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META-ANALYSIS

Consumption of red meat and processed meat and cancer incidence: a systematic review and meta-analysis of prospective studies

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Abstract

Red meat and processed meat consumption has been hypothesized to increase risk of cancer, but the evidence is inconsistent. We performed a systematic review and meta-analysis of prospective studies to summarize the evidence of associations between consumption of red meat (unprocessed), processed meat, and total red and processed meat with the incidence of various cancer types. We searched in MEDLINE and EMBASE databases through December 2020. Using a random-effect meta-analysis, we calculated the pooled relative risk (RR) and 95% confidence intervals (CI) of the highest versus the lowest category of red meat, processed meat, and total red and processed meat consumption in relation to incidence of various cancers. We identified 148 published articles. Red meat consumption was significantly associated with greater risk of breast cancer (RR = 1.09; 95% CI = 1.03–1.15), endometrial cancer (RR = 1.25; 95% CI = 1.01-1.56), colorectal cancer (RR = 1.10; 95% CI = 1.03–1.17), colon cancer (RR = 1.17; 95% CI = 1.09-1.25), rectal cancer (RR = 1.22; 95% CI = 1.01-1.46), lung cancer (RR = 1.26; 95% CI = 1.09–1.44), and hepatocellular carcinoma (RR = 1.22; 95% CI = 1.01-1.46). Processed meat consumption was significantly associated with a 6% greater breast cancer risk, an 18% greater colorectal cancer risk, a 21% greater colon cancer risk, a 22% greater rectal cancer risk, and a 12% greater lung cancer risk. Total red and processed meat consumption was significantly associated with greater risk of colorectal cancer (RR = 1.17; 95% CI = 1.08–1.26), colon cancer (RR = 1.21; 95% CI = 1.09–1.34), rectal cancer (RR = 1.26; 95% CI = 1.09–1.45), lung cancer (RR = 1.20; 95% CI = 1.09-1.33), and renal cell cancer (RR = 1.19; 95% CI = 1.04–1.37). This comprehensive systematic review and meta-analysis study showed that high red meat intake was positively associated with risk of breast cancer, endometrial cancer, colorectal cancer, colon cancer, rectal cancer, lung cancer, and hepatocellular carcinoma, and high processed meat intake was positively associated with risk of breast, colorectal, colon, rectal, and lung cancers. Higher risk of colorectal, colon, rectal, lung, and renal cell cancers were also observed with high total red and processed meat consumption.

Keywords Total red and processed meat · Red meat · Processed meat · Cancer · Meta-analysis

Introduction

Red meat and processed meat as rich sources of saturated fat and heme iron, as well as some carcinogens may be an important dietary risk factors leading to several cancers. Based on the International Agency for Research on Cancer (IARC) Working Group report, red meat (unprocessed) consumption including beef, lamb, veal, pork, mutton, goat, or horse meat may increase risk of colorectal, pancreatic, and prostate cancers, and processed meat including bacon, sausages, salami, hot dogs, or processed turkey may increase risk of colorectal cancer and stomach cancer [1]. However, in pooled analyses of prospective studies, high consumption of red meat or processed meat was not associated with

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risk of overall prostate cancer [2], renal cell cancer [3], or breast cancer [4]. In contrast, meta-analysis of prospective studies showed that processed meat consumption, but not red meat, was associated with higher breast cancer risk [5]. Higher risk of colorectal cancer, not rectal cancer, was reported with high consumption of both red meat and processed meat in a meta-analysis of prospective studies [6]. Zhao et al. reported in a meta-analysis that risk of pancreatic cancer may increase among men with high intake of red meat and processed meat, but not among women [7]. Furthermore, in meta-analyses of prospective studies, high intake of processed meat, but not red meat, was associated with higher risk of overall prostate cancer [8] and stomach cancer [9], and high intake of red meat, but not processed meat, was associated with higher risk of lung cancer [10] and hepatocellular carcinoma [11]. Processed meat intake was significantly associated with higher risk of renal cell cancer in a dose-response meta-analysis, but not in a meta-analysis comparing the highest versus the lowest category of intake [12]. However, in meta-analyses of prospective studies, red meat or processed meat intake was not associated with risk of ovarian cancer [13], endometrial cancer [14], esophageal cancer [15], bladder cancer [16], leukemia, non-Hodgkin lymphoma [17], or glioma [18]. The existing evidence from meta-analyses on red meat as well as processed meat consumption and cancer incidence is mixed and has several limitations, such as the inclusion of case–control studies, use of some identical studies twice, or inclusion of both cancer mortality and incidence in the meta-analyses. Furthermore, some of the meta-analyses needed to be updated by including newly published articles. This study addresses the gaps identified which will help clarify dietary recommendations for cancer prevention as part of an overall healthy lifestyle. In particular, we integrated the prospective studies into our analysis to identify the associations with various types of cancer incidence hypothesized to be related to consumption of red meat, processed meat, and total red and processed meat, using a systematic review and meta-analysis of prospective studies.

