Breast Cancer Res Treat (2015) 151:191–198
DOI 10.1007/s10549-015-3380-9

EPIDEMIOLOGY

Red and processed meat intake and risk of breast cancer: a meta-analysis of prospective studies

Jingyu Guo[1] · Wei Wei[1] · Lixing Zhan[1,2]

Received: 30 January 2015 / Accepted: 9 April 2015 / Published online: 19 April 2015

Abstract Epidemiological studies regarding the association between red and processed meat intake and the risk of breast cancer have yielded inconsistent results. Therefore, we conducted an updated and comprehensive meta-analysis which included 14 prospective studies to evaluate the association of red and processed meat intake with breast cancer risk. Relevant prospective cohort studies were identified by searching PubMed through October 31, 2014, and by reviewing the reference lists of retrieved articles. Study-specific relative risk (RR) estimates were pooled using a random-effects model. Fourteen prospective studies on red meat (involving 31,552 cases) and 12 prospective studies on processed meat were included in the meta-analysis. The summary RRs (95 % CI) of breast cancer for the highest versus the lowest categories were 1.10 (1.02, 1.19) for red meat, and 1.08 (1.01, 1.15) for processed meat. The estimated summary RRs (95 % CI) were 1.11 (1.05, 1.16) for an increase of 120 g/day of red meat, and 1.09 (1.03, 1.16) for an increase of 50 g/day of processed meat. Our findings indicate that increased intake of red and processed meat is associated with an increased risk of breast cancer. Further research with well-designed cohort or interventional studies is needed to confirm the association.

✉ Lixing Zhan
lxzhan@sibs.ac.cn

[1] Key Laboratory of Food Safety Research, Institute for Nutritional Sciences, Shanghai Institutes for Biological Sciences, Chinese Academy of Sciences, University of Chinese Academy of Sciences, 294 Taiyuan Road, Shanghai 200031, China

[2] Key Laboratory of Food Safety Risk Assessment, Ministry of Health, Beijing 100021, China

Keywords Red meat · Processed meat · Prospective studies · Meta-analysis · Breast cancer

Introduction

Breast cancer is the most common cancer in women worldwide. It is also the major cause of death from cancer among women globally [1]. It is reported that one in eight U.S. women (about 12.5 %) will be diagnosed with breast cancer in her lifetime [2]. In 2014, about 232,340 new cases of invasive breast cancer will be diagnosed in women, and 39,620 women will die from breast cancer in the United States [2]. Thus, to facilitate disease prevention, it is of great importance to identify potential risk factors for breast cancer, especially the modifiable lifestyle factors including diet [3]. Recently, an increasing number of studies have been carried out to explore the associations between red and/or processed meat intake and the risk of breast cancer, but the results have been inconsistent [4–9].

An early quantitative review done in 2010 demonstrated that red meat and processed meat intake does not appear to be independently associated with increased risk of breast cancer [9]. Since then, five more epidemiologic studies evaluating the association of red and processed meat intake with breast cancer risk have yielded inconsistent results [4–8]. Of these five studies, two prospective cohort studies in 2014 by Farvid et al. (including 88,803 and 44,231 women, respectively) found a positive association between red meat intake and breast cancer risk [4, 5]. Another study using data from the SU.VI.MAX study observed that processed meat intake was prospectively associated with increased breast cancer risk [6]. However, the other two studies reported null associations [7, 8]. Therefore, we conducted an updated and comprehensive meta-analysis of prospective studies to better characterize this issue.

Materials and methods

Search strategy

A computerized literature search was conducted in PubMed (http://www.ncbi.nlm.nih.gov/pubmed) from its inception through October 2014, by two independent researchers. We searched the relevant studies with the following medical subject-heading terms and/or text words: (1) breast cancer OR breast neoplasm; (2) meat OR red meat OR processed meat OR preserved meat OR pork OR beef OR veal OR mutton OR lamb OR ham OR sausage OR bacon; (3) cohort OR prospective OR nested case–control, following the meta-analysis of observation studies in epidemiology guidelines [10]. Furthermore, we carried out a broader search on diet or foods and breast cancer and reviewed lists of the relevant articles to identify additional studies. No language restriction was imposed.

Study selection

Studies were included in the meta-analysis if the studies met the following criteria: (1) peer-reviewed publications of prospective cohort studies or nested case–control studies; (2) the exposure studied was red meat or processed meat, and the outcome of interest was incidence of or mortality from breast cancer; and (3) relative risk (RR) with corresponding 95 % CI was presented. If the articles were duplicated or from the same study population, the more recent or complete study was included. Case–control studies, ecological assessments, correlation studies, experimental animal studies, and mechanistic studies were excluded. We finally identified 14 prospective studies that reported results for red meat or processed meat consumption in relation to risk of breast cancer according to the criteria listed above.

