JJCO Japanese Journal of Clinical Oncology

Japanese Journal of Clinical Oncology, 2015, 45(12) 1107–1115
doi: 10.1093/jjco/hyv150
Advance Access Publication Date: 21 October 2015
Original Article

OXFORD

Original Article

The association between overweight, obesity and ovarian cancer: a meta-analysis

Zhen Liu, Ting-Ting Zhang, Jing-Jing Zhao, Su-Fen Qi, Pei Du, Dian-Wu Liu, and Qing-Bao Tian*

Department of Epidemiology and Statistics, School of Public Health, Hebei Medical University, Shijiazhuang, China

*For reprints and all correspondence: Qing-Bao Tian, Department of Epidemiology and Statistics, School of Public Health, Hebei Medical University, 361 East Zhongshan Road, Shijiazhuang 050017, Hebei Province, China. E-mail: tqb1980@hebmu.edu.cn

Received 24 June 2015; Accepted 8 September 2015

Abstract

Objective: Epidemiological studies have reported an inconsistent association between obesity and ovarian cancer. To update the current knowledge of and further qualify the association between overweight, obesity and ovarian cancer risk, we conducted a meta-analysis of published observational studies.

Methods: Using the PubMed, MEDLINE and EMBASE databases, we performed a literature search of all of the case–control and cohort studies published as original articles in English before March 2015. We included 26 observational studies, of which 13 were case–control studies (7782 cases and 21 854 controls) and 13 were cohort studies (5181 cases). Fixed- and random-effects models were used to compute summary estimates and the corresponding 95% confidence intervals. Subgroup analyses were also performed.

Results: The pooled relative risk for overweight and obesity compared with normal weight (body mass index = 18.5–24.9 kg/m^2) was 1.07 (95% confidence interval: 1.02–1.12) and 1.28 (95% confidence interval: 1.16–1.41), respectively. In subgroup analyses, we found that overweight/obesity increased the risk of ovarian cancer in most groups, except for the postmenopausal group (overweight: pooled relative risk = 0.97, 95% confidence interval: 0.76–1.24; obesity: pooled relative risk = 0.93, 95% confidence interval: 0.61–1.42). There was no evidence of publication bias.

Conclusions: Increased body weight was associated with an increased risk of ovarian cancer; in particular, severe obesity demonstrated a stronger risk effect. No statistically significant association was observed in the postmenopausal period, but was in the premenopausal period.

Key words: ovarian cancer, obesity, body mass index, risk, meta-analysis

Introduction

Ovarian cancer (OC) is the eighth most common cancer and the seventh most common cause of death from cancer in women worldwide; it is the second most common cause of death among female reproductive malignancies and claims 140 200 lives each year (1). In addition, the majority of cases are diagnosed with OC at later stages. Despite efforts to improve early detection and treatment, OC is the most fatal gynaecologic cancer, with a 44% five-year survival rate (2).

While the debate regarding the reason for increased OC incidence continues, risk factors for OC are still not well established. Age, family history of OC, infertility treatment and assisted fertilization, hormonal substitution in menopause and obesity are potential factors in favour of developing OC (3,4). Because there are differences in the methodology and different means in defining obesity in the published research, an explanation of the results of epidemiological studies on the relation between obesity and OC has been hampered, and the

results of earlier observational studies were less conclusive. There have been several previous meta-analyses (5–8) that used different search methods and databases; these meta-analyses showed a significant association between body mass index (BMI) and OC risk. However, these studies have the conflicting conclusions as to whether increased body weight was associated with OC in different menopausal statuses. The aim of this meta-analysis was to update the current knowledge about the association of both cohort and case–control studies between overweight, obesity and OC risk and to explore whether this association was modified by menopausal status.

Patients and methods

Search strategy

A systematic search was performed in the PubMed, MEDLINE and EMBASE databases to find studies published in English before March 2015. We used the keywords 'body mass index', 'BMI', 'overweight' or 'obesity' in combination with 'ovarian carcinoma', 'ovarian cancer' or 'ovarian neoplasm'. Furthermore, we reviewed the reference lists of relevant articles to search for additional studies.

Selection criteria

Studies were included in the meta-analysis if they fulfilled the following criteria: (i) observational studies (case–control studies or cohort studies) in which OC incidence was an outcome; (ii) clear definition of overweight and obesity as defined by the BMI in kg/m^2 and (iii) reported effect estimates of the relative risk (RR), hazard ratio (HR) or odds ratio (OR) with 95% confidence intervals (CIs).

Statistical analysis

BMI was categorized as follows: <18.5, 18.5–24.9, 25.0–29.9 and ≥30 for underweight, normal weight, overweight and obese, respectively, according to World Health Organization (WHO) categories (9). Where non-standard categories of BMI were used, we selected the

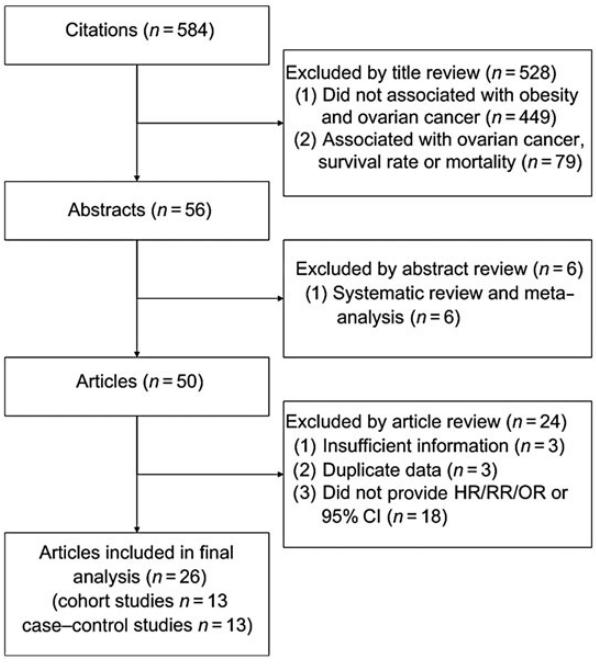

Figure 1. Flowchart of the study selection.