Subjects and methods

Study strategy

Design, analysis, and interpretation of findings have been done using the Meta-analysis of Observational Studies in Epidemiology (MOOSE) checklist [19]. Two databases, MEDLINE and EMBASE were used to identify publications of prospective studies that reported the associations of red meat, processed meat, or total red and processed meat, with any type of cancer until December 2020. The search string is presented in Supplementary Table S1. In addition, we searched references of related articles to find other relevant publications. We used the definition of IARC Working Group classification for red meat and processed meat [1]. In order to reduce the influence of recall and selection bias, we only selected prospective studies that evaluated the associations of red meat, processed meat, or total red and processed meat consumption as exposures and breast cancer, ovarian cancer, endometrial cancer, prostate cancer, colorectal cancer, colon cancer, rectal cancer, stomach cancer, esophageal squamous-cell carcinoma, esophageal adenocarcinoma, pancreatic cancer, lung cancer, bladder cancer, renal cell cancer, hepatocellular carcinoma, leukemia, non-Hodgkin lymphoma, melanoma, and glioma as endpoints. Case–control, cross-sectional, and ecological studies were excluded. We also excluded reviews and meeting abstracts. Furthermore, if there were several published papers from the same study population, we used the data reported in the most recent paper with the largest number of cancer cases (Fig. 1).

Data extraction

We summarized the characteristics of selected publications including first author, year of publication, study name, country of the study, design of study, follow up years, the total number of participants, number of cancer events, age at baseline, meat variable definition and method of assessment, amount of intake in the highest and the lowest categories, and covariates adjusted in the multivariable models. The relative risks (RRs) and 95% confidence intervals (CI) for the highest versus the lowest categories of intake were extracted from multivariable models with the highest number of covariates.

Data synthesis

We conducted separate analyses on various cancer sites using three exposure variables: “red meat” “processed meat” and “total red and processed meat.” In this meta-analysis, red meat means only unprocessed red meat; processed meat means processed red meat or other types of meat; and total red and processed meat means the sum of red meat and processed meat. The RRs for the highest versus the lowest category of intake of each exposure were pooled using random-effects models (DerSimonian and Laird method [20]). However, the amounts of intake in the highest and the lowest categories were not consistent across the studies. For one study that did not report the highest versus the lowest category of intake [21], assuming a normal distribution, the RRs and 95% CIs for the highest versus the lowest quintiles were calculated using 2.56 as a conversion factor for a one-standard deviation (SD) increase in total red and processed meat intake. For four studies, the RRs and 95% CIs for the

