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Association between butchers and cancer mortality and incidence

A systematic review and meta-analysis

Zhen-Lang Guo, MS[a], Jun-Yue Wang, MS[a], Yu-Si Li, MS[b], Lei-Liang Gong, MD[c], Shu Gan, MD[d,*], Shu-Sheng Wang, MD[d,*]

Abstract

Background: In this study, we evaluated whether increased risks of mortality and cancer incidence exist among butchers worldwide. To achieve this goal, we conducted a systematic review and meta-analysis to investigate the correlations of the risks of cancer death and incidence with male and female butchers.

Methods: We obtained data by performing a comprehensive literature search in several databases for eligible studies published before March 2017. Multivariable-adjusted standardized mortality ratios (SMRs) and odds ratio (OR), as well as associated 95% confidence intervals (CIs) and those by subgroups, were extracted and pooled.

Results: A total of 17 observational studies comprising 397,726 participants were included in the meta-analysis. The butcher occupation was not associated with all-cancer mortality risk, with pooled overall SMRs of 1.07 (95% CI 0.96–1.20). However, the pooled ORs revealed that butchers hold an elevated risk of total cancer incidence (OR, 1.51; 95% CI, 1.33–1.73). No proof of publication bias was obtained, and the findings were consistent in the subgroup analyses.

Conclusion: Our results suggest that working as butchers did not significantly influence all-cancer mortality risk but significantly contributed to elevated all-cancer incidence risk. Nevertheless, well-designed observational studies on this topic are necessary to confirm and update our findings.

Abbreviations: CIs = confidence intervals, HR = hazard ratio, MeSH = medical subject headings, NOS = Newcastle–Ottawa Scale, OR = odds ratio, PRISMA = Preferred Reporting Items for Systematic Reviews and Meta-Analyses, RR = risk ratio, SMRs = standardized mortality ratios.

Keywords: butcher, cancer, incidence, meta-analysis, mortality, systematic review

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[a] The Second Clinical College, [b] School of Basic Medical College, Guangzhou University of Chinese Medicine, [c] Department of Mechanical Engineering, National University of Singapore, Kent Ridge, Singapore, [d] Department of Urology, Guangdong Provincial Hospital of Chinese Medicine, Guangzhou, China.

[*] Correspondence: Shu-Sheng Wang, and Shu Gan, Yuexiu District, Guangzhou, Guangdong Province, China (e-mails: shushengwanggzy@163.com, ganshugzy@163.com).

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1. Introduction

Butchers constitute an occupational group exposed to potentially harmful agents, including environmental stressors, such as cold, explosions, fires, and combustion products.[1] They are also exposed suspected carcinogens, such as polycyclic aromatic hydrocarbons, nitrosamines, and potentially oncogenic animal viruses, which are formed during meat curing and slaughtering.[2–4] Despite its controversial health consequences, butchery is a prevalent occupation.

The number of reported cancers specific to butchers and related workers is relatively small. However, this finding may be biased because of the suspected excessive selective reporting of certain neoplasms.[5,6] Suspicions on the hazard in butchers originally arose from the routine investigations of occupational mortality and cancer incidence in Denmark and Sweden.[7,8] Subsequently, retrospective cohort studies of butchers in the USA also found increased risks of lung and colon cancer mortalities.[9] Moreover, increased risks of leukemia and stomach cancer were reported by several papers[10,11] but have not been confirmed in recent investigations.[12,13]

Knowledge is inadequate on the risks of cancer mortality and incidence and the small in this occupational group, and the magnitudes of the expected increases in these risks are small. Thus, we performed a comprehensive meta-analysis of published studies to clarify the above-mentioned contradictory results and evaluate the relationships of the risks of cancer mortality and incidence to male and female butchers globally.

2. Methods

2.1. Search strategies

This study was conducted in accordance with the guidelines of the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA)[14] and reported in compliance with the guidelines developed by the Meta-Analysis of Observational Studies in Epidemiology group.[15] We also registered the protocol on PROSPERO to document our methodological approach a priori. All analyses were based on previous published studies, thus no ethical approval and patient consent are required.

To identify eligible studies, 2 investigators (ZG and JW) performed a comprehensive literature search for eligible studies in the databases PubMed, Embase, Web of Science, Scopus, and Cochrane Library. Eligible studies included those on the relationships of the risks of cancer mortality and incidence to butchers from database inception to March 2017. Each database was searched without restrictions on language, publication type, and region using the following combinations of medical subject headings (MeSH) and non-MeSH search terms: "butcher"; "cancer, carcinoma, or tumor"; and "cancer risk, cancer mortality, or cancer incidence." We also identified other potentially relevant studies by manual searches through reference lists of all the included studies and previous reviews on the topic of interest. We contacted the authors of unpublished studies (abstracts only) and the most recurrent studies. Any discrepancy was resolved by consulting an investigator not involved in the initial procedure.

2.2. Study selection criteria

Two independent investigators (ZG and YL) chose the studies that explored the potential relationships of butchery to risks of cancer mortality and incidence. These works were selected using the following inclusion criteria. The studies contained predefined diagnosis criteria for both butchers and cancer. Participants were selected without limitations on region, age, and social status. The studies presented sufficient original data (excluding reviews) on standardized mortality ratio (SMR), odds ratio (OR), risk ratio (RR), and hazard ratio (HR) estimates as well as associated 95% confidence intervals (CIs) for the correlation of butchery with cancer mortality and incidence. The works used either a case-control, cross-sectional, retrospective, or prospective design. Lastly, the population included butchers employed in industries and meat cutters working outside the meat industry (e.g., in department stores and other sectors of the food industry). Any disagreement was resolved through the adjudication of senior authors.

2.3. Data extraction

Data from the included studies were extracted and independently summarized by 2 investigators from our team (JW and LG) using a predefined data extraction form. Specifically, we read the reports and independently extracted and tabulated the valuable information into a standardized evidence table. The data included the study design, baseline population characteristics (i.e., mean age, sex, sample size, and country), cancer types, endpoints, adjusted factors, cancer incidence, mortality, and risk estimates from the most fully adjusted model with 95% CIs from all the included studies. We also checked the data for accuracy. Moreover, whenever possible, we contacted the primary authors of the studies with insufficient information to acquire and verify the data. Disagreements were resolved by discussion or consensus with a third reviewer.