Data extraction

Two independent researchers extracted the following data from each study: the first author's last name, year of publication, country where the study was conducted, number of cases, cohort size, years of follow-up, type of meat, RR with corresponding 95 % CIs for the highest versus the lowest level, and adjusted variables. Attempts were also made to contact investigators if the data of interested were not directly presented in the publications. When several risk estimates were present, the estimates adjusted for the greatest number of potential confounders were extracted. The Newcastle–Ottawa scale was used to assess the study quality [22].

Statistical analysis

A random-effects model was used to calculate the summary relative risks and 95 % CIs for the highest *versus* the lowest level of red and processed meat intake. This model was developed by DerSimonian and Laird, which accounts for heterogeneity among studies [23]. For the dose-response meta-analysis, we used generalized least squares trend estimation analysis based on the methods proposed by Greenland and Longnecker [24] and Orsini [25]. This method requires the number of cases and non-cases (or person-time) and the RR with its variance estimate for at least three quantitative exposure categories. When studies did not provide this information, we estimated the slopes using variance-weighted least squares regression. When the included studies used different units (such as servings and times), we converted them into grams per day using 120 or 50 g as the average portion size for red meat or processed meat, respectively [26].

Statistical heterogeneity among studies was evaluated using the Cochran's Q and I^2 statistics [27]. Heterogeneity was considered present for $P < 0.05$ or $I^2 \geq 50$ %. Sources of heterogeneity were explored in stratified analysis by study location, menopausal status, and adjusted confounders. We also conducted sensitivity analysis to estimate the influence of each individual study on the summary results by repeating the random-effects meta-analysis after omitting one study at a time. Publication bias was assessed using funnel plots, and the further evaluated by Egger's linear regression and Begg's rank correlation test [28, 29]. A two-tailed P value < 0.05 was considered representative of significant statistical publication bias. All statistical analyses were performed using STATA, version 11.0 (STATA, College Station, TX).

Results

The flowchart of the identification of relevant studies is shown in Fig. 1. A total of 172 articles were identified by searching of the database, and 16 of these articles were retrieved for full-text review. After excluding 2 publications that represented the same population, 14 cohort/nest case–control studies were selected for use in our meta-analysis. Characteristics of the included studies are shown in Table 1. The 14 cohort studies [4, 6, 7, 11–21] comprised a total of 1588,890 participants and 31,552 breast cancer cases, and 3 studies were secondary analyses of randomized controlled trial data [6, 14, 20]. Among the 14 studies evaluated, 6 were conducted in the United States, 6

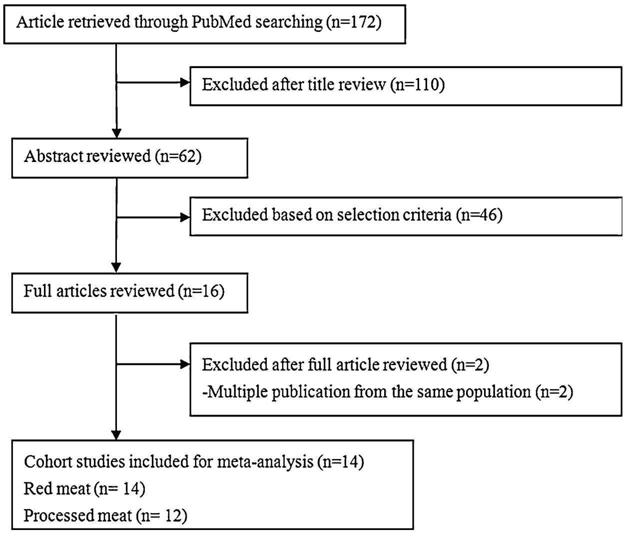

Fig. 1 Flow diagram of study selection process

in Europe, 1 in North America and Western Europe, and 1 in Asia.

Red meat and breast cancer

Fourteen cohort studies that examined the association between red meat intake and the risk of breast cancer were included in the meta-analysis. The summary RR of breast cancer was 1.10 (95 % CI, 1.02–1.19) for subjects in the highest category of red meat intake compared with those in the lowest category. Statistically significant heterogeneity was detected ($P = 0.001$, $I^2 = 62.2$ %). No publication bias was observed by Begg's test ($P = 0.44$) or by Egger's test ($P = 0.08$). Eleven studies [4, 7, 13–21] were eligible to have required data for dose-response analysis, and the estimated summary RR of breast cancer of an increase in red meat intake of 120 g/day was 1.11 (95 % CI, 1.05, 1.16); no significant heterogeneity was observed ($P_{heterogeneity} > 0.1$).

