Association of birth weight with cancer risk: A dose-response meta-analysis and Mendelian randomization study

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April 16, 2024

Abstract

Background Several articles have shown that birth weight is associated with the risk of many types of cancers. However, the results are inconsistent and whether the relationship has a casual effect remains unknown. Objectives To estimate the association between birth weight and cancer risk by dose-response meta-analysis and two-sample Mendelian randomization analysis. Search strategy PubMed and Embase library up to March 2021. Selection criteria Prospective cohort studies and case-control studies. Data collection and analysis Two reviewers collected data and the third reviewer check the accuracy. Summary relative risks (RRs) and 95% confidence intervals (CIs) were included. Main results In our dose-response meta-analysis, six cancers from 46 studies were found to had significant associations with the birth weight. (Ovarian cancer: RR: 1.21, 95%CI: 1.01-1.44; breast cancer: RR: 1.12, 95%CI: 1.08-1.16; colorectal cancer: RR: 1.20, 95%CI: 1.01-1.43; endometrial cancer: RR: 0.85, 95%CI: 0.78-0.93; prostate cancer: RR: 1.27, 95%CI: 1.01-1.61; testicular cancer: RR: 1.21, 95%CI: 1.03-1.43). As the birth weight gain, the slope of the dose-response curve of breast cancer increased continuously and the curve of testicular cancer was U-shaped. (Pnonlinearity<0.001) In the MR study, seven cancers were included. Only invasive mucinous ovarian cancer was found to have casual effect on birth weight (OR: 0.62; 95%CI: 0.39-0.97) while other cancers did not. Conclusions There is a nonlinear dose-response relationship between birth weight and breast cancer and testicular cancer. And birth weight has a casual effect on invasive mucinous ovarian cancer. Tweetable abstract Birth weight is associated with cancer risk but affects it indirectly.

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Abstract

Background

Several articles have shown that birth weight is associated with the risk of many types of cancers. However, the results are inconsistent and whether the relationship has a casual effect remains unknown.

Objectives

To estimate the association between birth weight and cancer risk by dose-response meta-analysis and two-sample Mendelian randomization analysis.

Search strategy

PubMed and Embase library up to March 2021.

Selection criteria

Prospective cohort studies and case-control studies.

Data collection and analysis

Two reviewers collected data and the third reviewer check the accuracy. Summary relative risks (RRs) and 95% confidence intervals (CIs) were included.

Main results

In our dose-response meta-analysis, six cancers from 46 studies were found to had significant associations with the birth weight. (Ovarian cancer: RR: 1.21, 95%CI: 1.01-1.44; breast cancer: RR: 1.12, 95%CI: 1.08-1.16; colorectal cancer: RR: 1.20, 95%CI: 1.01-1.43; endometrial cancer: RR: 0.85, 95%CI: 0.78-0.93; prostate cancer: RR: 1.27, 95%CI: 1.01-1.61; testicular cancer: RR: 1.21, 95%CI: 1.03-1.43). As the birth weight gain, the slope of the dose-response curve of breast cancer increased continuously and the curve of testicular cancer was U-shaped. ($P_{nonlinearity}<0.001$) In the MR study, seven cancers were included. Only invasive mucinous ovarian cancer was found to have casual effect on birth weight (OR: 0.62; 95%CI: 0.39-0.97) while other cancers did not.

Conclusions

There is a nonlinear dose-response relationship between birth weight and breast cancer and testicular cancer. And birth weight has a casual effect on invasive mucinous ovarian cancer.

Tweetable abstract

Birth weight is associated with cancer risk but affects it indirectly.

Keywords

Birth weight, Cancer, Dose-response Meta-analysis, Mendelian randomization analysis

Introduction

Cancer is one of the leading causes of death worldwide and the number of cancer cases is increasing. There were an estimated 19.3 million cancer cases and almost 10.0 million cancer deaths around the world in 2020[1]. With this growing global burden, the prevention of cancer is one of the most significant public health challenges of the 21st century. Therefore, it is urgent to find out cancer risk factors.

Birth weight (BW) is considered a marker of the intrauterine environment and has been widely studied in epidemiological researches. A mass of evidence implicates the essential role of early life factors in the occurrence of adult-onset diseases, including cancers[2]. According to the Developmental Origins of Health and Disease hypothesis, fetal adaptive strategies to the adverse intrauterine environment produce long-term consequences for poor health[3]. Over the decades, a number studies reported associations between BW and increased- or decreased- cancer risks, especially breast[4-23] and testicular cancers [24-33]. The World Cancer

Research Fund have concluded that the heavier people weighed at birth, the higher risk of some cancers they got. From their viewpoints, there is strong evidence that BW is causally associated with increased risk of breast cancer and so on[34].

However, after summarizing the most relating studies, it turns out that evidence to reliably establish a causal role of BW on cancer is obviously discrepant. One observational cohort study of BW and overall cancer found that BW was positively correlated with the risk of lung cancer and colon cancer. Yet, no significant trend was observed in breast cancer risk [35]. But another cohort study reported that breast cancer were positively correlated with BW[36].