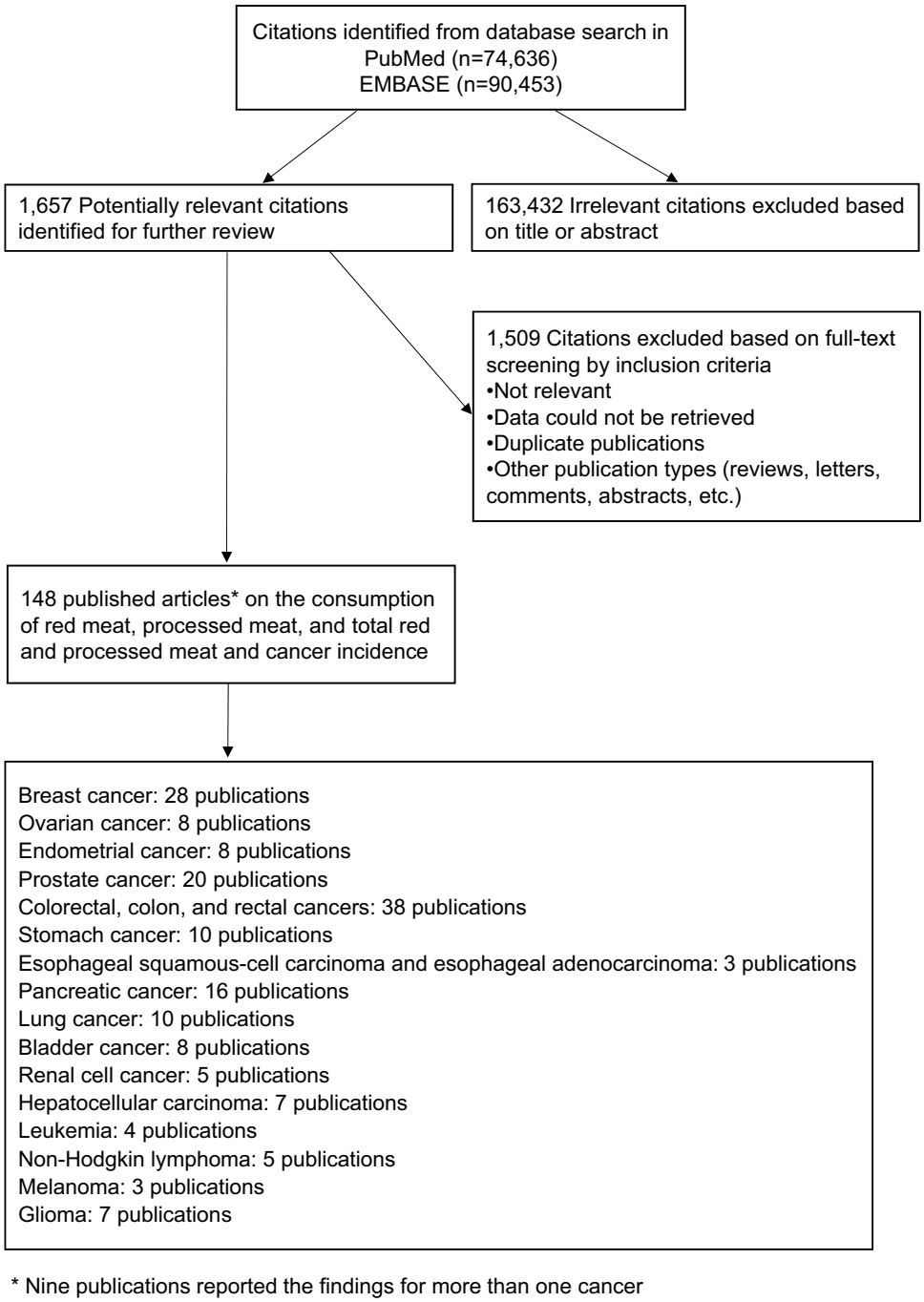

Fig. 1 Search, screening, and selection process of prospective studies of red meat, processed meat, and total red and processed meat intake and risk of cancer

highest versus the lowest quartiles or quintiles of intake have been provided *via* contacting authors [22–25].

We also calculated the RRs and 95% CI for each 100 g per day intake of red meat, and total red and processed meat, and each 50 g per day intake of processed meat in relation to each cancer, if data were available. We were able to do dose–response analyses for studies that reported the associations with exposures of interest as contentious variables or studies with information as follows: risk estimate, 95% CI or standard error, median intake, number of cases, person-years of follow-up or number of participants, for each exposure category. If ranges of intake were reported for each category of intake, we used the midpoint of the lower and upper bound of intake for each category. For an open-ended highest category, the range of amount of intake was estimated using the range of amount of intake in the previous category. For some of the studies, through correspondence with authors, relevant data (RRs and 95% CIs of exposures of interest as continuous variables, number of participants in each category, number of cases in each category, type of

red meat) were provided [23, 24, 26–38]. For studies that reported servings or times per day of intake, we converted them to g per day as follows: one serving or one time per day of red meat (unprocessed) equal to 120 g, one serving or one time per day of processed meat equal to 50 g, and one serving or one time per day of total red and processed meat equal to 100 g [39].

The RRs and 95% CIs for each study were presented using forest plots in the meta-analysis. To evaluate publication bias, we used visual inspection of a funnel plot [40] and the Begg and Mazumdar test [41]. To evaluate potential heterogeneity among studies, we used the I^2 statistic [42]. A two-tailed test at an alpha level of < 0.05 was considered statistically significant. All statistical analyses were conducted using STATA, version 16, software (STATA Corp, College Station, TX).

Results

Study characteristics

We identified 148 publications that examined the associations of red meat, processed meat, and total red and processed meat intake and various sites of cancer in prospective studies: 28 publications for breast cancer [22, 24, 26, 43–67] (Table S2); 8 publications for ovarian cancer [22, 23, 59, 68–72] (Table S3); 8 publications for endometrial cancer [22, 59, 73–78] (Table S4); 20 publications for prostate cancer [27, 28, 46, 59, 60, 62, 79–92] (Table S5); 38 publications for colorectal, colon, and rectal cancers [21, 29, 59, 60, 62, 64, 93–124] (Table S6); 10 publications for stomach cancer [59, 64, 70, 96, 125–130] (Table S7); 3 publications for esophageal squamous-cell carcinoma and esophageal adenocarcinoma [130–132] (Table S8); 16 publications for pancreatic cancer [30–32, 59, 133–144] (Table S9); 10 publications for lung cancer [33, 46, 59, 60, 64, 70, 145–148] (Table S10); 8 publications for bladder cancer [34, 59, 149–154] (Table S11); 5 publications for renal cell cancer [3, 59, 155–157] (Table S12); 7 publications for hepatocellular carcinoma [25, 35, 36, 59, 158–160] (Table S13), 4 publications for leukemia [59, 70, 161, 162] (Table S14), 5 publications for non-Hodgkin lymphoma [59, 163–166] (Table S15), 3 publications for melanoma [37, 59, 70] (Table S16), and 7 publications for glioma [38, 59, 167–171] (Table S17). Nine publications reported the findings for more than one cancer [22, 46, 59, 60, 62, 64, 70, 96, 130]. We did not observe publication bias for the