Table 1. Characteristics of the included cohort studies on overweight, obesity and ovarian cancer

Author, date, country	Year of study	Study name	Age	Cases	Cohort sizes	Exposure measure
Ma, 2013, China	1996–2000	Shanghai Women's Health Study (SWHS)	40–70	152	70 258	Measured at baseline
Brändstedt, 2011, Sweden	1991–96	The Malmö Diet and Cancer Study (MDCS)	Not given	93	17 035	Measured at baseline
Kotsopoulos, 2010, USA	NHS	Nurses' Health Study (NHS) and NHSII	NHS	862	NHS	Self-reported at baseline
	1979–2006		30–55		121 700	
	NHSII		NHSII		NHSII	
	1989–2005		25–42		116 430	
Lahmann, 2010, Europe	1992–2000	European Prospective Investigation into Cancer and Nutrition (EPIC) cohort study	35–70	611	226 798	Measured at baseline
Leitzmann, 2009, USA	1996–2003	The National Institutes of Health (NIH)-AARP Diet and Health Study	50–71	303	94 525	Self-reported at baseline
Reeves, 2007, UK	1996–2001	The Million Women Study	50–64	2406	1 222 630	Self-reported at baseline
Rapp, 2005, Austria	1985–2001	The Vorarlberg Health Monitoring and Promotion Program (VHM&PP) Study Cohort	19–93	121	78 484	Measured at baseline
Kuriyama, 2005, Japan	1984–92	A population-based prospective cohort study in Japan	≥40	5	15 054	Self-reported at baseline
Niwa, 2005, Japan	1988–99	Japanese Collaborate Cohort (JACC) study	40–79	38	36 456	Self-reported at baseline
Anderson, 2004, USA	1986–2000	The Iowa Women's Health Study Cohort	55–69	223	41 836	Measured at baseline; self-reported at age 18
Schouten, 2003, The Netherlands	1986–93	The Netherlands Cohort Study on Diet and Cancer	55–69	172	62 573	Self-reported at baseline; self-reported at age 20
Jonsson, 2003, Sweden	1969–97	Cohort and co-twin control studies based on the Swedish twin registry	44–83	118	11 598	Self-reported at baseline
Wolk, 2001, Sweden	1964–93	A population-based cohort of hospital patients with any discharge diagnosis of obesity	Not given	77	19 964	Height and weight recorded from hospital records

Table 2. Characteristics of the included case–control studies on overweight, obesity and ovarian cancer

Author, date, country	Year of study	Age	Cases/ controls	Case sources	Control sources	Exposure measure
Schildkraut, 2014, USA	2010–14	20–79	403/639	Newly diagnosed cases from Surveillance, Epidemiology and End Results (SEER) registries or gynaecologic oncology departments at individual hospitals	Population-based random-digit dialing (RDD) by an outside contractor (Kreider Research and Consulting)	Self-reported Current height and weight; age 18
Delort, 2009, France	1996–99 2005–06	24–84	55/857	Incident cases from hospitals within the Auvergne region, enrolled in the COSA (Breast and Ovarian Cancer in Auvergne) programme	Population-based gathered in a mammographic screening centre	Self-reported Current height and weight; age 20
Olsen, 2008, Australia	2002–05	18–79	1580/1509	Newly diagnosed, histologically confirmed cases from state cancer registries throughout Australia	Population-based randomly selection from the national electoral roll	Self-reported One year prior to diagnosis/ interview; age 20
Rossing, 2006, USA	1994–98	35–54	355/1637	Incident cases from SEER registry in metropolitan Atlanta, Detroit and Seattle	Population-based RDD in metropolitan Atlanta, Detroit and Seattle	Self-reported Five years before diagnosis/ reference date; age 18, 30
Peterson, 2006, USA	1993–95 1998–2001	20–79	700/5943	Newly diagnosed, state cancer registries in Wisconsin and Massachusetts	Population-based randomly selection from lists of licensed drivers and rosters of Medicare beneficiaries compiled by the Centers for Medicare and Medicaid Services	Self-reported One year prior to diagnosis/ interview; age 20
Beehler, 2006, USA	1982–98	Not given	427/854	Incident cases from Roswell Park Cancer Institute (RPCI) in Buffalo, NY	Hospital-based randomly selection from who were not diagnosed with a pathological condition in Roswell Park Cancer Institute (RPCI)	Self-reported BMI calculated from 'usual weight'
Hoyo, 2005, USA	1999–2003	20–74	593/628	Newly diagnosed, North Carolina Central Cancer Registry	Population-based RDD and ascertained through Health Care Financing Administration lists	Self-reported One year prior to diagnosis/ interview; age 18
Riman, 2004, Sweden	1993–95	50–74	655/3899	Incident cases from regional tumour registries	Population-based randomly selection from a national population registry	Self-reported One year prior to interview
Pike, 2004, USA	1992–98	18–74	467/660	Histologically confirmed cases from the cancer registry of Los Angeles County	Population-based randomly selection from Los Angeles County	One year prior to diagnosis/ interview
Pan, 2004, Canada	1994–97	21–76	442/2492	National Enhanced Cancer Surveillance System (NECSS) in Canada	Population-based stratified random sample and RDD	Self-reported Two years prior to interview
Kuper, 2002, USA	1992–97	Not given	563/523	Incident cases from hospital tumour boards and statewide cancer registries in eastern Massachusetts (MA) or New Hampshire (NH)	Population-based RDD and selection from community lists (townbooks)	Self-reported One year prior to diagnosis/ interview
Purdie, 2001, Australia	1990–93	18–79	775/846	Incident cases from gynaecological oncology treatment centres in New South Wales, Victoria and Queensland	Population-based randomly selection from state electoral roll	Self-reported 'Usual weight before their illness'
Ness, 2000, USA	1994–98	20–69	767/1367	Newly diagnosed, 39 hospitals around the Delaware Valley	Population-based RDD in the same geographic region and ascertained through Health Care Financing Administration lists	Self-reported Six months prior to interview