2.4. Methodological quality assessment

The methodological quality of the included studies was assessed by 2 independent reviewers (SW and SG) using the modified Newcastle–Ottawa Scale (NOS).[16] This scale consists of the following domains: patient selection, study group comparability, and outcome assessment. A score of 0 to 9 (denoted by stars) was allocated for observational studies. Disagreements were also settled through a discussion among the authors.

2.5. Statistical analyses

For the meta-analysis, the total effectiveness rates of the extracted data were pooled using SMR and OR with associated 95% CIs to determine the relationships of the risks of cancer mortality and incidence to male and female butchers worldwide. Since the absolute risk of caner is low, the measures of association are expected to yield similar estimates of ORs. Consequently, we therefore reported all results as the OR simplicity, as appropriate, so that comprehensiveness of the analysis and maximization of the statistical power are ensured.[17–19] The aggregated results and 95% CIs for the effect size were calculated using inverse-variance weighted meta-analysis. An *I*-square (I^2) test was performed to assess the effect of study heterogeneity on the meta-analysis results. In this test, I^2 values of 0%, 25%, 50%, and 75% represented no, low, moderate, and high heterogeneities, respectively. According to the Cochrane review guidelines, a severe heterogeneity of $I^2 \geq 50\%$ warrants the use of the random-effects model. Otherwise, a fixed-effects model is appropriate. Statistical significance was set at $P < .05$. Sensitivity analysis was conducted to eliminate 1 study at a time by evaluating the quality and consistency of the results. Funnel-plot visual inspection and Egger linear regression test were conducted to assess for publication bias. Subgroup analyses by country, sex, and study design were performed.

3. Results

3.1. Study selection process

Figure 1 presents a flowchart describing the selection process of our literature screening. Our search yielded 241 unique reports, from which only 189 studies were retrieved after the removal of duplicates. After screening the titles and abstracts, only 36 studies were retained and the reasons are as follows: 36 studies did not match the butcher definition, 30 studies were not human studies, 24 studies were not related to cancer, 28 studies were mechanistic/genetic studies, 22 studies did not provide eligible endpoints, 8 studies were reviews, and 5 studies were published as abstracts. Finally, 19 full-text articles were discarded for the following reasons: 4 studies did not provide eligible outcomes, 4 studies did not match the butcher definition, and 11 studies did not provide sufficient data for extraction. Therefore, 17 observational studies[9–13,20–31] comprising 397,726 participants were included in our meta-analysis on the basis of the inclusion criteria.

3.2. Study characteristics and methodological quality

The characteristics of the 17 included studies[9–13,20–31] are shown in Table 1. Among the included works, 11 were case-control studies,[11,21–25,27–31] 5 were retrospective cohort studies,[9,10,12,13,20] and 1 was a prospective cohort study.[26] Their publication years ranged from 1989 to 2011. Among the

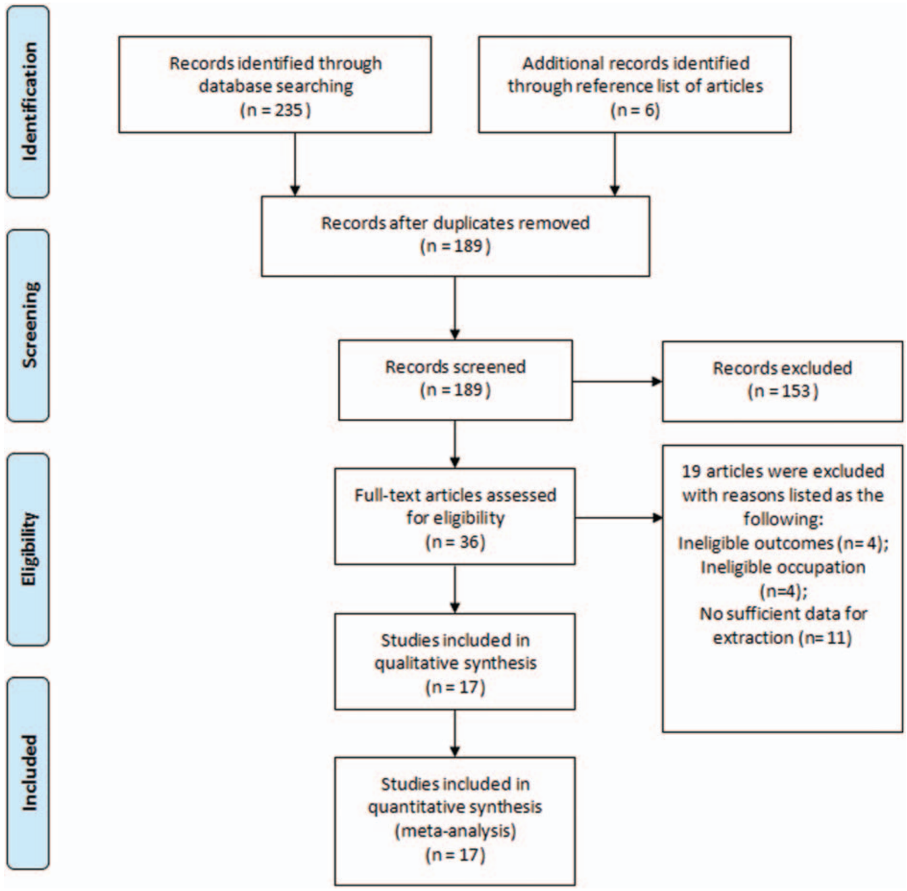

Figure 1. Flow diagram of study selection. Note: Our search yielded 241 unique reports and from this, only 189 studies were retrieved after removal of duplicates. Following the screening of titles and abstracts, only 36 studies remained. A total of 19 full-text articles were discarded after their full texts were read.

Table 1

Basic characteristics of the included studies.