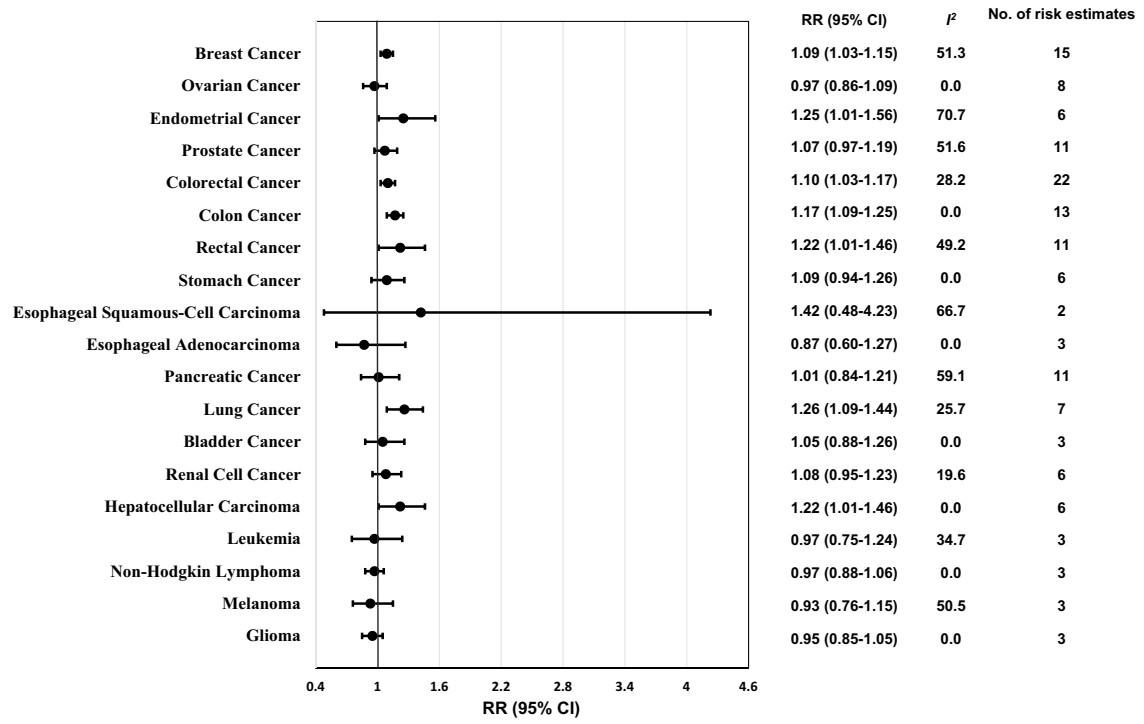

Fig. 2 Pooled relative risks and 95% confidence intervals of various cancer incidence associated with red meat intake (highest category versus lowest category), using random-effect models

associations of red meat, processed meat, or total red and processed meat intake with various sites of cancer, using visual inspection of a funnel plot or Begg and Mazumdar test (Fig. S1–S3).

Red meat (unprocessed) intake and cancer risk

The random-effects summary of RRs comparing the highest versus the lowest category of red meat intake and various cancer types are presented in Fig. 2. Red meat consumption was associated with increased breast cancer, endometrial cancer, colorectal cancer, colon cancer, rectal cancer, lung cancer, and hepatocellular carcinoma risk. The pooled RR comparing the highest versus the lowest category of red meat intake was 1.09 (95% CI = 1.03-1.15; $I^2 = 51.3\%$; 15 risk estimates) for breast cancer (Fig. S4), 1.25 (95% CI = 1.01-1.56; $I^2 = 70.7\%$; 6 risk estimates) for endometrial cancer (Fig. S6), 1.10 (95% CI = 1.03–1.17; $I^2 = 28.2\%$; 22 risk estimates) for colorectal cancer (Fig. S8), 1.17 (95% CI = 1.09-1.25; $I^2 = 0.0\%$; 13 risk estimates) for colon cancer (Fig. S9), 1.22 (95% CI = 1.01-1.46; $I^2 = 49.2\%$; 11 risk estimates) for rectal cancer (Fig. S10), 1.26 (95% CI = 1.09-1.44; $I^2 = 25.7\%$; 7 risk estimates) for lung cancer (Fig. S15), and 1.22 (95% CI = 1.01-1.46; $I^2 = 0.0\%$; 6 risk estimates) for hepatocellular carcinoma (Fig. S18). Red meat consumption was not associated with risk of ovarian, prostate, and stomach cancers, as well as esophageal squamous-cell carcinoma, esophageal adenocarcinoma, pancreatic cancer, bladder cancer, renal cell cancer, leukemia, non-Hodgkin lymphoma, melanoma, and glioma (Figs. S5, S7, S11-S14, S16, S17, S19–S22). In dose–response analysis, using available data, each 100 g per day of red meat intake was associated with an 11% higher risk of breast cancer, a 14% higher risk of colorectal cancer, a 17% higher risk of colon cancer, a 26% higher risk of rectal cancer, and a 29% higher risk of lung cancer (Table S18).

