacity, cancer registries, and/or research output are more likely to report a higher incidence of CRC than other regions.

In this study, we identified several potential risk factors that could be used for primary and secondary prevention of CRC in Africa and should be investigated in future longitudinal studies.

A family history of any cancer was associated with CRC in one study [36]. This might point toward a shared genetic linkage between CRC and several other malignancies. It might also be due to shared environmental and lifestyle risk factors. Similarly, a study conducted among African Americans showed that people with a family history of other cancers such as breast cancer and other gastrointestinal malignancies had a higher risk of developing CRC [48]. Screening based on a family history of CRC has become an important strategy for early detection and prevention of CRC; however, only one study has reported the association between a family history of CRC

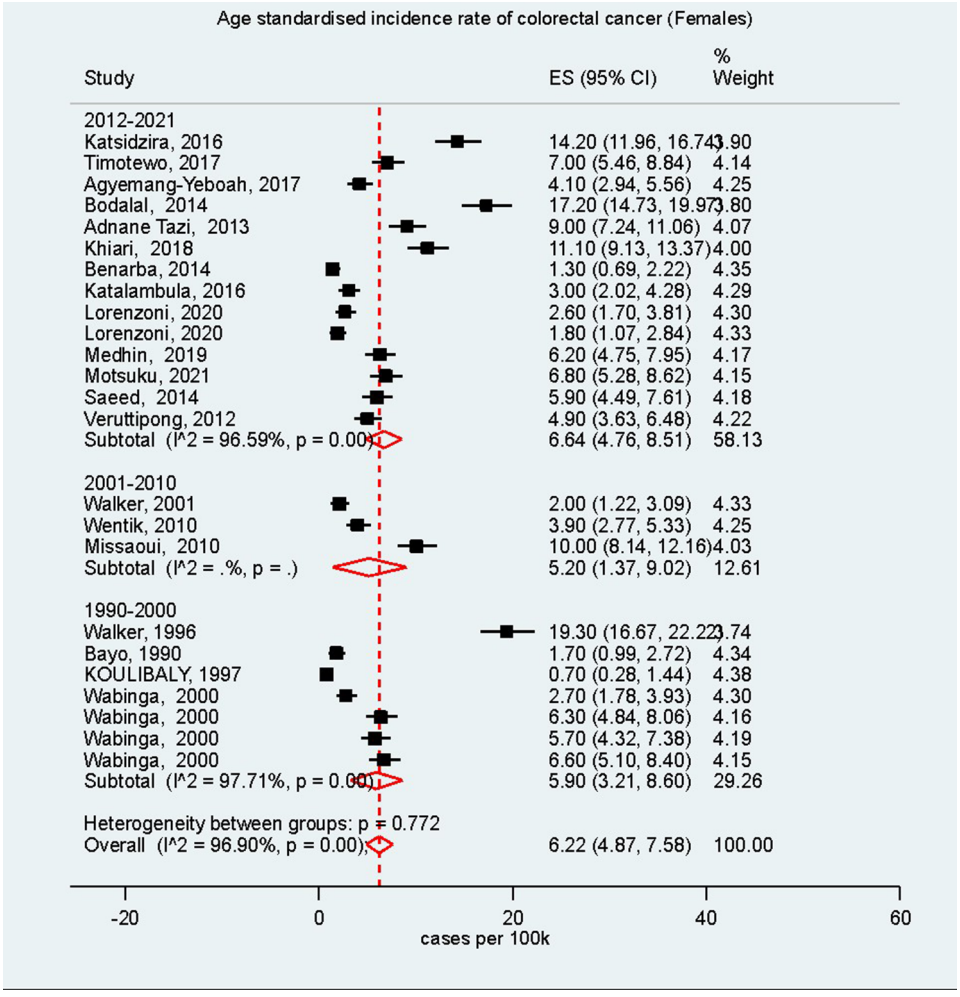

Fig. 5 Age-standardized incidence rates (ASIR) per 100,000 persons of colorectal cancer among females in Africa by decade