In stratified analysis by menopausal status, the summary RR of breast cancer for subjects in the highest category of red meat intake compared with those in the lowest category was 1.08 (95 % CI, 0.95–1.22; $n = 5$, $P_{heterogeneity} = 0.22$, $I^2 = 30.9$ %) for premenopausal women, and 1.20 (95 % CI, 1.00–1.44; $n = 6$, $P_{heterogeneity} = 0.04$, $I^2 = 56.6$ %) for postmenopausal women. Furthermore, in stratified analysis by geographic region, the summary RR was similar for studies conducted in the United States [RR, 1.10 (95 % CI, 0.97–1.25), $n = 6$, $P_{heterogeneity} = 0.024$, $I^2 = 61.3$ %] and Europe [RR, 1.16 (95 % CI, 1.01–1.32), $P_{heterogeneity} = 0.038$, $I^2 = 57.5$ %] (Fig. 2).

When the overall homogeneity and effect size were calculated by removing one study at a time, we confirmed the stability of the positive association between red meat intake and breast cancer risk (data not shown).

Processed meat and breast cancer

Twelve cohort studies [6, 7, 12–21] that examined the association between processed meat intake and the risk of breast cancer were included in the meta-analysis. The summary RR of breast cancer was 1.08 (95 % CI, 1.01–1.15) for subjects in the highest category of processed meat intake compared with those in the lowest category. Statistically significant heterogeneity was detected ($P = 0.006$, $I^2 = 58.3$ %), and publication bias was not evidenced by Begg's test ($P = 0.30$), but was observed by Egger's test ($P < 0.01$). Seven studies [7, 13, 16–20] were eligible to have required data for dose-response analysis, and the estimated summary RR of breast cancer of an increase in processed meat intake of 50 g/day was 1.09 (95 % CI, 1.03, 1.16); no significant heterogeneity was observed ($P_{heterogeneity} > 0.1$) (Fig. 3).

In stratified analysis by menopausal status, the summary RR of breast cancer for subjects in the highest category of processed meat intake compared with those in the lowest category was 1.03 (95 % CI, 0.89–1.18; $n = 3$, $P_{heterogeneity} = 0.29$, $I^2 = 20.4$ %) for premenopausal women, and 1.23 (95 % CI, 0.98–1.55; n = 4, $P_{heterogeneity} = 0.06$, $I^2 = 60.4$ %) for postmenopausal women. Furthermore, in stratified analysis by geographic region, the summary RR was 1.04 (95 % CI, 0.97–1.12) ($n = 4$, $P_{heterogeneity} = 0.8$, $I^2 = 0.0$ %) for studies conducted in the United States, and 1.16 (95 % CI, 1.05–1.28) ($n = 6$, $P_{heterogeneity} = 0.21$, $I^2 = 30.4$ %) for studies conducted in the Europe (Fig. 4).

Discussion

In this comprehensive updated meta-analysis, higher red and processed meat intake was found to be associated with an increased risk of breast cancer. The summary risk of breast cancer for the highest *versus* the lowest categories increased by 10 % for red meat, and 8 % for processed meat. The results were consistent when using dose-response analysis.

A previous meta-analysis of red and processed meat consumption and breast cancer was conducted by Alexander et al. in 2009 [9]. That study found weak positive summary associations across all meta-analysis models, with the majority being non-statistically significant. Moreover, only 11 studies were included in the previous meta-analysis. However, since then, a number of large-scale prospective epidemiologic studies have evaluated the association between red and processed meat intake and breast cancer risk. For example, one study with

Table 1 Characteristics of prospective studies of red meat and processed meat consumption and breast cancer risk