Processed meat intake and cancer risk

The pooled RRs comparing the highest versus the lowest category of processed meat intake and various cancer types are presented in Fig. 3. Processed meat consumption was significantly associated with increased risk of breast cancer (pooled RR = 1.06; 95% CI = 1.01–1.12; $I^2 = 39.0\%$; 16 risk estimates; Fig. S4), colorectal cancer (pooled RR = 1.18; 95% CI = 1.13–1.24; $I^2 = 1.9\%$; 23 risk estimates; Fig. S8), colon cancer (pooled RR = 1.21; 95% CI = 1.13–1.29; $I^2 = 0.0\%$; 15 risk estimates; Fig.

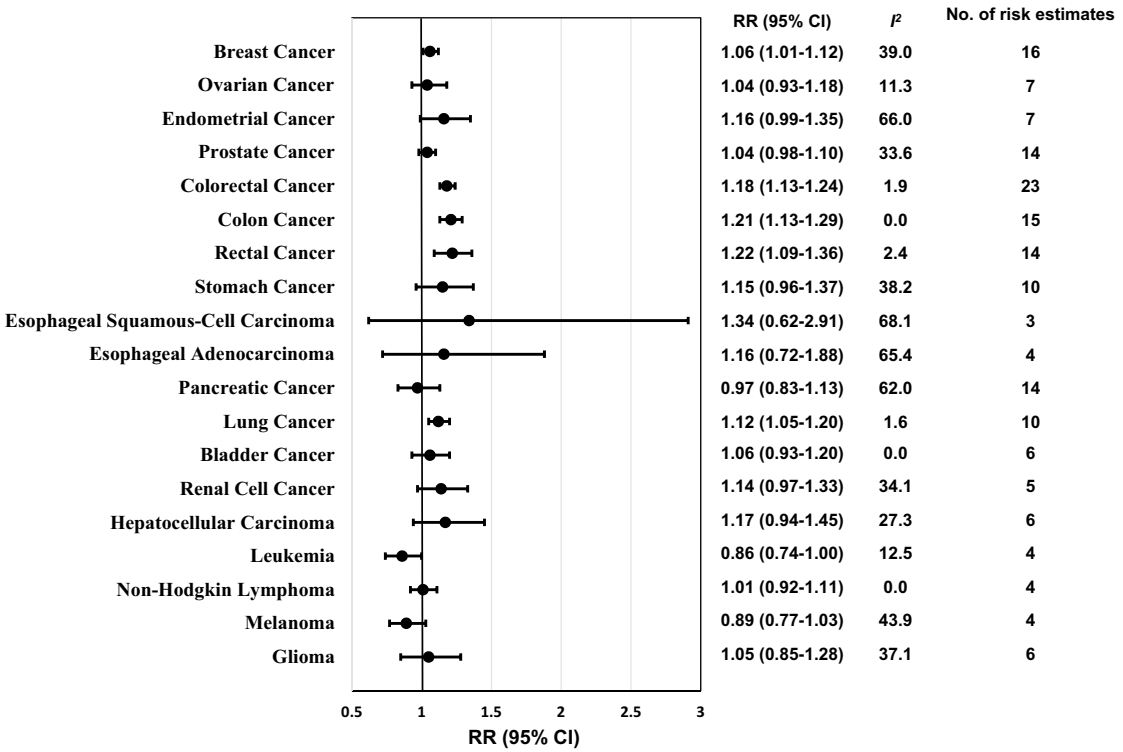

Fig. 3 Pooled relative risks and 95% confidence intervals of various cancer incidence associated with processed meat intake (highest category versus lowest category), using random-effect models

S9), rectal cancer (pooled RR = 1.22; 95% CI = 1.09-1.36; I^2 = 2.4%; 14 risk estimates; Fig. S10), and lung cancer (pooled RR = 1.12; 95% CI = 1.05–1.20; I^2 = 1.6%; 10 risk estimates; Fig. S15). Processed meat consumption was not associated with risk of ovarian cancer, endometrial cancer, prostate cancer, stomach cancer, esophageal squamous-cell carcinoma, esophageal adenocarcinoma, pancreatic cancer, bladder cancer, renal cell cancer, hepatocellular carcinoma, leukemia, non-Hodgkin lymphoma, melanoma, and glioma (Figs. S5-S7, S11-S14, S16–S22). In dose–response analysis, using available data, each 50 g per day of processed meat intake was associated with a 16% higher risk of colorectal cancer, a 17% higher risk of colon cancer, a 25% higher risk of rectal cancer, and an 8% higher risk of renal cell cancer (Table S18).