Author, year	Study design	Country	Number of participants (male/female)	Age (y)	Study period	Cancer type	Endpoints
Aragonés et al [10]	Retrospective cohort	Sweden	8763/0	25–59	1971–1989	Stomach cancer	Cancer incidence
Greenland [17]	Retrospective cohort	USA	17,165/1474	71	1984–1998	Colon and lung cancer	Cancer mortality
Bethwaite et al[11]	Case-control	New Zealand	144/165	30–70	1989–1991	Leukemia	Cancer incidence
Boffetta[12]	Retrospective cohort	Sweden	NA	NA	1971–1989	Oral cavity, pharynx, stomach, colon, larynx, lung, prostate, kidney, and leukemia	Cancer incidence
Larsson et al[18]	Case-control	UK	6080/0	NA	1961–1992	Lung cancer	Cancer mortality
Adami et al[19]	Case-control	New Zealand	658/591	20–70	2007–2008	Lung cancer	Cancer incidence
Besson et al[20]	Case-control	Romania, Hungary, Poland, UK, Russia, Slovakia, and Czech Republic	2202/2305	50–70	1998–2002	Lung cancer	Cancer incidence
Guberan[13]	Retrospective cohort	Netherlands	862/887	32.5 (male)/ 31.0 (female)	1901–1990	Oral cavity, pharynx, stomach, colon, liver, laryngeal, lung, prostate, kidney, lymphoma, leukaemia	Cancer incidence
Coggon and Wield[21]	Case-control	Sweden	230 (NA)	38–87	1971–1982	Lung cancer	Cancer incidence
Johnson et al[9]	Retrospective cohort	USA	301/209	33	1950–2006	Colon and lung cancer	Cancer mortality
Corbin et al[22]	Case-control	USA	159 (NA)	NA	1949–1980	Leukemia	Cancer incidence
Durusoy et al[23]	Prospective cohort	Denmark, Italy, The Netherlands, Norway, Spain, Sweden and, UK, Germany, Greece and France	106,813/241,742	35–70	1992–2000	Lymphoma	Cancer incidence
Gustavsson et al[24]	Case-control	USA	640/648	>18	1994–1998	Glioma	Cancer incidence
Metayer et al[25]	Case-control	USA	1458/515	18–80	1995–1998	Glioma	Cancer incidence
Neasham et al[26]	Case-control	Uruguay	621 (NA)	30–75	1993–1995	Laryngeal cancer	Cancer incidence
Roos et al[27]	Case-control	Uruguay	1352 (NA)	30–89	1994–2000	Lung cancer	Cancer incidence
Ruder et al[28]	Case-control	USA	1742 (NA)	20–85	1969–1980	Liver cancer	Cancer incidence

NA = not available.

studies, 6 were conducted in the USA,[9,20,25,27,28,31] 3 in Sweden,[10,12,24] 2 in New Zealand,[11,22] 2 in Uruguay,[29,30] and 1 in the Netherlands.[13] Moreover, 1 was conducted in 10 participating centers in the following locations: Denmark, Italy, the Netherlands, Norway, Spain, Sweden, UK, Germany, Greece, and France.[26] Finally, 1 was performed in 7 participating centers located in Romania, Hungary, Poland, UK, Russia, Slovakia, and the Czech Republic.[23] Meanwhile, 14 studies were performed among populations older than 18 years,[9–11,13,20,22–24,26–31] but 3 studies did not report the exact ages.[12,21,25] The cancer types varied across the included studies, and only 2 studies reported estimates without adjustments.[9,21] The follow-up length ranged from 2 years to 99 years. In the included clinical trials, the sample sizes varied between 159 and 348,555 participants.

In addition, 11 studies were of high methodological quality,[9,10,13,20,22,23,26–28,30,31] 3 studies[11,24,29] were of moderate quality, and 3 studies[12,21,25] were of poor quality based on the modified NOS. The main deficiency was the selection bias related to the insufficient adjustment of confounding factors among the included studies.

3.3. Association between butchers and the risk of cancer mortality

The data on cancer mortality were analyzed from 3 studies (2 retrospective cohort studies[9,20] and 1 case-control study[21]; Fig. 2) with the random-effects model. We found that the butchers did not show a significantly different all-cancer mortality risk from that in the general population. The pooled overall SMRs were 1.07 (95% CI 0.96–1.20), and 1.07 (95% CI 0.93–1.21) for lung cancer, 1.54 (95% CI 0.59–4.01) for colon cancer, respectively. Nevertheless, moderate heterogeneity was found (I^2=69.3%, P=.011), and the subgroup analyses were restricted by the small number of studies evaluated.

3.4. Association between butchers and the risk of cancer incidence

The pooled ORs revealed that butchers were at an elevated risk of total cancer incidence (OR, 1.51; 95% CI, 1.33–1.73) (Table 2, Figs. 3–6). Significant associations were demonstrated for glioma (OR, 1.95; 95% CI, 1.19–3.17, P=.584) as well as cancers of the stomach (OR, 1.41; 95% CI, 1.14–1.76, P=.726), oral cavity and pharynx (OR, 1.60; 95% CI, 1.07–2.40, P=.989), lung (OR, 1.47; 95% CI, 1.23–1.74, P=.356), and liver (OR, 2.56; 95% CI, 1.52–4.32, P=.682). However, no significant association was found for leukemia (OR, 1.58; 95% CI, 0.97–2.57, P=.312) and lymphoma (OR, 0.79; 95% CI, 0.13–4.95, P=.097) as well as cancers of the larynx (OR, 1.86; 95% CI, 0.92–3.76, P=.321), colon (OR, 1.35; 95% CI, 0.38–4.81, P=.356), kidney (OR, 1.14; 95% CI, 0.68–1.89, P=.357), and prostate (OR, 1.44; 95% CI, 0.97–2.14, P=.070). The between-study heterogeneity was insignificant among the individual studies (I^2=40.4%, P=.013). Thus, the fixed-effects model was used to estimate the cancer incidence among women. Moreover, the combined results were further confirmed by sensitivity analysis, and subgroup