BMI, body mass index.

category that was most similar to those defined by the WHO. Because cancer could be considered to be a relatively rare event, we assumed that the ORs, risk ratios and rate ratios were all comparable estimates of the RR (10). Thus, we collected maximally adjusted HR, RR or OR estimates (for the comparison of individuals in the 'overweight' and 'obesity' category with those with 'normal weight') in our analysis. We included studies that used a reference BMI category that was less than the WHO defined 'normal BMI' if the RR estimate for the 'normal BMI' category was 1.0 compared with the reference category (5). Some studies did not provide the required risk estimates for analysis; thus, we combined the risk estimates into a single required category with the fixed-effect model.

The statistical heterogeneity among studies was tested with the Q statistic, and inconsistency was quantified with the I^2 statistic (11). For the Q statistic, statistical significance was set at $P < 0.1$. When heterogeneity was detected, the random-effects model was used (12). To evaluate the potential for publication bias, a visual inspection of asymmetry in funnel plots was performed, and the symmetry of the funnel plot was tested using Egger's test and Begg's test ($P < 0.05$ was considered to be a representative of statistically significant publication bias) (13). We also conducted a sensitivity analysis in which one study was removed and the rest were analysed to confirm the stability of the overall result.

Subgroup analyses were carried out based on the study design (cohort and case–control), race (Caucasian and Asian), body size assessment (measured and self-reported) and menopausal status (premenopausal and postmenopausal). All of the statistical analyses were performed using STATA12.0 (StataCorp, College Station, TX, USA).

Results

Characteristics of studies that were included in the meta-analysis

We identified 584 potential relevant studies by a primary computerized literature search. After screening titles and abstracts and reviewing the full-text articles, 13 cohort studies (14–26) and 13 case–control studies (27–39) were obtained (Fig. 1). Of these studies, 11 were conducted in the United States, 9 in Europe, 3 in Asia, 2 in Australia and 1 in Canada. The main characteristics of the studies that were included in the meta-analysis are summarized in Tables 1 and 2 for cohort and case–control studies, respectively.

Association of overweight, obesity and risk for OC

As shown in Fig. 2, we compared the 'overweight' category with 'normal weight' (BMI = 18.5–24.9 kg/m^2) to estimate the RR. There was a statistically significant association (pooled RR = 1.07, 95% CI: 1.02–1.12) between overweight and OC risk.

In Fig. 3, the analysis of all of the studies revealed a statistically significant association between obesity and OC risk (pooled RR = 1.28,

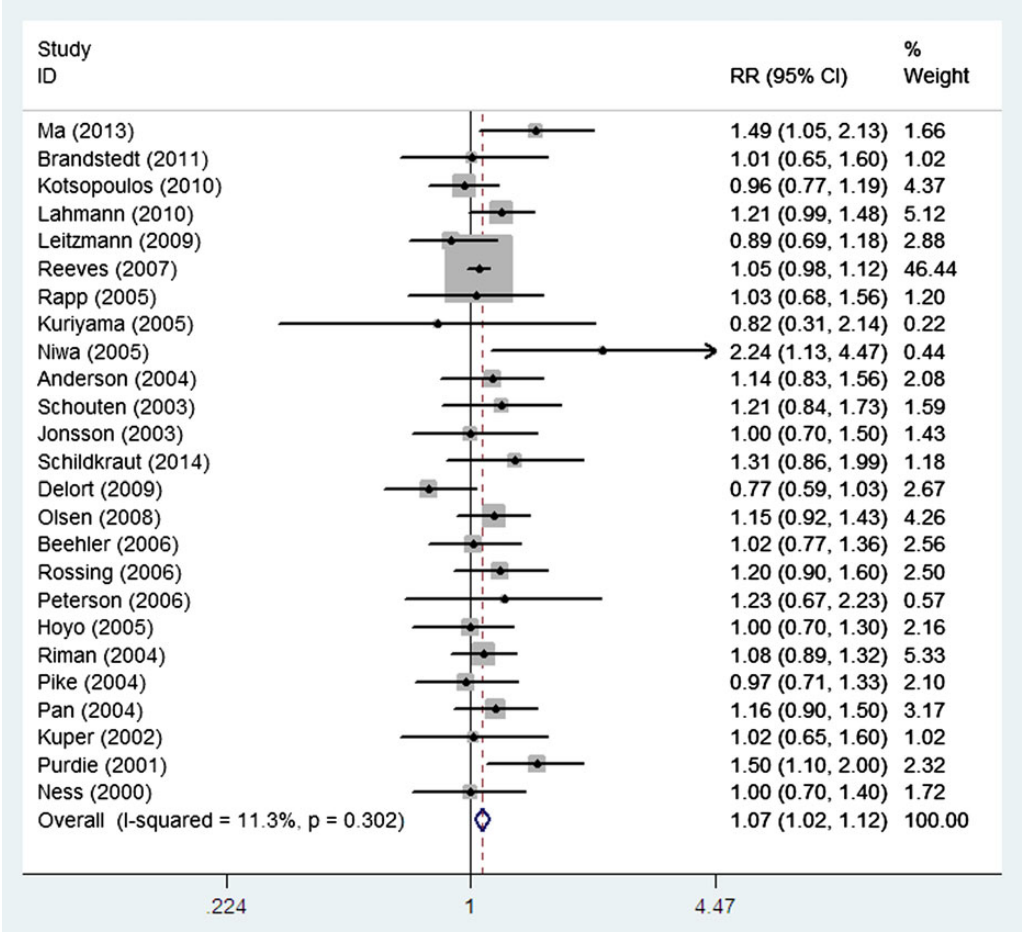

Figure 2. Forest plot for the association between overweight and ovarian cancer risk. Relative risk estimates are for the comparison of individuals in the 'overweight' category with those in the 'normal weight' category.