Total red and processed meat intake and cancer risk

The pooled RRs comparing the highest versus the lowest category of total red and processed meat intake and various cancer types are presented in Fig. 4. Total red and processed meat consumption was significantly associated with higher risk of colorectal cancer (pooled RR = 1.17; 95% CI = 1.08–1.26; I^2 = 32.7%; 20 risk estimates; Fig. S8), colon cancer (pooled RR = 1.21; 95% CI = 1.09–1.34; I^2 = 33.7%; 12 risk estimates; Fig. S9), rectal cancer (pooled RR = 1.26; 95% CI = 1.09–1.45; I^2 = 29.4%; 10 risk estimates; Fig. S10), lung cancer (pooled RR = 1.20; 95% CI = 1.09–1.33; I^2 = 30.9%; 10 risk estimates; Fig. S15), and renal cell cancer (pooled RR = 1.19; 95% CI = 1.04–1.37; I^2 = 0.0%; 4 risk estimates) (Fig. S17). Findings were similar for the associations between total red and processed meat intake and colorectal cancer (pooled RR = 1.19; 95% CI = 1.11–1.29; I^2 = 23.3%; 19 risk estimates), colon cancer (pooled RR = 1.29; 95% CI = 1.19–1.40; I^2 = 0.0%; 11 risk estimates), and rectal cancer (pooled RR = 1.30; 95% CI = 1.11–1.53; I^2 = 25.5%; 9 risk estimates), when the study by Nguyen et al. [21] was excluded; as mentioned above, we calculated the RRs and 95% CIs of the highest versus the lowest quintile of intake for that study using 2.56 as a conversion factor for a one-SD increase in total red and processed meat intake, assuming a normal distribution. Based on results from one study, high total red and processed meat intake was associated with higher risk of esophageal squamous-cell carcinoma (RR= 1.79; 95% CI = 1.07-3.01; Fig. S12). High intake of total red and processed meat was suggestively associated with higher risk of pancreatic cancer (pooled RR = 1.13; 95% CI = 1.00-1.27; I^2 = 41.2%; 12 risk estimates; Fig. S14). Total red and processed meat consumption was not associated with risk of breast cancer, ovarian

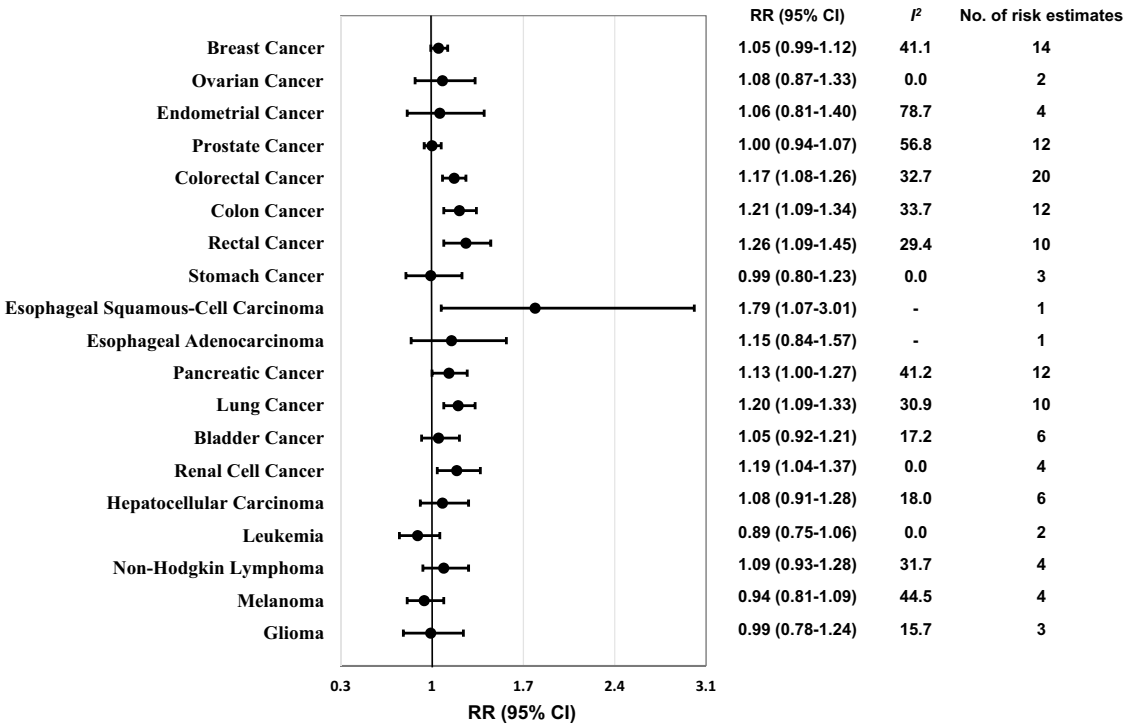

Fig. 4 Pooled relative risks and 95% confidence intervals of various cancer incidence associated with total red and processed meat intake (highest category versus lowest category), using random-effect models

cancer, endometrial cancer, prostate cancer, stomach cancer, esophageal adenocarcinoma, bladder cancer, hepatocellular carcinoma, leukemia, non-Hodgkin lymphoma, melanoma, and glioma (Figs. S4–S7, S11, S13, S16, S18–S22). Each 100 g per day of total red and processed meat intake was associated with a 12% higher risk of endometrial cancer, an 18% higher risk of colorectal cancer, a 25% higher risk of colon cancer, a 25% higher risk of rectal cancer, and a 35% higher risk of lung cancer (Table S18).