Author/publication year/country	Cohort	Cases/cohort size	Follow-up	Exposure details	RR (95 % CI) (highest vs. lowest)	Controlled variables
Byrne et al./1996/United States	NHANES I/NHEFS cohort	53/6156	1982–1987	Beef	0.5 (0.3, 1.1)	Age
Missmer et al./2002/North America and Western Europe	North America and Western Europe	7379/351,041	1976–1997	Red meat	0.94 (0.87, 1.02)	Age at menarche, interaction between parity and age at first birth, oral contraceptive use, history of benign breast disease, family history of breast cancer, smoking status, education, BMI, height, alcohol, intake, total energy intake, menopausal status, interaction of BMI and menopausal status, postmenopausal hormone use
				Processed meat	0.98 (0.96, 1.00)	
van der Hel et al./2004/Dutch	Monitoring Project on CVD Risk Factors	229/551	1987–1997	Fresh red meat	1.30 (0.83, 2.02)	Age, menopausal status, town, energy intake
				Processed meat	1.05 (0.67, 1.64)	
Shannon et al./2005/China	Shanghai breast self-exam trial	378/1448	1989–2000	Red meat	1.24 (0.77, 1.99)	Age, total energy intake, breast-feeding
				Cured meat	1.20 (0.82, 1.74)	
Cho et al./2006/United States	Nurses' Health Study II	1021/90,659	1991–2003	Red meat	1.27 (0.96, 1.67)	Age, calendar year of interview, smoking, height, parity, age at first birth, BMI, age at menarche, family history of breast cancer, history of benign breast disease, oral contraceptive use, alcohol intake, energy intake
				Processed meat	1.08 (0.89, 1.31)	
Taylor et al./2007/UK	UK Women's Cohort Study	678/35,372	1995–2004	Red meat	1.41 (1.11, 1.81)	Age, energy intake, menopausal status, BMI, physical activity, smoking status, HRT use, OCP use, parity, total fruit and vegetable intake
				Processed meat	1.39 (1.09, 1.78)	
Cross et al./2007/United states	NIH-AARP Diet and Health study	5872/500,000	1995–2003	Red meat	1.02 (0.93, 1.12)	Age, sex, education, marital status,, family history of cancer, race, BMI, smoking, physical activity, total energy intake, alcohol intake, and fruit and vegetable consumption
				Processed meat	1.03 (0.94, 1.12)	
Egeberg et al./2008/Denmark	Diet, Cancer and Health Cohort Study	378/24,697	1993–2000	Red meat	1.65 (1.09, 2.50)	Parity, age at first birth, education, duration of HRT, intake of alcohol, and BMI
				Processed meat	1.59 (1.02, 2.47)	
Larsson et al./2009/Sweden	Swedish Mammography Cohort	2952/61,433	1987–2007	Total red meat	0.98 (0.80, 1.12)	Education, BMI, height, parity, age at first birth, age at menarche, age at menopause, use of oral contraceptives, use of postmenopausal hormones, family history of breast cancer, intakes of total energy and alcohol

Table 1 continued

Author/publication year/country	Cohort	Cases/cohort size	Follow-up	Exposure details	RR (95 % CI) (highest vs. lowest)	Controlled variables
				Processed meat	1.08 (0.96, 1.22)	
Ferrucci et al./2009/United States	Prostate, Lung, Colorectal, and Ovarian Cancer Screening Trial	1205/52,158	1993–2001	Red meat	1.23 (1.00, 1.51)	Age, race, education, study center, randomization group, family history of breast cancer, age at menarche, age at menopause, age at first birth and number of live births, history of benign breast disease, number of mammograms during past 3 years, menopausal hormone therapy use, BMI, alcohol intake, total fat intake, and total energy intake
				Processed meat	1.12 (0.92, 1.36)	
Pala et al./2009/European	European Prospective Investigation into Cancer and Nutrition Cohort	7119/319,826	1992–2003	Red meat	1.06 (0.98, 1.14)	Energy, height, weight, years of schooling, smoking, and menopause
				Processed meat	1.10 (1.00, 1.20)	
Genkinger et al./2013/United States	Black Women's Health Study (BWHS)	1268/52,062	1995–2007	Red meat	1.02 (0.83, 1.24)	Energy intake, age at menarche, BMI, family history of breast cancer, education, parity and age at first live birth, oral contraceptive use, menopausal hormone use, vigorous physical activity, smoking status, and alcohol intake
				Processed meat	0.99 (0.82, 1.20)	
Takemi et al./2014/United States	Nurses' Health Study II	2830/88,803	1991–2011	Total red meat	1.22 (1.06, 1.40)	Age, height, weight, family history of breast cancer, history of benign breast disease, smoking, race, age at menarche, parity, age at first birth, menopausal status, postmenopausal hormone use, age at menopause and oral contraceptive use
Pouchieu et al./2014/France	SU.VI.MAX Study	190/4684	1994–2007	Red meat	1.19 (0.79, 1.80)	Age, intervention group, number of dietary records, smoking status, educational level, physical activity, height, BMI, family history of breast cancer, menopausal status at baseline, use of HTM at baseline, number of live births, without-alcohol energy intake, alcohol intake, total lipid intake. In addition, the red meat model is adjusted for processed meat intake and conversely
				Processed meat	1.45 (0.92, 2.27)	

RR relative risk, *CI* confidence interval, *BMI* body mass index, *OCP* oral contraceptive pill, *HRT* hormone replacement therapy, *HTM* hormonal treatment for menopause, *NHANES* National Health and Nutrition Examination Survey

20 years of follow-up among 88,803 premenopausal women from the Nurses' Health Study II found that greater intake of total red meat was associated with an increased risk of breast cancer (highest vs. lowest quintiles, RR, 1.22; 95 % CI, 1.06–1.40; P trend = 0.01) [4]. Another study with 13-year follow-up by Farvid MS et al. (including