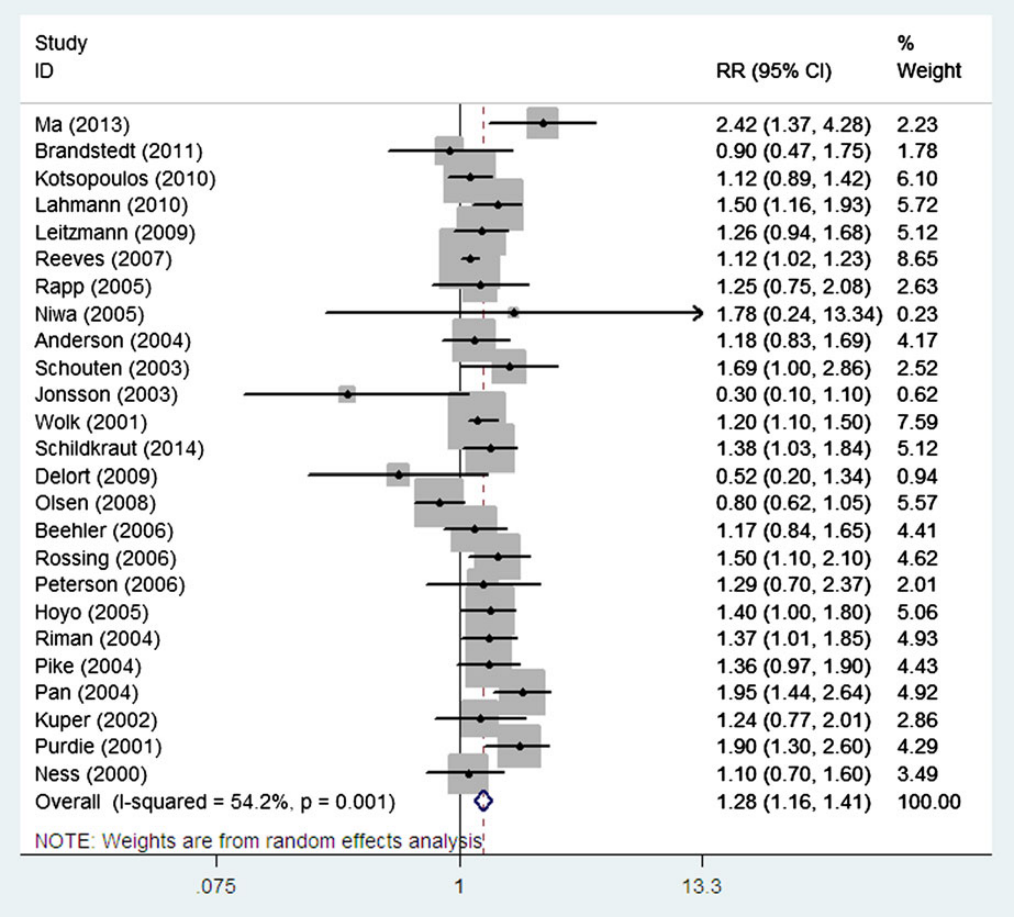

Figure 3. Forest plot for the association between obesity and ovarian cancer risk. Relative risk estimates are for the comparison of individuals in the 'obesity' category with those in the 'normal weight' category.

95% CI: 1.16–1.41) compared with normal weight (BMI = 18.5–24.9 kg/m^2).

Subgroup analyses

The results of subgroup analyses according to the study design, race, body size assessment and menopausal status are presented in Table 3. Increased body weight was associated with an increased risk of OC in both the cohort studies (overweight: pooled RR = 1.07, 95% CI: 1.01–1.13; obesity: pooled RR = 1.23, 95% CI: 1.10–1.39) and the case–control studies (overweight: pooled RR = 1.09, 95% CI: 1.00–1.18; obesity: pooled RR = 1.31, 95% CI: 1.21–1.54). As shown in Table 3, overweight and obesity were associated with an increased risk of OC in both the Caucasian studies (overweight: pooled RR = 1.06, 95% CI: 1.02–1.11; obesity: pooled RR = 1.26, 95% CI: 1.15–1.39) and the Asian studies (overweight: pooled RR = 1.52, 95% CI: 1.13–2.05; obesity: pooled RR = 2.37, 95% CI: 1.37–4.09). When stratifying for menopausal status, overweight and obesity were associated with an increased risk of OC in the premenopausal period (overweight: pooled RR = 1.31, 95% CI: 1.04–1.65; obesity: pooled RR = 1.50, 95% CI: 1.12–2.00). However, no statistically significant association was observed in the postmenopausal period (overweight: pooled RR = 0.97, 95% CI: 0.76–1.24; obesity: pooled RR = 0.93, 95% CI: 0.61–1.42). Overweight and obesity were associated with an increased risk of OC risk in both the self-reported studies (overweight: pooled RR = 1.06, 95% CI: 1.01–1.11; obesity: pooled RR = 1.27, 95% CI: 1.13–1.43) and the measured studies (overweight: pooled RR = 1.19, 95% CI: 1.04–1.37; obesity: pooled RR = 1.28, 95% CI: 1.14–1.44).