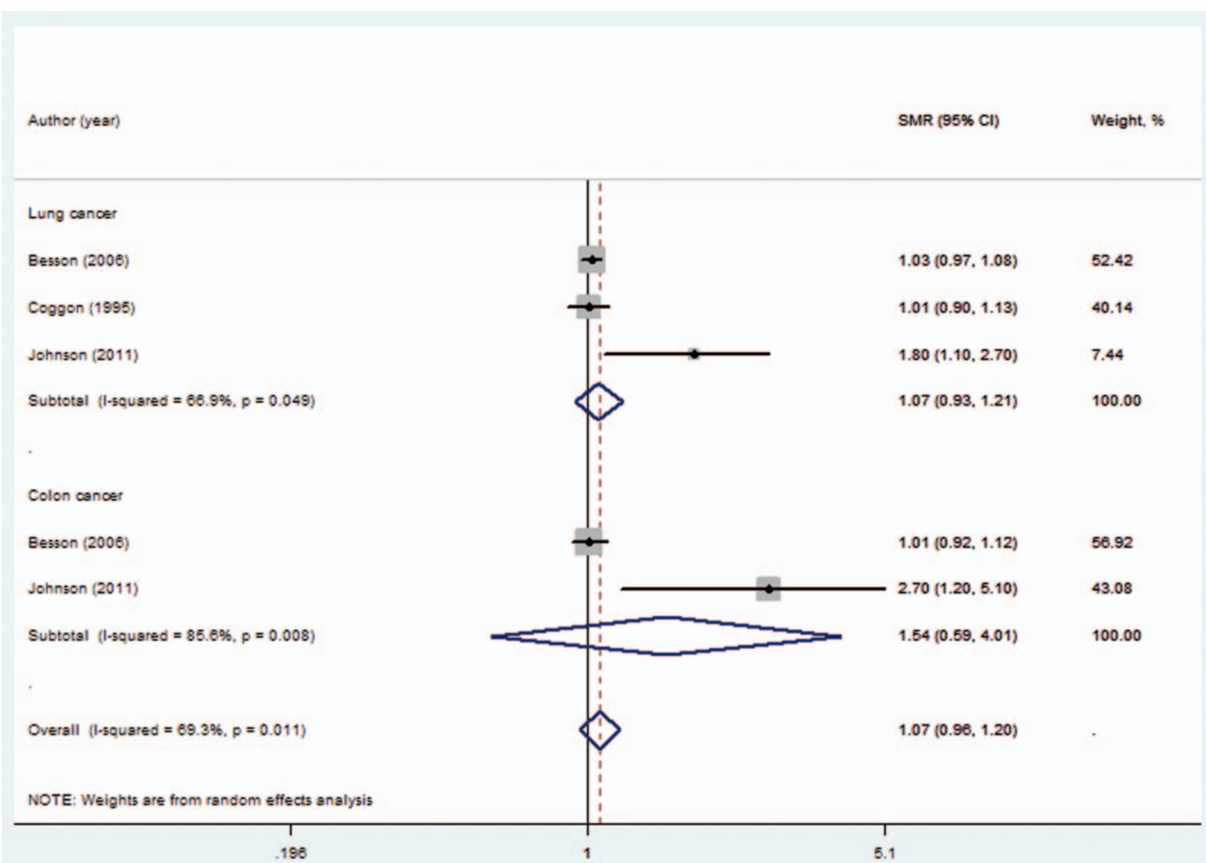

Figure 2. Association between butchers and the risk of cancer mortality. Note: The summary estimates were obtained using the random-effects model. The dots indicate the adjusted SMRs (*100). The size of the shaded square is proportional to the percent weight of each study. The horizontal lines represent 95% CIs. The diamond data markers indicate the summary SMR. CI=confidence interval; SMR=standardized mortality ratio.

Table 2

Summary of meta-analysis results for the association between butchers and the risk of cancer incidence.

Cancer types	Participants,N	OR (95% CI)	*P* Value	*P* of heterogeneity	I^2 (%)
Stomach cancer	10,512	1.42 (1.14–1.76)	.002	.726	0
Leukemia	2217	1.58 (0.97–2.57)	.063	.312	15.9
Oral cavity, pharynx cancer	1749	1.60 (1.07–2.40)	.022	.989	0
Colon cancer	1749	1.35 (0.38–4.81)	.001	.000	95.3
Laryngeal cancer	2370	1.86 (0.92–3.76)	.083	.321	11.9
Lung cancer	9087	1.47 (1.23–1.74)	.000	.356	9.4
Prostate cancer	1749	1.44 (0.97–2.14)	.003	.070	69.5
Kidney cancer	1749	1.14 (0.68–1.89)	.627	.357	0
Liver cancer	3491	2.56 (1.52–4.32)	.000	.682	0
Lymphoma	350,304	0.79 (0.13–4.95)	.096	.097	63.8
Glioma	3,261	1.95 (1.19–3.17)	.008	.584	0

CI=confidence interval; OR=odds ratio.