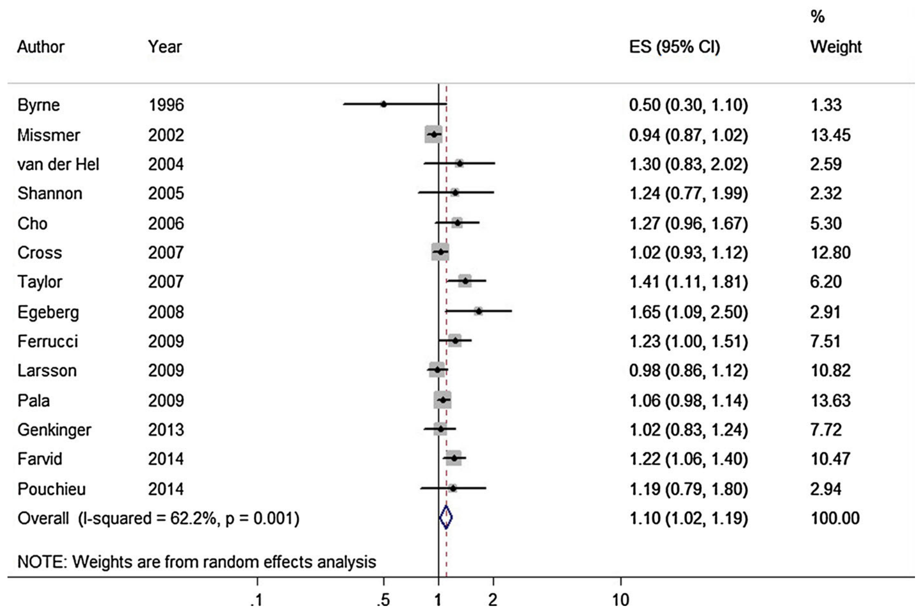

Fig. 2 Relative risks of breast cancer comparing the highest with the lowest category of red meat consumption. *Squares* indicate study-specific relative risks (size of the square reflects the statistical weight that each study contribute to the summary estimate); *horizontal lines* indicate 95 % CI; *diamond* indicates summary relative risk estimate with corresponding 95 % CI

44,231 women) also observed that higher consumption of total red meat in adolescence was significantly associated with increased premenopausal breast cancer risk (highest vs. lowest quintiles, RR, 1.43; 95 % CI, 1.05–1.94; *P* trend = 0.007) [5]. Using the data from the SU.VI.MAX study, Pouchieu C et al. demonstrated that processed meat intake was prospectively associated with increased breast cancer risk (highest vs. lowest quartiles, RR, 1.45; 95 % CI, 0.92–2.27, *P* trend = 0.03) [6]. In the current updated meta-analysis, after excluding the studies from the same study population, we finally included 14 prospective studies and found statistically significant relationship between red and processed meat consumption and breast cancer risk (highest vs. lowest categories, summary RR, 1.10; 95 % CI, 1.02–1.19 for red meat, and summary RR, 1.08; 95 % CI, 1.01–1.15 for processed meat).

Several suggested biological mechanisms might explain the positive association between red meat or processed meat intake and breast cancer risk. The first mechanism concerns the heme iron and non-heme iron. Iron, which has a pro-oxidant activity, has been suggested as a risk factor for many types of cancers [30]. However, epidemiological studies have yielded mixed and contentious results regarding the relationship between iron and breast cancer [20]. Moreover, a cohort study included in our meta-analysis revealed that adjusting for heme iron did not appreciably change the association between red meat intake and breast cancer risk [4], indicating that heme iron might not be a major causal fact for the association between red meat intake and breast cancer risk. Another important mechanism that may explain the positive association relates to the presence of some carcinogenic compounds like the heterocyclic amines (HCAs) and polycyclic aromatic hydrocarbons (PAHs), by-products that are produced in the process of high-temperature cooking of red meat [31, 32]. Several human studies have demonstrated a positive association between HCA and PAH intake and overall breast cancer risks [31, 33–38]. In addition, hormone residues of the exogenous hormones used to treat beef cattle also are recognized as possible sources of the positive association between red meat intake and breast cancer risk [39, 40]. Recently, a new study published on PNAS has revealed that the animal sugar molecule *N*-glycolylneuraminic acid (Neu5Gc), which is highly enriched in red meat, would be absorbed and accumulated in human tissues, and eventually lead to chronic inflammation and tumor formation [41].