Observational epidemiological studies are prone to confounding, reverse causation, and various biases and have generated findings that proved to be unreliable indicators of the causal effects of modifiable exposures on disease outcomes [37]. To avoid these disadvantages, Mendelian randomization (MR) analysis came into existence. It is analogous to a randomized clinical trial where randomization to genotype takes place at conception which is less likely to be affected by confounding. The approach is being widely applied in many studies[38].

Thus, this analysis aims to explore the effect of BW on cancer by a dose-response meta-analysis and MR analysis. The genetic data for BW were used as an instrumental variable to perform an MR analysis and observational studies were selected to establish a dose-response meta-analysis.

Methods

1. Dose-response meta-analysis

1.1 Database search

We searched PubMed and Embase library to identify the works of literature reporting the relationship between BW and the risk of any adult-onset cancers published before March 2021. The following keywords were used for retrieval: ("Birth weight" OR "Birth size") AND ("Cancer" OR "tumor" OR "brain cancer" OR "breast cancer" OR "bladder cancer" OR "colorectal cancer" OR "endometrial cancer" OR "esophageal cancer" OR "kidney cancer" OR "lung cancer" OR "leukemia" OR "lymphoma" OR "liver cancer" OR "nervous system tumors" OR "malignant melanoma" OR "osteosarcoma" OR "ovarian cancer" OR "prostate cancer" OR "testicular cancer"). The detailed search strategy was shown in Table S1. Then we add studies included in systematic reviews and meta-analyses and duplicate articles were excluded.

1.2 Inclusion and exclusion criteria

We only included the observational studies which satisfied the following criteria: (1) assessed the effect of BW on the risk of adult-onset cancers; (2) the effect values including hazard ratios (HRs) or odds ratios (ORs) and 95% confidence intervals (95% CIs) were reported or provided sufficient data to calculate them; (3) studies have a clear dose representation of BW, a number of cancer cases corresponding to BW or provide sufficient data to calculate them; (4) prospective cohort studies or case-control studies. We did not include conference abstracts or unpublished or grey literature, anecdotal reports, or case series, or manuscripts published in any language other than English.

1.3 Data extraction

Two reviewers (CC and CXY) retrieved articles independently about the titles and abstracts. If there was any contradiction, we would discuss it with the third author (WDH) and decide it together.

We searched 17 types of cancer including 6,139 articles in total. Then 240 observational articles were collected after reading the title/abstract. Finally, after careful review of the inclusion and exclusion criteria, 46 articles of 6 types of cancers were identified for dose-response meta-analysis. The study selection process and results from the literature search are presented in Figure S1.

Data from all eligible articles were collected by two authors (CC and CXY), including the first author's name, publication year, BW range (kg), BW measure methods, cancer type, number of cancer case, sample size,

and the baseline status of the study populations such as age, sex, ethnicity. (Table S2) For dose-response meta-analysis, we extracted some data that need to be calculated including the first author, publication years, BW dose, total participants, HRs or ORs, 95% confidence interval, the logarithm for HRs or ORs, standard error of HRs or ORs (SE). All of them were inputted into Excel for analysis. If the article provided more than one HRs or ORs, we chose the most adjusted one to exclude as many confounding factors as possible. If there were some missing data, we used appropriate statistical methods to calculate[39, 40]. 5 studies did not report the number of participants exposed under different BW categories [14, 35, 41-43], we averaged the total sample sizes of all BW groups (C) to each group. And 3 studies lacked the number of cases of each BW group (N_x) [36, 41, 42], so we calculated them deriving from the HRs or ORs (RR_x) and sample sizes (M_x) at each BW group. ($Nx=RRx\times M_r/N_rM_x$; $C=N_{x1}+\ldots\ldots+N_{xn}$; M_r: sample sizes of reference BW group; N_r: cases of reference BW group)

1.4 Quality assessment

We used the Newcastle-Ottawa Scale (NOS) to assess the quality of each cohort and case-control studies [44]. It evaluated the quality of articles from case and control selection, exposure record, the comparability and the outcome. The average score of quality assessment was 8.1 of the cohort studies and 8.0 of the case-control studies. The lowest was 7 and the highest was 9. (Table S3- S4)

2. Mendelian randomization analysis

2.1 GWAS summary data for BW and cancers

The public Genome-wide association study (GWAS) relative to BW we chose was reported by Horikoshi M et al. in 2013 [45]. It identified 60 loci associated with BW which was transformed into Z-score separately in males and females excluding non-singletons and premature births to standardize the data. All meta-analyses were derived from the European population of Early Growth Genetics (EGG) Consortium. The lead SNPs were up to the standard of the threshold of genome-wide significance ($P¡5x10^{-8}$) and the limitation of the linkage disequilibrium (LD) analysis ($R^2¡0.05$). To identify the relationship between BW and different types of cancers, we chose several GWAS meta-analyses including seven cancers. All the population was from Europe and derived from the authoritative consortium. (Table 1)

3. Statistical analyses

3.1 Dose-response meta-analysis

In order to analyze the correlation between BW and the risk of cancers, we used the dose-response meta-analysis to reflect the overall trend change of exposure (BW) level and the risk of outcome (cancer risk) indicators [46]. Firstly, for all collected studies, we chose the most adjusted risk estimates and 95% confidence interval for the highest BW group versus the lowest group (reference). And the reported HRs and ORs were approximately considered RRs[47]. Then, we used both "Random-effects models" and "Fixed-effects models" to calculate the summarized RR estimates. If the heterogeneity was low ($I^2<50\%$), we used the value of fixed-effects models. Otherwise, we preferred to used random-effects models.