Discussion

This comprehensive systematic review and meta-analysis study shows that high intake of red meat as well as high intake of processed meat are associated with increased risk of breast cancer, colorectal cancer, colon cancer, rectal cancer, and lung cancer. In Addition, high red meat intake was associated with higher risk of endometrial cancer and hepatocellular carcinoma. Furthermore, significant positive associations were observed between high total red and processed meat consumption and risk of colorectal cancer, colon cancer, rectal cancer, lung cancer, and renal cell cancer. Based on results from one study, high total red and processed meat intake was associated with higher risk of esophageal squamous-cell carcinoma. High intake of total red and processed meat was suggestively associated with higher risk of pancreatic cancer.

Evidence on biological mechanisms explaining the association between high red meat and processed meat intake and cancer is mounting. Processing meat, which includes curing and smoking, produces carcinogens such as N-nitroso compounds (NOC) and polycyclic aromatic hydrocarbons (PAHs) [1, 172]. Cooking meat, especially at high temperature like grilling, barbecuing, or frying, also results in the production of known or suspected carcinogenic substances, such as heterocyclic aromatic amines (HAAs) and PAHs [173]. 2-Amino-1-methyl-6-phenylimidazo[4,5-b]pyridine (PhIP), one of the most frequent HAAs formed during cooking meat, has been shown to be potently estrogenic, with the potential to increase cell proliferation, migration, and invasion [174, 175]. Additionally, PAHs may cause cancer through the DNA adduct formation and interference with apoptosis [176]. A positive dose–response association between meat doneness levels and risk of breast cancer was observed in the Iowa Women's Health Study; consistently consuming very well-done hamburger, beef steak, and bacon was associated with a 4.62 times higher risk of breast cancer, compared with consuming rare or medium-done meat [177].

Heme iron from red and processed meat has been found to induce cytotoxicity and promote apoptosis and hyperplasia of epithelial cell, to induce lipid peroxidation, and free radical and DNA adduct formation in epithelial cells, as well as to catalyze N-nitroso compound formation, which can promote carcinogenesis [178]. High animal protein intake has been shown to be associated with a significantly higher risk of inflammatory bowel disease [179]; inflammatory bowel diseases are associated with elevated colorectal cancer risk [180]. In addition, animal-derived products contain antibiotics which may adversely affect the compositions and functions of the gut microbiota [181] and may affect local immunity as well as systemic immune responses [181]. The combined effects of these factors promote carcinogenesis [182]. Protein from animal sources is rich in dietary branched-chain and aromatic amino acids, which have been found to increase risk of insulin resistance [183, 184]. Insulin resistance has been linked to an increased risk of various cancers, such as breast cancer, prostate cancer, colorectal cancer, and endometrial cancer [185–190]. The high intake of red meat elevates insulin-like growth factor I (IGF-I) levels [191, 192]. IGF-I plays significant roles in cell growth, cancer development, and tumor progression [193]. Several studies have suggested that high circulating IGF-I has been associated with greater risk of colorectal, prostate, and breast malignancies [194–197]. The circulating level of IGF-I was lower among women with a plant-based (vegan) diet, compared with those with a meat-eating or lacto-ovo-vegetarian diet [198]. The increased release of bile acids, cholecystokinin, and prostaglandins from the high total fat content of meat also increases the risk of colorectal and pancreatic cancers [199–201]. Further, Persistent Organic Pollutants (POPs), which accumulate in animal fat cells [202, 203], may adversely affect endocrine pathways and increase risk of various chronic diseases, including cancer [203]. They are also present in lipoproteins and have been shown to be higher in participants with cancer compared to healthy individuals [204].

Higher red meat and processed meat consumption has been associated with increased oxidative stress and plasma concentrations of inflammatory biomarkers, including C-reactive protein [205, 206]. Nonhuman sialic acid N-glycolylneuraminic acid (Neu5Gc) and methionine, which are abundant in red meat, have been shown to promote chronic inflammation contributing to cancer development and tumor progression [207, 208]. Decreased proliferation of numerous cancer cell lines has been reported with reduced methionine consumption [209].

The most widely used growth promoting sex hormones in cattle raised in the US are estrogens, including estradiol-17β [210]. Estradiol-17β was reported as a carcinogen by the IARC [211], primarily due to its effects in increasing risk of breast cancer and endometrial cancer [212, 213]. Estrogens have also been shown in the development and progression of prostate cancer as well [214]. Some metabolites of estrogens may lead to the free radical formation, epigenetic, immunotoxic, and inflammatory changes, as well as, genotoxicity

and hyperprolactinemia [214]. Therefore, consumption of meat from animals treated with hormones is likely to positively influence carcinogenesis [210].

Increased red meat or processed meat consumption has been shown to be associated with shorter telomere length [215, 216], which in turn result in chromosomal instability and promoting cancer risk [217, 218]. Indeed, studies have shown inverse associations between telomere length and risk of cancer incidence and mortality [219–221].