Our meta-analysis has several strengths. Firstly, the assessment was based on prospective studies, which tend to be less likely to have recall and selection bias than retrospective case–control studies. Moreover, our studies included a large sample size (1588,890 participants and 31,552 breast cancer cases) which would have a much greater possibility of reaching detecting smaller associations and performing subgroup analysis. However, there were also some limitations in this meta-analysis. First, the inherent problems of residual confounders in the included studies are of concern in the meta-analysis of observational studies. Most of the studies included in our meta-analysis controlled for a wide range of confounders (such as age, BMI, and total energy intake), and some of these studies even had controlled for postmenopausal hormone treatment and Hormone replacement therapy (of note, adjustment for all possible confounders might result in over-adjustment.). However, we still cannot exclude the possibility that other inadequately measured factors such as environmental pollution [42, 43] and sleep quality [44], which might confound the association,

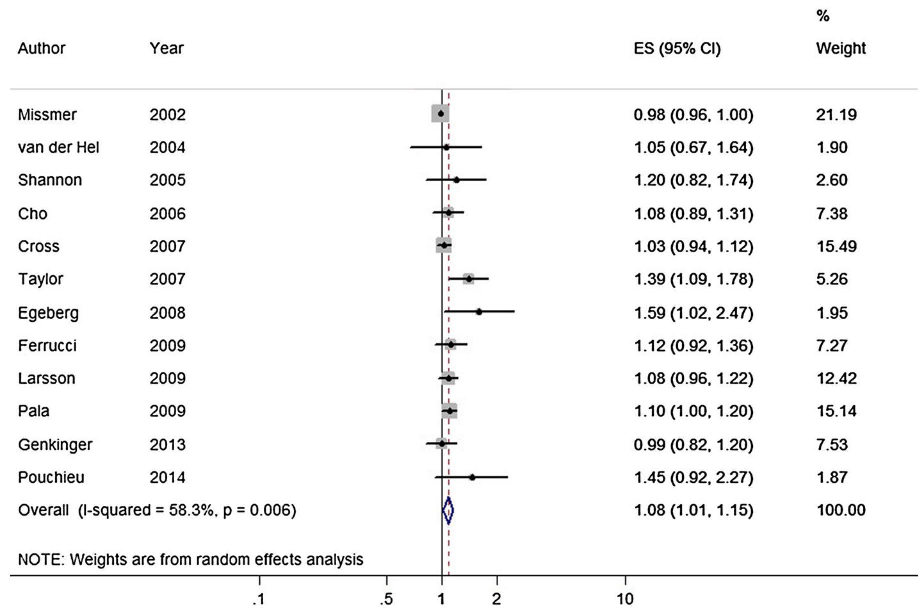

Fig. 3 Relative risks of breast cancer comparing the highest with the lowest category of processed meat consumption. *Squares* indicate study-specific relative risks (size of the square reflects the statistical weight that each study contribute to the summary estimate); *horizontal lines* indicate 95 % CI; *diamond* indicates summary relative risk estimate with corresponding 95 % CI

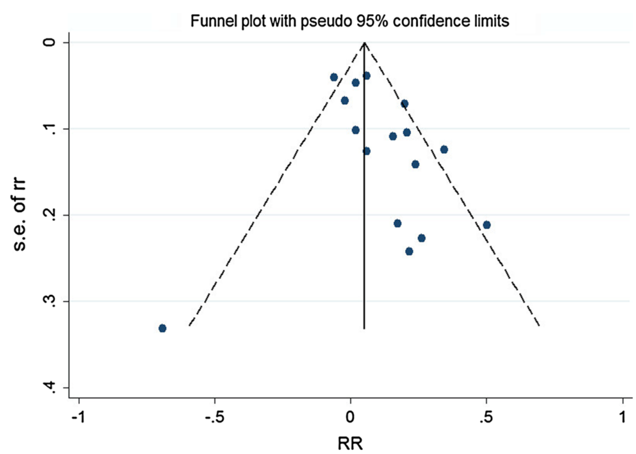

Fig. 4 Funnel plot for prospective studies of red meat and breast cancer. (*SE* standard error, *rr*/*RR* relative risk.)

should be included in the future studies. Second, our findings are likely to be affected by the misclassification of meat. In the studies included in our meta-analysis, the term "red meat" referred to total red meat, corresponding to processed red meat in some studies and to unprocessed red meat in other studies. However, misclassification is generally non-differential in cohort studies, which would most likely attenuate the association. Third, the intake quantity and consumption levels in the highest and lowest categories varied across studies, which might contribute the heterogeneity among studies in the analysis of the highest *versus* the lowest intake categories. To account for these differences, we also estimated the relative risks of breast cancer for an increase intake of red meat of 120 g/day and of processed meat of 50 g/day, and similar results were observed. Finally, as with any meta-analysis, publication bias could be of concern, because studies with null results or small sample sizes tend not to be published. Thus, the summary results may overestimate the relative risk of breast cancer with red and/or processed meat intake.