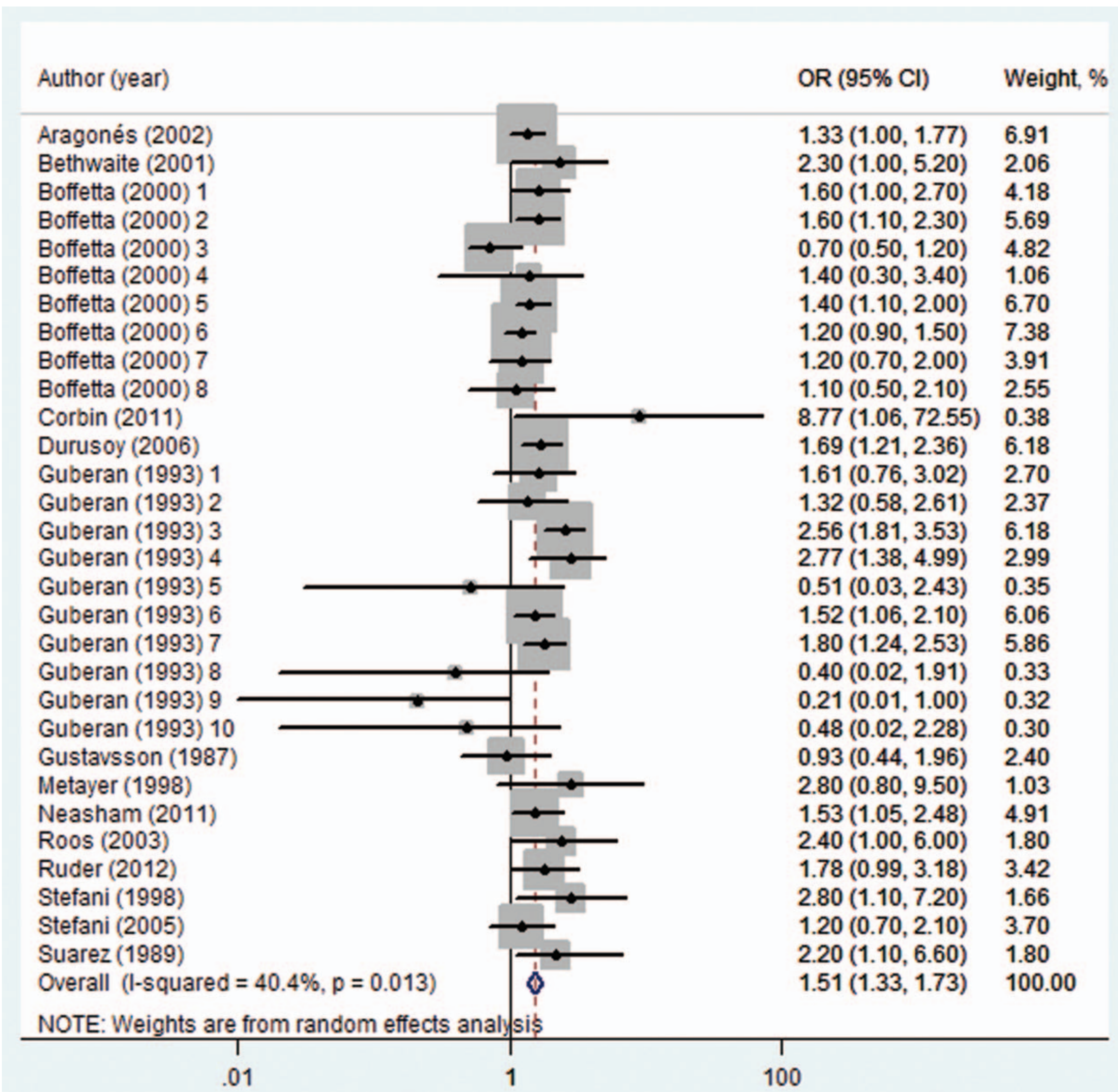

Figure 3. Association between butchers and the risk of cancer incidence. Note: The summary estimates were obtained using the fix-effects model. The dots indicate the adjusted ORs from a comparison between cancer mortality risk and butcher occupation. The size of the shaded square is proportional to the percent weight of each study. The horizontal lines represent the 95% CIs. The diamond data markers indicate the summary OR. Boffetta[12] 1 to 8 represent oral cavity and pharynx cancer, stomach cancer, colon cancer, laryngeal cancer, lung cancer, prostate cancer, kidney cancer, and leukemia, respectively. Guberan[13] 1 to 10 represent oral cavity and pharynx cancer, stomach cancer, colon cancer, liver cancer, laryngeal cancer, lung cancer, prostate cancer, kidney cancer, lymphoma, and leukaemia, respectively. CI=confidence interval; OR=odds ratio.

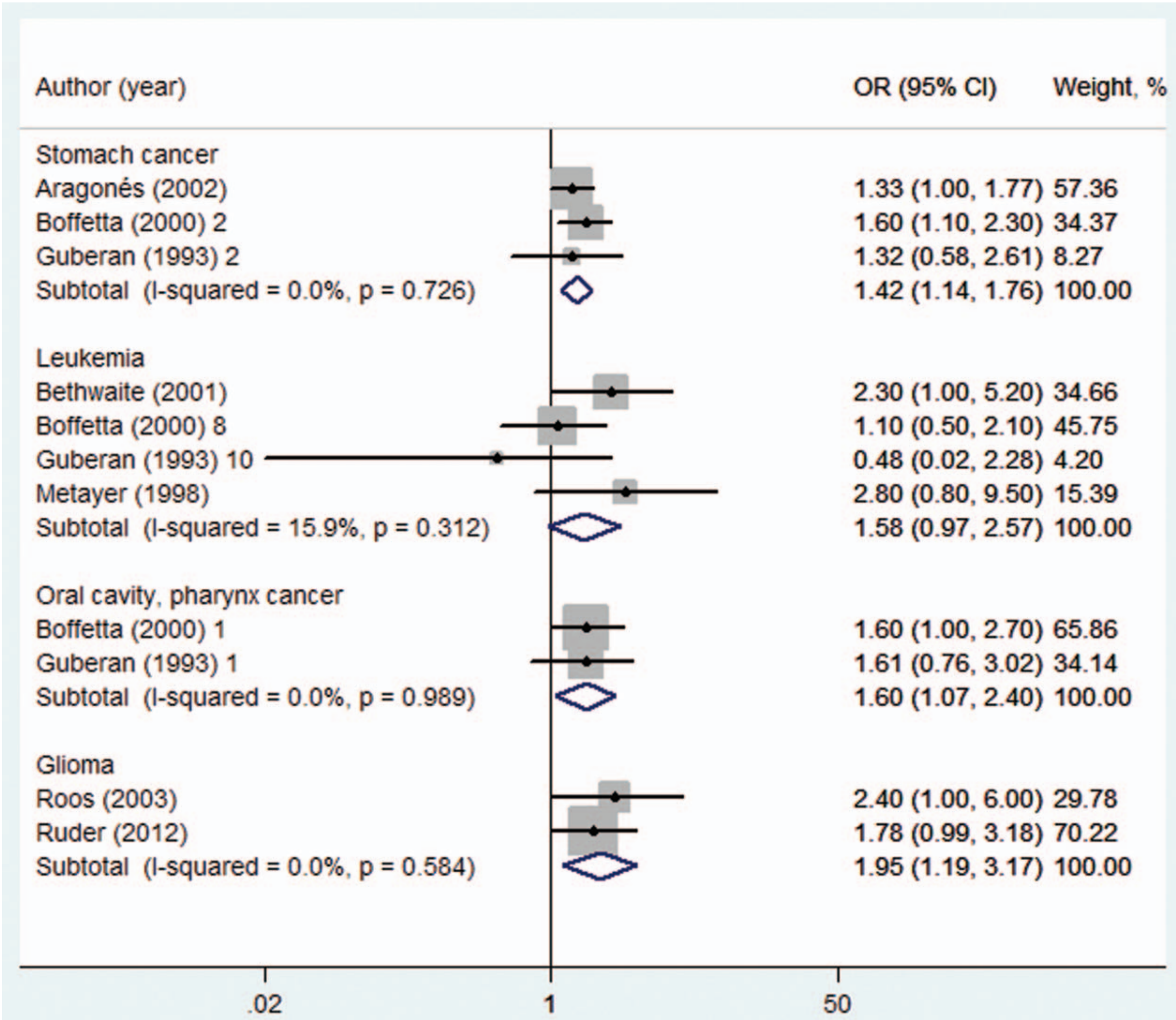

Figure 4. Association between butchers and the risk of cancer incidence (glioma, leukemia; and stomach, and oral cavity, pharynx cancer). Note: The summary estimates were obtained using the fix-effects model. The dots indicate the adjusted ORs from a comparison between cancer mortality risk and butcher occupation. The size of the shaded square is proportional to the percent weight of each study. The horizontal lines represent the 95% CIs. The diamond data markers indicate the summary OR. CI=confidence interval; OR=odds ratio.

analyses were conducted to investigate the potential factors that may substantially affect the between-study heterogeneity.