Publication bias and sensitivity analysis

We detected no publication bias in the literature on BMI and OC risk in the 'overweight' and 'obesity' groups based on either Egger's test ($P = 0.31$ and 0.37, respectively) or Begg's test ($P = 0.30$ and 0.83, respectively). In the sensitivity analyses, there was no significant variation in the pooled RR by excluding any of the studies, supporting the robustness of our results (Figs 4 and 5).

Discussion

A total of 12 963 cases in 26 independent studies were identified in this current meta-analysis. The results of this current meta-analysis, including 13 case–control and 13 cohort studies, indicate that overweight and obesity are associated with an increased risk of OC. When stratified by the degree of obesity, the overweight studies were associated with a slightly increased risk of OC, and the results from the obesity studies demonstrated a stronger risk effect.

In subgroup analyses, we found that overweight and obesity could increase the risk of OC in most groups, except for the postmenopausal group. The summary RR estimate was slightly lower for cohort studies than for case–control studies. Olsen et al. (5) also reported that the summary estimate was slightly lower in cohort studies, but these

Table 3. Pooled RRs of ovarian cancer for overweight/obesity compared with normal weight and corresponding 95% CIs

Studies groups	No. of studies	Fixed-effects RR (95% CI)	Random-effects RR (95% CI)	*Q*-test for heterogeneity	
				I^2 score (%)	*P* value
Overweight					
Study design					
Cohort studies	12	1.07 (1.01, 1.13)	1.08 (0.99, 1.17)	17.9	0.268
Case–control studies	13	1.09 (1.00, 1.18)	1.09 (1.00, 1.19)	11.1	0.334
Race					
Caucasian	22	1.06 (1.02, 1.11)	1.06 (1.02, 1.11)	0	0.604
Asian	3	1.52 (1.13, 2.05)	1.51 (1.01, 2.28)	28.6	0.246
Menopausal status					
Premenopausal	6	1.31 (1.04, 1.65)	1.32 (0.98, 1.77)	36.1	0.166
Postmenopausal	6	1.00 (0.87, 1.14)	0.97 (0.76, 1.24)	64.1	0.016
Body size assessment					
Self-reported	20	1.06 (1.01, 1.11)	1.06 (1.00, 1.13)	12.8	0.296
Measured	5	1.19 (1.04, 1.37)	1.19 (1.04, 1.37)	0	0.623
Obesity					
Study design					
Cohort studies	12	1.18 (1.11, 1.26)	1.23 (1.10, 1.39)	41.5	0.065
Case–control studies	13	1.32 (1.20, 1.45)	1.31 (1.12, 1.54)	60.5	0.002
Race					
Caucasian	23	1.22 (1.15, 1.29)	1.26 (1.15, 1.39)	53.2	0.001
Asian	2	2.37 (1.37, 4.09)	2.37 (1.37, 4.09)	0	0.773
Menopausal status					
Premenopausal	6	1.50 (1.12, 2.00)	1.50 (1.12, 2.00)	0	0.501
Postmenopausal	6	1.02 (0.86, 1.21)	0.93 (0.61, 1.42)	77.6	0
Body size assessment					
Self-reported	19	1.21 (1.14, 1.29)	1.27 (1.13, 1.43)	58.5	0.001
Measured	6	1.28 (1.14, 1.44)	1.32 (1.10, 1.58)	39.5	0.142

RR, relative risk; CI, confidence interval.

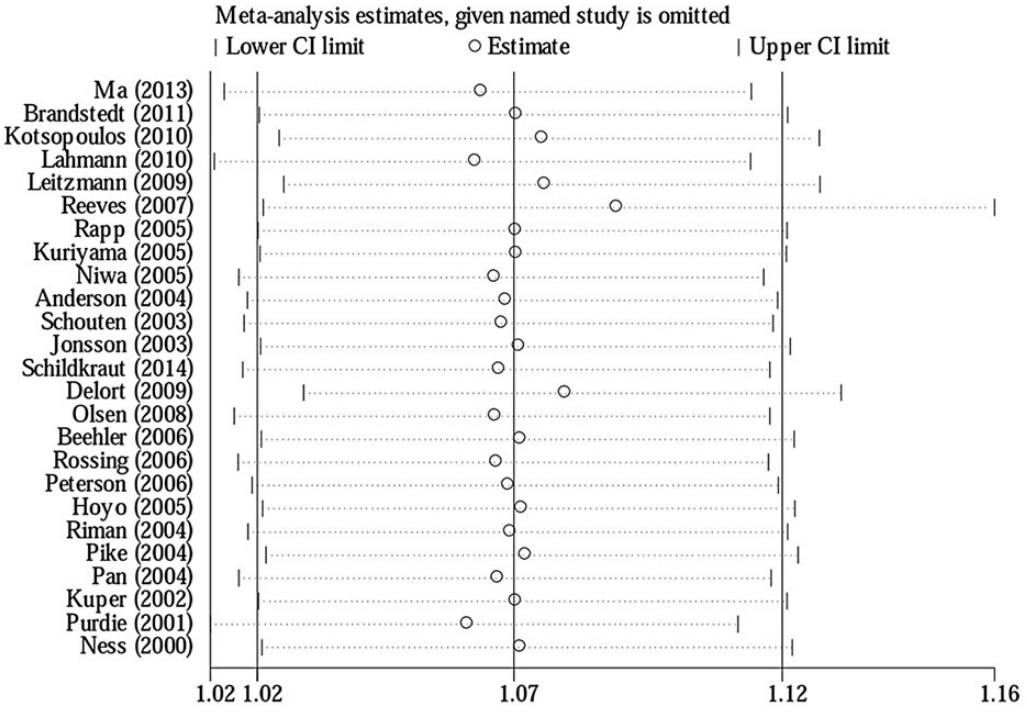

Figure 4. Sensitivity analyses for overweight versus normal weight.