In conclusion, the overall results of the present study suggest that high intake of red and/or processed meat is associated with an increased risk of breast cancer. However, additional well-designed cohort or interventional studies will be needed to confirm the association.

Acknowledgments The study was supported by grants from the Ministry of Science and Technology of China (2011CB510104 and 2012CB945004), the National Natural Science Foundation of China (31090362), the National Natural Science Foundation of China (81071684), the Hundred Talents Program (2010OHTP11), Shanghai PuJiang Talent program (11PJ1411200), and the Ministry of Science and Technology of China (2012BAK01B00).

Conflict of interest The authors of this study have no conflict of interest or any financial disclosures to make.

References

1. Parkin DM, Pisani P, Ferlay J (1999) Global cancer statistics. CA 49:33–64
2. DeSantis C, Ma JM, Bryan L, Jemal A (2014) Breast cancer statistics, 2013. CA 64:52–62
3. de Lorgeril M, Salen P (2014) Helping women to good health: breast cancer, omega-3/omega-6 lipids, and related lifestyle factors. BMC Med 12:54
4. Farvid MS, Cho E, Chen WY, Eliassen AH, Willett WC (2014) Dietary protein sources in early adulthood and breast cancer incidence: prospective cohort study. BMJ 348:g3437

5. Farvid MS, Cho E, Chen WY, Eliassen AH, Willett WC (2014) Adolescent meat intake and breast cancer risk. Int J Cancer 136:1909–1920
6. Pouchieu C, Deschasaux M, Hercberg S et al (2014) Prospective association between red and processed meat intakes and breast cancer risk: modulation by an antioxidant supplementation in the SU.VI.MAX randomized controlled trial. Int J Epidemiol 43:1583–1592
7. Genkinger JM, Makambi KH, Palmer JR, Rosenberg L, Adams-Campbell LL (2013) Consumption of dairy and meat in relation to breast cancer risk in the Black Women's Health Study. Cancer Causes Control 24:675–684
8. Lee HJ, Wu K, Cox DG et al (2013) Polymorphisms in xenobiotic metabolizing genes, intakes of heterocyclic amines and red meat, and postmenopausal breast cancer. Nutr Cancer 65:1122–1131
9. Alexander DD, Morimoto LM, Mink PJ, Cushing CA (2010) A review and meta-analysis of red and processed meat consumption and breast cancer. Nutr Res Rev 23:349–365
10. Stroup DF, Berlin JA, Morton SC et al (2000) Meta-analysis of observational studies in epidemiology: a proposal for reporting. Meta-analysis Of Observational Studies in Epidemiology (MOOSE) group. JAMA 283:2008–2012
11. Byrne C, Ursin G, Ziegler RG (1996) A comparison of food habit and food frequency data as predictors of breast cancer in the NHANES I/NHEFS cohort. J Nutr 126:2757–2764
12. Missmer SA, Smith-Warner SA, Spiegelman D et al (2002) Meat and dairy food consumption and breast cancer: a pooled analysis of cohort studies. Int J Epidemiol 31:78–85
13. van der Hel OL, Peeters PH, Hein DW et al (2004) GSTM1 null genotype, red meat consumption and breast cancer risk (The Netherlands). Cancer Causes Control 15:295–303
14. Shannon J, Ray R, Wu C et al (2005) Food and botanical groupings and risk of breast cancer: a case-control study in Shanghai, China. Cancer Epidemiol Biomark Prev 14:81–90
15. Cho EY, Chen WY, Hunter DJ et al (2006) Red meat intake and risk of breast cancer among premenopausal women. Arch Intern Med 166:2253–2259
16. Taylor EF, Burley VJ, Greenwood DC, Cade JE (2007) Meat consumption and risk of breast cancer in the UK Women's Cohort Study. Br J Cancer 96:1139–1146
17. Cross AJ, Leitzmann MF, Gail MH et al (2007) A prospective study of red and processed meat intake in relation to cancer risk. PLoS Med 4:1973–1984
18. Egeberg R, Olsen A, Autrup H et al (2008) Meat consumption, *N*-acetyl transferase 1 and 2 polymorphism and risk of breast cancer, in Danish postmenopausal women. Eur J Cancer Prev 17:39–47
19. Pala V, Krogh V, Berrino F et al (2009) Meat, eggs, dairy products, and risk of breast cancer in the European prospective investigation into cancer and nutrition (EPIC) cohort. Am J Clin Nutr 90:602–612