3.5. Subgroup analyses

In the subgroup analyses by study design and country (Table 3), the findings on the associations of butchers with the risks of cancer mortality and incidence were consistent. Accordingly, under stratification analysis by country, the pooled ORs showed that working as butchers was significantly related to an elevated risk of cancer incidence in the USA, Sweden, New Zealand, and the Netherlands but not in Uruguay. Under stratification analysis by study design, the pooled ORs revealed that butchers were significantly related to an elevated risk of cancer incidence in all study designs. However, subgroup analyses were not performed for age and sex considering the limited number of independent datasets.

3.6. Sensitivity analysis

Sensitivity analysis was conducted to determine whether a certain study strongly influences the estimates between butchers and the risks of cancer mortality and incidence or affected the final heterogeneity. We evaluated the effect of each study on the methodological quality by the sequential exclusion of each study. The stability of the results did not significantly change (Fig. 7); thus, the rationality and reliability of our analysis were validated.

3.7. Evaluation of publication bias

Funnel-plot visual inspection and Egger linear regression test were conducted to check for publication bias (Fig. 8). The Egger test showed an insignificant result ($P=.979$), which indicates that our study possesses a low probability of publication bias.

4. Discussion

In this study, we analyzed the associations of butchers with the risks of cancer-related mortality and incidence using a meta-analysis of 17 included studies[9–13,20–31] to obtain a powerful conclusion. To the best of our knowledge, this research is the first meta-analysis that provides comprehensive insights into the

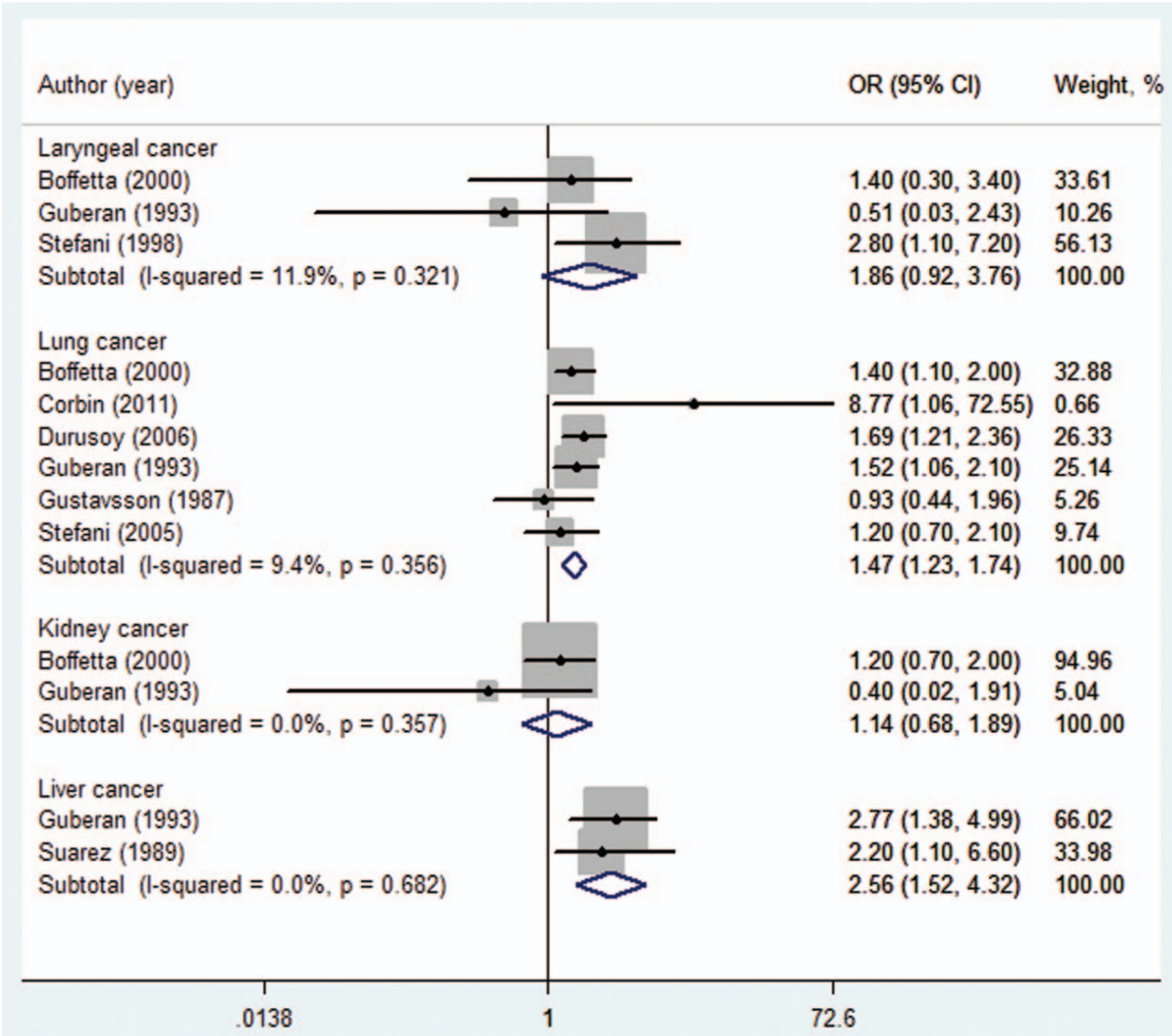

Figure 5. Association between butchers and the risk of cancer incidence (laryngeal, lung, kidney, and liver cancer). Note: The summary estimates were obtained using the fix-effects model. The dots indicate the adjusted ORs from a comparison between cancer mortality risk and butcher occupation. The size of the shaded square is proportional to the percent weight of each study. The horizontal lines represent the 95% CIs. The diamond data markers indicate the summary OR. CI = confidence interval; OR = odds ratio.

relationships between butcher occupation and risks of cancer mortality and incidence through a summary and review of previously published quantitative studies to answer various clinical questions related to this field. Overall, our results demonstrated that working as butchers significantly increased cancer incidence risk by 1.51 times, particularly for glioma as well as stomach, oral cavity, pharynx, lung, and liver cancers. By contrast, no positive association was found for leukemia; lymphoma; and laryngeal, colon, kidney, and prostate cancers. The current meta-analysis provided evidence that butchers were not associated with an elevated risk of total cancer mortality. The overall estimates were robust in the subgroup and sensitivity analyses. No evident publication bias was detected by visual inspection of funnel plot and Egger test.