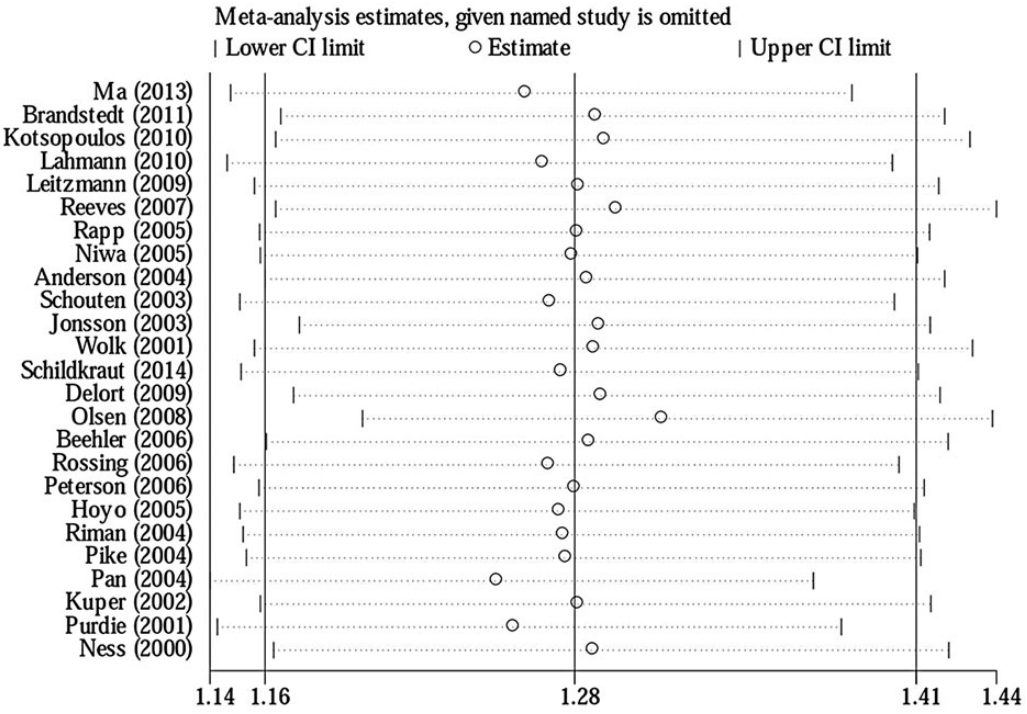

Figure 5. Sensitivity analyses for obesity versus normal weight.

authors did not perform a subgroup analysis. Another meta-analysis was conducted by the Collaboration Group on Epidemiological Studies of Ovarian Cancer, who reported highly significant variation in the findings by study design (6). The reasons for these results may be as follows: in case–control studies, the under-reporting of weight could be a potential bias if it occurred unequally among cases and controls, and there may also be bias if the individuals in the control group were more 'health conscious' and thus less likely to be overweight than the other cases (40). It seemed that most of the case–control cases were incorporated into our paper, including the young adults about 20. Most of the target subjects in cohort studies were over age 40, as shown in Tables 1 and 2, which may also lead to a higher RR estimate for the case–control studies. However, we found the young adults accounting for a very small part of all cases in the case–control studies, in which an age distribution was adopted (27,31,33,35,39). There was also the possibility that the age of the cases may have no obvious difference between cohort and case–control studies. When we used self-reported weight and height at study entry to calculate the BMI, the small error that exists is generally systematic, with an overestimation of height and an underestimation of weight, especially at higher weights (41–43). Consequently, we could observe a stronger association in the measured studies. The measured studies were more accurate, and the conclusion drawn from them was more credible. Furthermore, the Asian studies demonstrated a stronger risk effect in our results. Few observational studies were conducted among Asian women: one Japanese study (20) and three Chinese studies (14,44,45) revealed a statistically significant association between obesity and OC, whereas Kuriyama et al. (25) and Weiderpass et al. (46) reported no association. Additional studies are needed to support this thesis: there exist some differences in the risk of OC caused by overweight/obesity between Asians and Caucasians. In addition, the summary of the RR estimate was higher for obesity groups than for overweight groups in all of the above categories.

In our meta-analysis, we found no association between BMI and OC risk in the postmenopausal period. However, the associations of overweight and obesity with OC risk appeared stronger for postmenopausal women than for premenopausal women in the European Prospective Investigation into Cancer and Nutrition (EPIC) cohort study (16). In a meta-analysis that was conducted by Poorolajal et al. (7), when stratifying for menopausal status, these authors reported that an increase in BMI could increase the risk of OC regardless of the menopausal status. In contrast, Schouten et al. (8) revealed that no association between BMI and OC risk existed in the postmenopausal period; many epidemiological studies (32,37,47) have supported our findings. The potential biological mechanism for the association between overweight, obesity and OC was not clear and consistent. Kuper et al. (37) suggested that progesterone and leptin may be potential endocrine mediators of the effect of weight on OC risk. This effect may also be as a result of the increased insulin levels (48), androgens and free IGF-I (49) caused by obesity. Because there was no association between BMI and OC risk in postmenopausal women, Reeves et al. (18) suggested that OC and the relation with BMI might be mediated by hormones, as the effect of BMI on risk seems to differ markedly in premenopausal and postmenopausal women. Interestingly, BMI was inversely associated with sex hormone-binding globulin and progesterone and positively associated with free testosterone in premenopausal women (50). All of the above hormone factors probably play an independent or cooperative role in the carcinogenic process. As previous findings remained inconclusive, additional studies are needed to confirm these findings and to explore the possible mechanism.