The multiple, but not exhaustive, cancer-promoting mechanisms cited above, appear to support our findings of increased risk of the various cancer types with increased red meat and processed meat consumption. However, current evidence does not support a significant positive association between high red meat and/or high processed meat intakes and risk of several cancers including ovarian cancer, prostate cancer, stomach cancer, esophageal adenocarcinoma, bladder cancer, leukemia, non-Hodgkin lymphoma, melanoma, and glioma. The lack of significant associations for some sites of cancer may be due to the small number of available studies or no biological relationship between red meat, processed meat, and those cancers. Further investigations are warranted to confirm the safety of red and processed meat intake for prevention of those cancers.

The strength of this meta-analysis should be noted. We analyzed comprehensively all the prospective studies which evaluated the risk of cancer in relation to red meat, processed meat, and total red and processed meat consumption. We only selected prospective studies for this meta-analysis, so recall and selection biases were minimized. Despite wide variations in the amount of red meat and processed meat intake as well as population characteristics across studies, for the majority of cancer sites, there was low to moderate heterogeneity across studies using the I^2 statistic. This supports the external validity of pooling RRs of studies from different populations.

The limitations of this meta-analysis should be noted as well. In the interpretation of findings, publication bias should be considered even though we did not observe publication bias using visual inspection of a funnel plot or Begg and Mazumdar test for either red meat, processed meat, or total red and processed meat. Residual confounding is possible even though major cancer risk factors were controlled in most of the studies. The under- or over-reporting of the amount of red meat and processed meat items, as well as measurement errors, are possible when dietary intake was assessed using the food frequency questionnaire (FFQ). However, this bias may be observed in both cases and non-cases; therefore, it is more likely to attenuate findings. Moreover, we pooled RRs in the highest versus the lowest levels of intake, but levels of intake may be different across studies. We observed almost similar associations using dose–response analysis, though data from all of the studies were not included for dose–response analysis. Even though both intakes of red meat and processed meat were associated with higher risk of breast cancer, we did not observe a significant association with total red and processed meat intake; thus, further studies are needed. The significant positive association of total red and processed meat with esophageal squamous-cell carcinoma was based on only one study, and hence, more studies are needed to confirm this finding. In addition, most of the findings related to associations of red meat and processed meat were from studies in North America and Europe, generalizability to other regions with differences across social and physical environments, as well as sociodemographic factors such as race and ethnicity may be an important issue.

It is important to note that our findings provide robust evidence that high intake of red meat or processed meat increase risk of breast cancer, endometrial cancer, colon cancer, rectal cancer, esophageal squamous-cell carcinoma, lung cancer, renal cell cancer, and hepatocellular carcinoma in addition to colorectal cancer and pancreatic cancer previously reported by IARC [1]. Furthermore, this study supports dietary guidelines promoting limiting or avoiding red meat and processed meat intake to decrease cancer risk as proposed by the World Cancer Research Fund and American Institute for Cancer Research (WCRF/AICR) [222, 223]. Findings also support the American Cancer Society (ACS) dietary guidelines to limit or eliminate red meat and processed meat intake [224]. Evidence on the protective effects of high intake of wholefoods, plant-based diets, including legumes which are healthy substitutes for meat [24, 225–228], and the adverse effects of high red meat and processed meat intake, as well as supporting mechanisms for their actions on the risk of various types of cancer, continue to increase. Reduction of red meat and processed meat consumption has been shown to not only reduce cancer risk, but also other diseases such as diabetes and cardiovascular diseases [229–232]. Given the current available evidence, it seems prudent for practitioners and public health officials to encourage the adoption of a lifestyle that incorporates limiting or avoiding red meat and processed meat intake to decrease cancer risk burden in the US and worldwide.

Conclusion

Findings from this comprehensive systematic review and meta-analysis of prospective studies provide evidence that lower consumption of red meat and processed meat could be a key modifiable lifestyle factor in reducing the types of cancer identified in this paper.

Supplementary Information The online version contains supplementary material available at https://doi.org/10.1007/s10654-021-00741-9.

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Author contributions Maryam S. Farvid: Study concept and design, data extraction and statistical analysis, interpretation of data, drafting of manuscript, critical revision of the manuscript for important intellectual content, and approval of the final manuscript for submission. Elkhansa Sidahmed: Helped with data extraction, interpretation of data, critical revision of the manuscript for important intellectual content, and approval of the final manuscript for submission. Nicholas D. Spence: Helped with interpretation of data, critical revision of the manuscript for important intellectual content, and approval of the final manuscript for submission. Kingsly Mante Angua: Helped with data extraction, and approval of the final manuscript for submission. Bernard A. Rosner: Helped with the interpretation of data and approval of the final manuscript for submission. Junaidah B. Barnett: Helped with the interpretation of data and writing the discussion section, critical revision of the manuscript for important intellectual content, and approval of the final manuscript for submission.

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Compliance with ethical standards

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Data sharing Data are available to share.

Ethical approval NA.

Patient and public involvement NA.

Transparency All authors affirm that the manuscript is an honest, accurate, and transparent account of the study being reported; that no important aspects of the study have been omitted; and that any discrepancies from the study as planned (and, if relevant, registered) have been explained.

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