Recent searches have documented that butchers hold a higher risk of developing cancers, such as lung and colon cancer.[20–22] Actually, zoonotic viruses and chemicals may contribute to the emergence of the lymphatic and hematopoietic system cancers among butchers and animals.[32,33] Moreover, some human retroviruses, such as sarcoma and avian leukosis virus, are known to cause cattle and chicken leukemia because of their frequent contact with the animals' fluids and organs.[34–37] Several studies have confirmed that antibodies to avian reticuloendotheliosis viruses are present in the butcher's serum during meat curing and processing, respectively.[38,39] Therefore, future studies should further classify exposure not only by job category, but also by specific tasks and job titles. Our understanding of the effects of participant age and sex in the included studies on the overall results remains insufficient, although these factors have been investigated, but inadequately, in other studies. Thus, further research is needed to verify the findings of this meta-analysis with regard to different ethnic populations, low-bias risk, and adjusted confounding factors on extensive consequences. Nevertheless, the subgroup and sensitivity analyses did not modify the pooled results.

In general, our meta-analysis exhibited significant strengths. First, this meta-analysis is the first to assess the potential correlations of butcher occupation with the risks of cancer

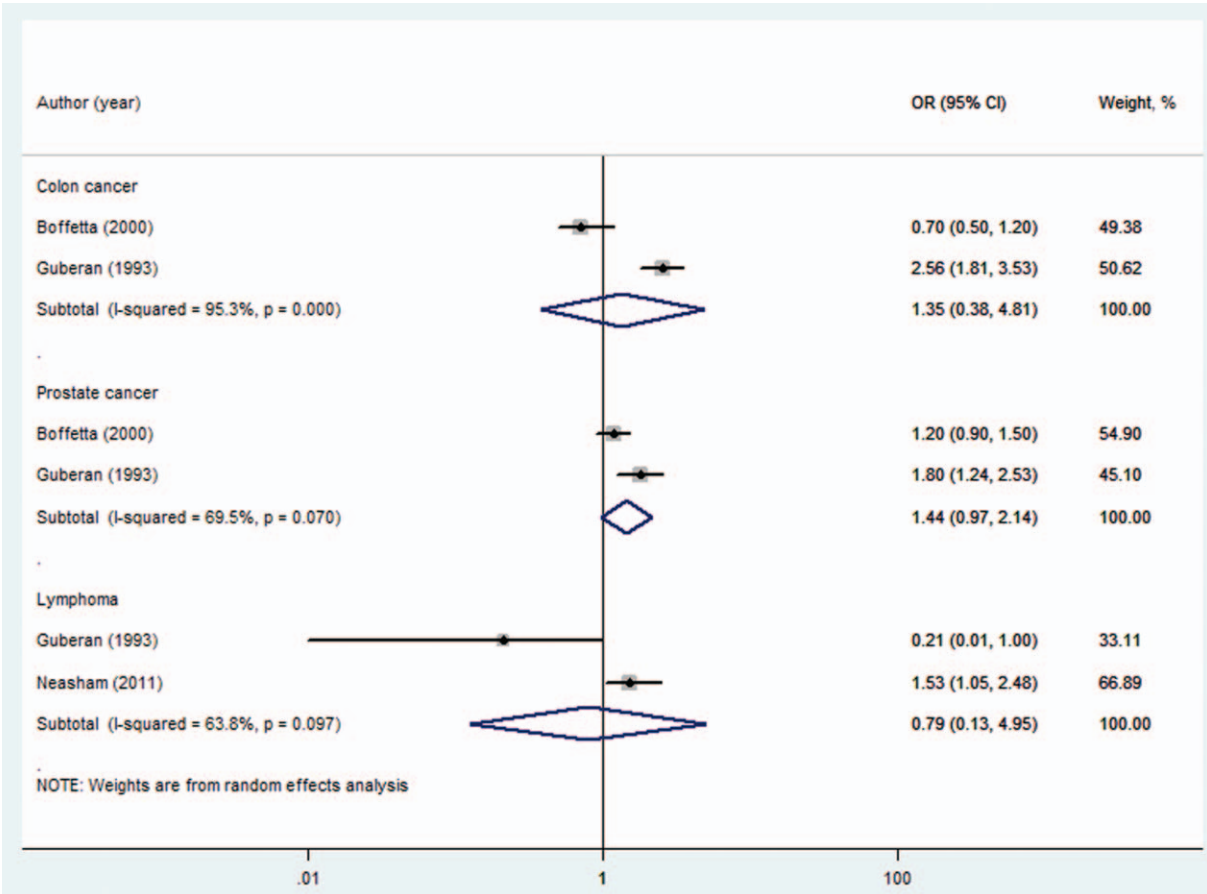

Figure 6. Association between butchers and the risk of cancer incidence (lymphoma; and colon, and prostate cancer). Note: The summary estimates were obtained using the fix-effects model. The dots indicate the adjusted ORs from a comparison between cancer mortality risk and butcher occupation. The size of the shaded square is proportional to the percent weight of each study. The horizontal lines represent the 95% CIs. The diamond data markers indicate the summary OR. CI = confidence interval; OR = odds ratio.

mortality and incidence in populations worldwide by a thorough systematic search and rigorous analytical approaches. Second, the rationality and reliability of our meta-analysis were remarkably improved by overall combined estimates based on a large sample size. Third, multivariable-adjusted risk estimates were used to minimize the confounding factors, such as smoking, which might have influenced the overall results. These estimates were also used to reflect the correlations of butchers with the risks of cancer mortality and incidence accurately and obtain well-founded conclusions. Sufficient subgroup analyses and sensitivity analyses were performed to ensure study reliability.

However, the current meta-analysis was restricted by several limitations. First, residual confounding and non-measurable factors were present in the included observational studies. The accuracy of the results may be increased by adjusting other confounding factors, such as age, sex, and ethnicity. Second, most

Table 3

Results of overall subgroup analysis.

	Studies, N	Participants, N	OR (95% CI)	*P* value	*P* of heterogeneity	I^2 (%)
Total	14	372,497	1.51 (1.33–1.73)	.000	.013	40.4
Country						
Sweden	3	8,993	1.26 (1.11–1.43)	.000	.275	18.3
USA	4	5,162	2.08 (1.38–3.11)	.000	.895	0
New Zealand	1	1,249	2.75 (1.27–5.92)	.010	.247	25.2
Netherlands	1	1,749	1.84 (1.55–2.20)	.000	.088	40.4
Uruguay	2	1,973	1.49 (0.93–2.39)	.100	.127	57.1
Study design						
Case-control study	10	13,430	1.72 (1.40–2.12)	.000	.005	51.3
Retrospective cohort	3	10,512	1.44 (1.30–1.60)	.000	.393	5.1
Prospective cohort	1	107,796	1.53 (1.00–2.35)	.052	NA	NA

CI = confidence interval; NA = not available; OR = odds ratio.