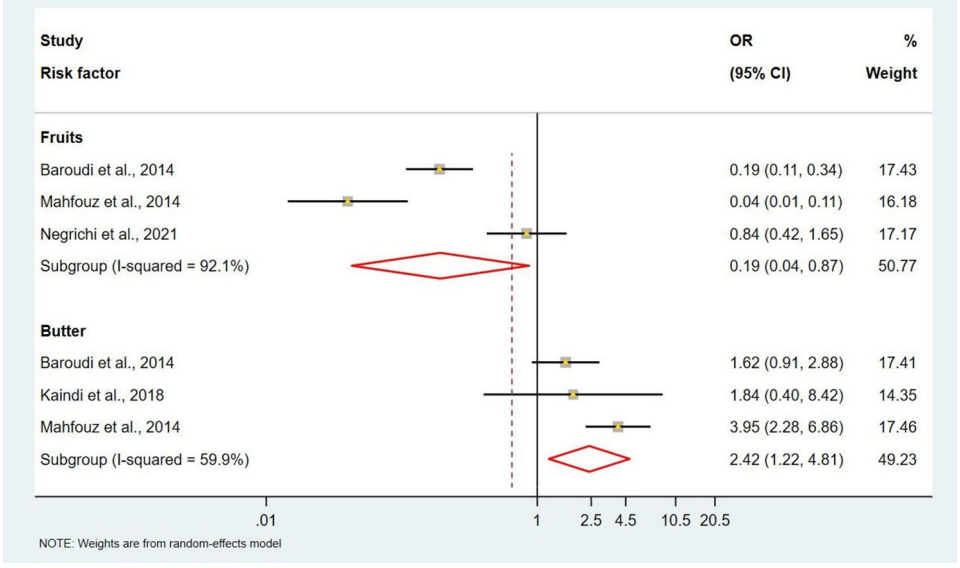

Fig. 6 Estimated odds ratio of developing colorectal cancer associated with regular consumption of butter and fruits. DL, DerSimonian-Laird; CI, confidence interval

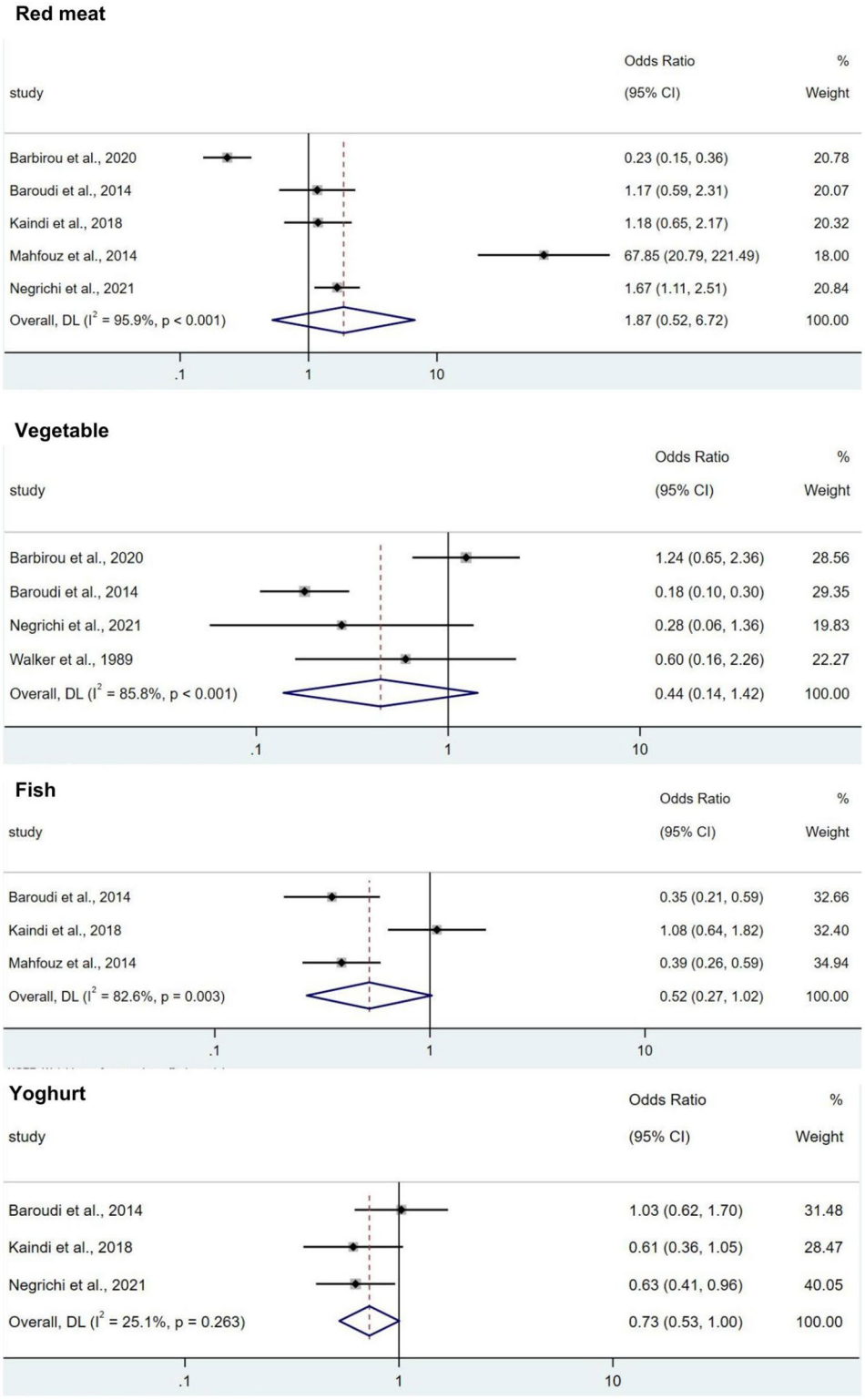

Fig. 7 Estimated odds ratio of developing colorectal cancer associated with regular consumption of red meat, vegetables, fish, and yogurt. DL, DerSimonian-Laird; CI, confidence interval