20. Ferrucci LM, Cross AJ, Graubard BI et al (2009) Intake of meat, meat mutagens, and iron and the risk of breast cancer in the Prostate, Lung, Colorectal, and Ovarian Cancer Screening Trial. Br J Cancer 101:178–184
21. Larsson SC, Bergkvist L, Wolk A (2009) Long-term meat intake and risk of breast cancer by oestrogen and progesterone receptor status in a cohort of Swedish women. Eur J Cancer 45:3042–3046
22. Stang A (2010) Critical evaluation of the Newcastle–Ottawa scale for the assessment of the quality of nonrandomized studies in meta-analyses. Eur J Epidemiol 25:603–605
23. DerSimonian R, Laird N (1986) Meta-analysis in clinical trials. Control Clin Trials 7:177–188
24. Greenland S, Longnecker MP (1992) Methods for trend estimation from summarized dose-response data, with applications to meta-analysis. Am J Epidemiol 135:1301–1309
25. Orsini N, Bellocco R, Greenland S (2006) Generalized least squares for trend estimation of summarized dose–response data. Stata J 6:40–57
26. Norat T, Lukanova A, Ferrari P, Riboli E (2002) Meat consumption and colorectal cancer risk: dose-response meta-analysis of epidemiological studies. Int J Cancer 98:241–256
27. Higgins JP, Thompson SG, Deeks JJ, Altman DG (2003) Measuring inconsistency in meta-analyses. BMJ 327:557–560
28. Egger M, Davey Smith G, Schneider M, Minder C (1997) Bias in meta-analysis detected by a simple, graphical test. BMJ 315:629–634
29. Begg CB, Mazumdar M (1994) Operating characteristics of a rank correlation test for publication bias. Biometrics 50:1088–1101
30. Fonseca-Nunes A, Jakszyn P, Agudo A (2014) Iron and cancer risk-a systematic review and meta-analysis of the epidemiological evidence. Cancer Epidemiol Biomark 23:12–31
31. Kazerouni N, Sinha R, Hsu CH, Greenberg A, Rothman N (2001) Analysis of 200 food items for benzo[a] pyrene and estimation of its intake in an epidemiologic study. Food Chem Toxicol 39:423–436
32. Knize MG, Salmon CP, Pais P, Felton JS (1999) Food heating and the formation of heterocyclic aromatic amine and polycyclic aromatic hydrocarbon mutagens/carcinogens. Adv Exp Med Biol 459:179–193
33. De Stefani E, Ronco A, Mendilaharsu M, Guidobono M, Deneo-Pellegrini H (1997) Meat intake, heterocyclic amines, and risk of breast cancer: a case-control study in Uruguay. Cancer Epidemiol Biomark 6:573–581
34. Rundle A, Tang DL, Hibshoosh H et al (2000) The relationship between genetic damage from polycyclic aromatic hydrocarbons in breast tissue and breast cancer. Carcinogenesis 21:1281–1289
35. Sinha R, Gustafson DR, Kulldorff M et al (2000) 2-amino-1-methyl-6-phenylimidazo [4,5 b] pyridine, a arcinogen in high-temperature -cooked meat, and breast cancer risk. J Natl Cancer Inst 92:1352–1354
36. Gammon MD, Santella RM, Neugut AI et al (2002) Environmental toxins and breast cancer on long Island. I. Polycyclic aromatic hydrocarbon DNA adducts. Cancer Epidemiol Biomark 11:677–685
37. Bonner MR, Han D, Nie J et al (2005) Breast cancer risk and exposure in early life to polycyclic aromatic hydrocarbons using total suspended particulates as a proxy measure. Cancer Epidemiol Biomark 14:53–60
38. Zheng W, Lee SA (2009) Well-done meat intake, heterocyclic amine exposure, and cancer risk. Nutr Cancer 61:437–446
39. Andersson AM, Skakkebaek NE (1999) Exposure to exogenous estrogens in food: possible impact on human development and health. Eur J Endocrinol 140:477–485
40. Stephany RW (2001) Hormones in meat: different approaches in the EU and in the USA. Apmis 109:S357–S363
41. Samraj AN, Pearce OM, Laubli H et al (2015) A red meat-derived glycan promotes inflammation and cancer progression. Proc Natl Acad Sci USA 112:542–547
42. Brody JG, Rudel RA (2003) Environmental pollutants and breast cancer. Environ Health Perspect 111:1007–1019
43. Brody JG, Moysich KB, Humblet O, Attfield KR, Beehler GP, Rudel RA (2007) Environmental pollutants and breast cancer: epidemiologic studies. Cancer 109:2667–2711
44. Girschik J, Heyworth J, Fritschi L (2013) Self-reported sleep duration, sleep quality, and breast cancer risk in a population-based case-control study. Am J Epidemiol 177:316–327