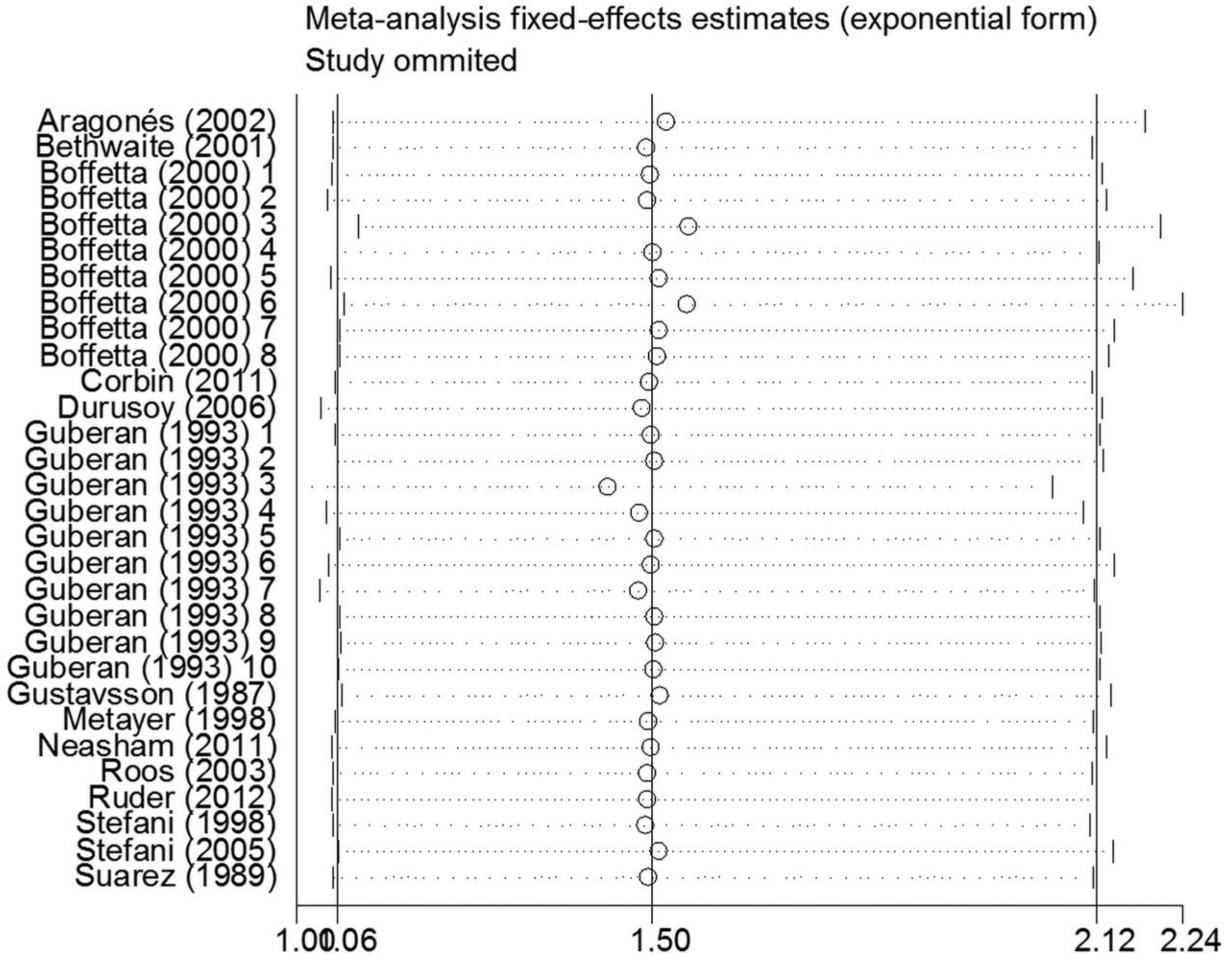

Figure 7. Sensitivity analysis. Note: This figure shows the pooled analysis result after a certain study was omitted. The stability of results did not significantly change; thus, the rationality and reliability of our analysis were validated.

of the included studies were performed in Europe, America, and Oceania. Therefore, the conclusions should be considered cautiously for other ethnic populations. We suggest that population-based cohort studies be conducted to explore the association in study under each ethnicity. Third, a potential publication bias likely exists despite the lack of evidence for this occurrence gained from our statistical tests. Lastly, only English language reports were included. Hence, we may have missed data from important studies published in other languages.

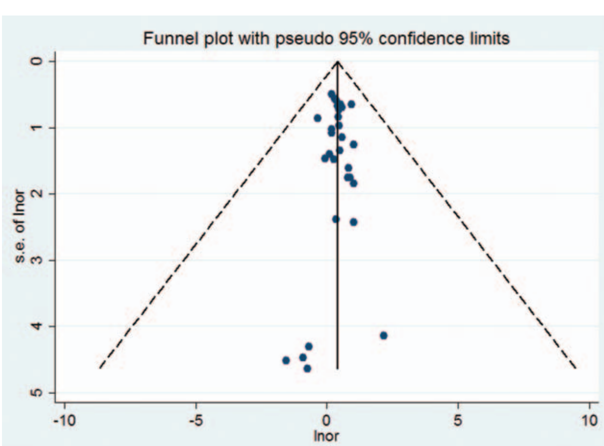

Figure 8. Funnel plot. Note: Funnel-plot visual inspection and Egger linear regression test were performed to assess publication bias. The Egger test ($P=.979$) achieved an insignificant result. Hence, our study possesses a low probability of publication bias.

5. Conclusions

In summary, our meta-analysis suggests that the overall cancer incidence among butchers is higher than that among the general population, particularly for glioma as well as stomach, oral cavity, pharynx, lung, and liver cancers. However, butchers do not exhibit elevated cancer mortality risk, specifically, in colon and lung cancers. Additional studies should be conducted to confirm whether the mortality from other cancers can be attributed to chance. Further investigation must also be performed to clarify the potential biological mechanisms further and update the findings of this analysis.

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