The strength of our meta-analysis lies in its large sample size (12 963 OC cases and 2 164 977 participants) and a lack of significant evidence of publication bias. Furthermore, we incorporated a maximal bias adjustment in the pooled estimate; thus, the effect of potential confounders was minimized. However, there were a few limitations

in our study as follows: (i) Due to the inherited limitation of observational studies, the possibility of recall, selection and information biases cannot be ruled out and might have distorted the results. (ii) We only searched for relevant articles in English and did not include literature of other languages. (iii) We could not avoid the effect of confounding variables completely, such as nulliparity and a family history of OC, dietary intake, physical activity, tumour type and hormone replacement therapy. Despite some limitations, this meta-analysis could efficiently assess the association between overweight, obesity and OC based on these studies.

In conclusion, the findings of this meta-analysis suggest that increased body weight is associated with an increased risk of OC, in Caucasians and Asians; in particular, severe obesity demonstrated a stronger risk effect. No statistically significant association was observed in the postmenopausal period, but was in the premenopausal period. Note that OC can be prevented by maintaining a healthy body weight; the results of this study will have a positive impact on public health.

Funding

This research received no specific grant from any funding agency in the public, commercial or not-for-profit sectors.

Conflict of interest statement

None declared.

References

1. Jemal A, Bray F, Center MM, Ferlay J, Ward E, Forman D. Global cancer statistics. *CA Cancer J Clin* 2011;61:69–90.
2. Cancer Facts & Figures 2012. American Cancer Society (ACS). *J Consum Health Internet* 2012;16:366–7.
3. Gates MA, Rosner BA, Hecht JL, Tworoger SS. Risk factors for epithelial ovarian cancer by histologic subtype. *Am J Epidemiol* 2010;171:45–53.
4. Devita VT, Hellman S, Rosenberg SA. Cancer: principles & practice of oncology[M]// Lippincott Williams & Wilkins, 2005.
5. Olsen CM, Green AC, Whiteman DC, Sadeghi S, Kolahdooz F, Webb PM. Obesity and the risk of epithelial ovarian cancer: a systematic review and meta-analysis. *Eur J Cancer* 2007;43:690–709.
6. Collaborative Group on Epidemiological Studies of Ovarian Cancer. Ovarian cancer and body size: individual participant meta-analysis including 25,157 women with ovarian cancer from 47 epidemiological studies. *PLoS Med* 2012;9:e1001200.
7. Poorolajal J, Jenabi E, Masoumi SZ. Body mass index effects on risk of ovarian cancer: a meta- analysis. *Asian Pac J Cancer Prev* 2014;15:7665–71.
8. Schouten LJ, R Alexandra G, Brandt PAVD. Height, weight, weight change, and ovarian cancer risk in the Netherlands cohort study on diet and cancer. [J]. *Am J Epidemiol* 2003;157:424–33.
9. Eveleth, Phyllis B. Physical Status: The Use and Interpretation of Anthropometry. Report of a WHO Expert Committee[J]. *Am J Human Biol* 1996;8:786–7.
10. Greenland S. Quantitative methods in the review of epidemiologic literature. *Epidemiol Rev* 1987;9:1–30.
11. Higgins JP, Thompson SG. Quantifying heterogeneity in a meta-analysis. *Stat Med* 2002;21:1539–58.
12. DerSimonian R, Laird N. Meta-analysis in clinical trials. *Control Clin Trials* 1986;7:177–88.
13. Egger M, Davey Smith G, Schneider M, Minder C. Bias in meta-analysis detected by a simple, graphical test. *BMJ* 1997;315:629–34.
14. Ma X, Beeghly-Fadiel A, Shu X-O, et al. Anthropometric measures and epithelial ovarian cancer risk among Chinese women: results from the Shanghai Women's Health Study. *Br J Cancer* 2013;109:751–5.
15. Kotsopoulos J, Baer HJ, Tworoger SS. Anthropometric measures and risk of epithelial ovarian cancer: results from the nurses' health study. *Obesity* 2010;18:1625–31.
16. Lahmann PH, Cust AE, Friedenreich CM, et al. Anthropometric measures and epithelial ovarian cancer risk in the European Prospective Investigation into Cancer and Nutrition. *Int J Cancer* 2010;126:2404–15.
17. Brandstedt J, Nodin B, Manjer J, Jirstrom K. Anthropometric factors and ovarian cancer risk in the Malmo Diet and Cancer Study. *Cancer Epidemiol* 2011;35:432–7.
18. Reeves GK, Pirie K, Beral V, Green J, Spencer E, Bull D. Cancer incidence and mortality in relation to body mass index in the Million Women Study: cohort study. *BMJ* 2007;335:1134.
19. Rapp K, Schroeder J, Klenk J, et al. Obesity and incidence of cancer: a large cohort study of over 145,000 adults in Austria. *Br J Cancer* 2005;93:1062–7.
20. Niwa Y, Yatsuya H, Tamakoshi K, et al. Relationship between body mass index and the risk of ovarian cancer in the Japanese population: findings from the Japanese Collaborate Cohort (JACC) study. *J Obstet Gynaecol Res* 2005;31:452–8.
21. Anderson JP, Ross JA, Folsom AR. Anthropometric variables, physical activity, and incidence of ovarian cancer: The Iowa Women's Health Study. *Cancer* 2004;100:1515–21.
22. Schouten LJ, Goldbohm RA, van den Brandt PA. Height, weight, weight change, and ovarian cancer risk in the Netherlands cohort study on diet and cancer. *Am J Epidemiol* 2003;157:424–33.
23. Jonsson F, Wolk A, Pedersen NL, et al. Obesity and hormone-dependent tumors: cohort and co-twin control studies based on the Swedish Twin Registry. *Int J Cancer* 2003;106:594–9.
24. Wolk A, Gridley G, Svensson M, et al. A prospective study of obesity and cancer risk (Sweden). *Cancer Causes Control* 2001;12:13–21.
25. Kuriyama S, Tsubono Y, Hozawa A, et al. Obesity and risk of cancer in Japan. *Int J Cancer* 2005;113:148–57.
26. Leitzmann MF, Koebnick C, Danforth KN, et al. Body mass index and risk of ovarian cancer. *Cancer* 2009;115:812–22.
27. Schildkraut JM, Alberg AJ, Bandera EV, et al. A multi-center population-based case-control study of ovarian cancer in African-American women: the African American Cancer Epidemiology Study (AACES). *BMC Cancer* 2014;14:688.
28. Delort L, Kwiatkowski F, Chalabi N, Satih S, Bignon YJ, Bernard-Gallon DJ. Central adiposity as a major risk factor of ovarian cancer. *Anticancer Res* 2009;29:5229–34.
29. Olsen CM, Nagle CM, Whiteman DC, Purdie DM, Green AC, Webb PM. Body size and risk of epithelial ovarian and related cancers: a population-based case-control study. *Int J Cancer* 2008;123:450–6.
30. Rossing MA, Tang MT, Flagg EW, Weiss LK, Wicklund KG, Weiss NS. Body size and risk of epithelial ovarian cancer (United States). *Cancer Causes Control* 2006;17:713–20.
31. Peterson NB, Trentham-Dietz A, Newcomb PA, et al. Relation of anthropometric measurements to ovarian cancer risk in a population-based case-control study (United States). *Cancer Causes Control* 2006;17:459–67.
32. Beehler GP, Sekhon M, Baker JA, et al. Risk of ovarian cancer associated with BMI varies by menopausal status. *J Nutr* 2006;136:2881–6.
33. Hoyo C, Berchuck A, Halabi S, et al. Anthropometric measurements and epithelial ovarian cancer risk in African-American and White women. *Cancer Causes Control* 2005;16:955–63.
34. Riman T, Dickman PW, Nilsson S, Nordlinder H, Magnusson CM, Persson IR. Some life-style factors and the risk of invasive epithelial ovarian cancer in Swedish women. *Eur J Epidemiol* 2004;19:1011–9.
35. Pike MC, Pearce CL, Peters R, Cozen W, Wan P, Wu AH. Hormonal factors and the risk of invasive ovarian cancer: a population-based case-control study. *Fertil Steril* 2004;82:186–95.
36. Pan SY, Johnson KC, Ugnat AM, Wen SW, Mao Y, Canadian Cancer Registries Epidemiology Research Group. Association of obesity and cancer risk in Canada. *Am J Epidemiol* 2004;159:259–68.