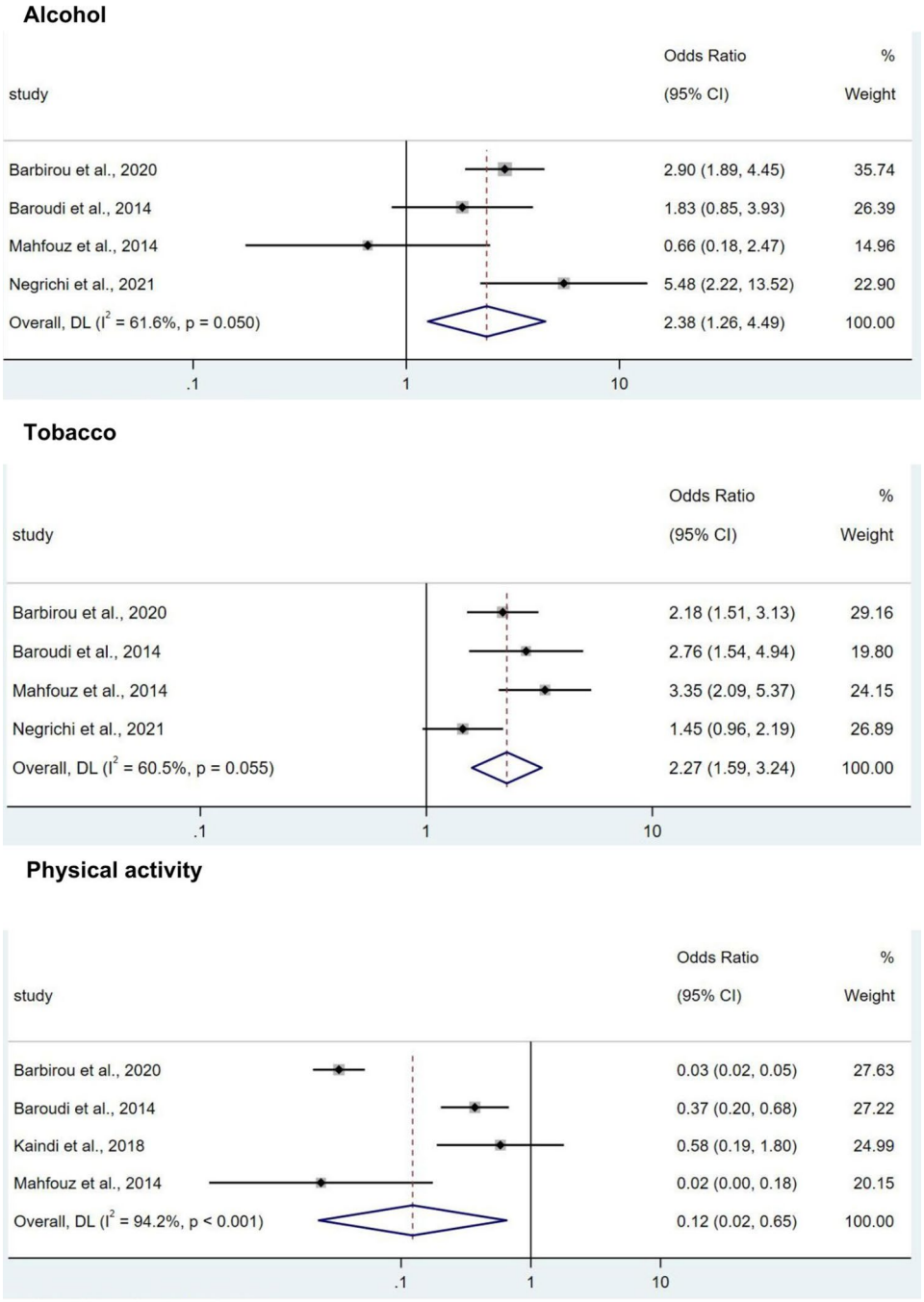

Fig. 8 Estimated odds ratio of developing colorectal cancer associated with alcohol consumption, tobacco smoking, and physical activity. DL, DerSimonian-Laird; CI, confidence interval

and the development of CRC in Africa. [36, 49] *Negrichi et al.* observed an increased risk of CRC associated with a family history of CRC in first, second, and third-degree relatives [36]. To estimate the true association between a family history of CRC and the development of CRC in Africa more studies need to be conducted with family history as a predictor variable.