37. Kuper H, Cramer DW, Titus-Ernstoff L. Risk of ovarian cancer in the United States in relation to anthropometric measures: does the association depend on menopausal status? *Cancer Causes Control* 2002;13:455–63.
38. Purdie DM, Bain CJ, Webb PM, Whiteman DC, Pirozzo S, Green AC. Body size and ovarian cancer: case-control study and systematic review (Australia). *Cancer Causes Control* 2001;12:855–63.
39. Ness RB, Grisso JA, Klapper J, et al. Risk of ovarian cancer in relation to estrogen and progestin dose and use characteristics of oral contraceptives. SHARE Study Group. Steroid Hormones and Reproductions. *Am J Epidemiol* 2000;152:233–41.
40. Berrington de Gonzalez A, Sweetland S, Spencer E. A meta-analysis of obesity and the risk of pancreatic cancer. *Br J Cancer* 2003;89:519–23.
41. Palta M, Prineas RJ, Berman R, Hannan P. Comparison of self-reported and measured height and weight. *Am J Epidemiol* 1982;115:223–30.
42. Stewart AW, Jackson RT, Ford MA, Beaglehole R. Underestimation of relative weight by use of self-reported height and weight. *Am J Epidemiol* 1987;125:122–6.
43. Stevens J, Keil JE, Waid LR, Gazes PC. Accuracy of current, 4-year, and 28-year self-reported body weight in an elderly population. *Am J Epidemiol* 1990;132:1156–63.
44. Su D, Pasalich M, Binns CW, Lee AH. Is body size associated with ovarian cancer in southern Chinese women? *Cancer Causes Control* 2012; 23:1977–84.
45. Zhang M, Xie X, Holman CD. Body weight and body mass index and ovarian cancer risk: a case-control study in China. *Gynecol Oncol* 2005;98:228–34.
46. Weiderpass E, Sandin S, Inoue M, et al. Risk factors for epithelial ovarian cancer in Japan—results from the Japan Public Health Center-based Prospective Study cohort. *Int J Oncol* 2012;40:21–30.
47. Fairfield KM, Willett WC, Rosner BA, Manson JE, Speizer FE, Hankinson SE. Obesity, weight gain, and ovarian cancer. *Obstet Gynecol* 2002;100:288–96.
48. Calle EE, Kaaks R. Overweight, obesity and cancer: epidemiological evidence and proposed mechanisms. *Nat Rev Cancer* 2004;4:579–91.
49. Risch HA. Hormonal etiology of epithelial ovarian cancer, with a hypothesis concerning the role of androgens and progesterone. *J Natl Cancer Inst* 1998;90:1774–86.
50. Tworoger SS, Eliassen AH, Missmer SA, et al. Birthweight and body size throughout life in relation to sex hormones and prolactin concentrations in premenopausal women. *Cancer Epidemiol Biomarkers Prev* 2006;15: 2494–501.