Red meat and processed meat have been classified by the International Agency for Research on Cancer as probably carcinogenic (Group 2 A) and carcinogenic to humans, respectively [50]. Our study findings suggest that patients who consume red and processed meat in Africa more likely to develop CRC. However, more studies are needed to examine the relationship of different types of meat, methods of processing and quantity

of consumption with the development of CRC. Several studies have hypothesized a protective effect of a high-fiber diet on colon carcinogenesis. [51, 52] In this study, we found that consumption of foods rich in fiber such as fruits and vegetables was associated with a decreased risk of CRC. Our study suggests that adherence to diets rich in fiber can help prevent CRC.

Alcohol consumption and smoking are established risk factors for many types of cancers and have both been shown to increase the risk of CRC in a dose-dependent manner. [53] Similarly, our study demonstrated an increased risk of CRC associated with alcohol consumption and smoking. However, no studies from the African continent has investigated the effect of dose and duration of tobacco smoking and alcohol consumption on the development of CRC. Having a sedentary lifestyle has also been implicated as a major risk factor for CRC in recent studies. Physical activity is known to improve immune system function, reduce inflammation, reduce stress, optimize metabolic rate, help regulate hormone level and prevent obesity and, as a result, help protect against cancer development [1]. In our review, all studies that investigated the association between regular exercise and CRC reported an inverse relationship, suggesting the benefits of regular exercise in this age of rapidly increasing rates of CRC.

Despite our study providing information on high-risk groups that can be targeted by disease prevention programs, other established risk factors of CRC such as gender, diets low in calcium and vitamin D, diabetes mellitus, inflammatory bowel disease, and gut microbiota were largely underreported in the included studies. In addition, studies that examine non-traditional risk factors, occupational exposures, and exposures that occur early in life are necessary to determine whether there are exposures unique to recent cohorts that are driving the increase of CRC in Africa.

Our study has several limitations. First, we included only studies that were published in English, which makes it possible that some non-English studies might have been omitted. Secondly, despite there being a high degree of heterogeneity in the risk estimates across studies for the majority of risk factors, we were unable to explore sources of this heterogeneity (including differences in study design, study quality, or control for confounding) because of an insufficient number of studies included in each meta-analysis. Furthermore, the majority of included studies were of modest quality, suggesting that the results of this study could be biased and subject to residual confounding. Similarly, our results on incidence should be interpreted cautiously due to the high level of heterogeneity. Third, because a limited number of studies were available to include in each meta-analysis, it was difficult to determine whether publication bias was present with formal methods; therefore, publication bias cannot be ruled out for any of the analyses. Lastly, only 17 out of 54 African countries had publications included in this review. There are several strengths of this study. First, our estimates of ASIR are externally validated when compared to GLOBOCAN data. Secondly, this is one of the largest systematic reviews and meta-analyses of CRC in Africa acknowledging the heterogeneity and regional differences throughout the continent. Thirdly, this is one of the first and most comprehensive analyses of risk factors for the development of colorectal cancer in Africa. Lastly, the DerSimonian and Laird method of random-effects model accounts for the heterogeneity across the included studies.

Conclusion

In conclusion, the incidence of CRC in Africa seems to be on the rise, with the accuracy of estimates being hampered by a lack of screening guidelines, a shortage of diagnostic services, and a shortage of high-quality cancer reporting systems such as population-based cancer registries. A family history of cancer, red meat and processed consumption, alcohol consumption, smoking, and physical activity appear to be significant contributors to CRC in Africa. High-quality studies conducted on generalizable populations that comprehensively examine risk factors for CRC are required to inform initiatives aimed at primary and secondary prevention against CRC in Africa.

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s12876-024-03385-7.

Supplementary Material 1

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Author contributions
A.W.A, M.M, N.N.T, E.F.P, K.S, E.S.C: conception of the study. K.S.: Performed literature search. N.N.T, E.F.P, A.D.A, K.B, E.S.C, S.C.E, C.A: screened the articles and extracted the data. A.W.A, M.M, M.F.M: reviewed conflicts. J.F.G and J.S: analyzed the data. N.N.T, S.C.E, J.S and A.W.A wrote the manuscript. All authors reviewed and approved the manuscript.

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Data availability
The datasets used and/or analyzed during the current study are available from the corresponding author upon reasonable request.

Declarations

Ethics approval and consent to participate
Not applicable.

Consent for publication
Not applicable.

Competing interests
The authors declare no competing interests.

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