To estimate study-specific dose-response curves between BW and different types of cancer risk, we chose three models for fitting. The generalized least squares (GLS) model estimated the linear dose-response calculating the study-specific RR of per 500g BW increment. The restricted cubic spline model was used to estimate the nonlinear trend of the dose-response relation [48]. In the dose distribution, three knots were set to fit the model adjusting appropriately according to different cancer data. The accuracy of nonlinear fitting was assessed by the Wald test to determine whether the combined dose-response relationship is nonlinear. In addition, the quadratic model was also applied to estimate the nonlinear relationship between exposure and outcome which using the maximum likelihood estimation method as parameter estimation method. The heterogeneity across included studies was tested by the Q test and I^2 test. We also tested the sensitivity by excluding one study at a time. The Egger's test and the symmetry of the funnel plot were used to evaluate potential publication bias [49]. All analyses were performed R (version 4.0.5) software with the packages of "dosresmeta", "metaphor", "mvmeta", "rms" and "metafor".

3.2 Mendelian randomization analysis

To make sure the causal relationship in MR analysis is reasonable, the instrumental variable (IV) assumptions must meet the following three conditions: (1) It must closely relate to BW. (2) It must not be relevant to other confounding factors. (3) It only affects cancers through BW. Before the MR analysis, we calculated the power value and F statistic of each cancer GWAS studies we chose to test whether the IV was strong enough to explain the exposure under the existing sample size[50]. (power>80%, F>100) It is based on simulations and specific parameters for two-stage least squares (2SLS) MR analyses to make sure that the degree of deviation in estimating causal correlation was within an acceptable range. The main statistical test we used to estimate BW for different cancers is a random-effects inverse-variance weighted (IVW) meta-analysis of the Wald ratio for individual SNPs. Besides, we also applied other methods including the weighted median, weighted mode and MR-Egger regression methods to test the third assumption. Then we analyzed the accuracy of MR results in three aspects. First, we conducted a heterogeneity test to identify the differences between each IVs. Furthermore, the intercept of MR-Egger and MR-PRESSO were used to check the gene pleiotropy ensuring the feasibility of the second assumption. The MR-PRESSO was a recently published method for testing gene-level pleiotropy which could assess it more accurately [51]. At last, we employed a leave-one-out sensitivity analysis to assess the sensitivity of each IVs to MR results. Several palindromic SNPs were moved to decreased the bias of our MR analysis. (Table S5) Our MR analysis was conducted using the package "Two Sample MR (version 0.5.5)".

4. Patient involvement

No patient were involved in our study.

5.Funding

None.

Result

1. Meta-analysis of pooled RR comparing cancer risk of the high with low BW

We compared the highest dose of BW with the low group of each study and subsequently combined them to calculate the pooled RR. Our analysis found that the risk of six cancers we selected has a significant relationship with BW. Five of them showed that higher BW was the risk factor. (Ovarian cancer: pooled RR=1.21, 95%CI=1.01-1.44, I^2=11%, p=0.34; breast cancer: pooled RR=1.12, 95%CI=1.08-1.16, I^2=48%, p<0.01; colorectal cancer: pooled RR=1.20, 95%CI=1.01-1.43, I^2=0%, p=0.87; prostate cancer: pooled RR=1.27, 95%CI=1.01-1.61, I^2=0%, p=0.93; testicular cancer: pooled RR=1.21, 95%CI=1.03-1.43, I^2=0%, p=0.84) However, higher BW were likely to be the protective factor of endometrial cancer (pooled RR=0.78, 95%CI=0.78-0.93, I^2=0%, p=0.63). (Figure S2- S7)

2. Dose-response association between BW and cancer risk

Totally 20 studies were collected on the relationship between BW and breast cancer including 9 case-control studies [4-12]and 11 cohort studies [13-23]. We selected the non-linear model with three knots in the splines at the 35th, 55th, 75th percentiles, the slope of the dose-response curve increased continuously with the BW gain (X^2=5.3, $P_{nonlinearity}$<0.01). (Figure 1) The RRs (95% CIs) of breast cancer risk were 0.98 (0.96-1.00), 1.00 (0.96-1.03), 1.07 (1.02-1.12) and 1.11 (1.03-1.18) for 2.0, 3.0, 4.0, and 4.5 kg, respectively. Yet the simulation of the linear model and quadratic model were not statistically significant ($P_{linearity}$=0.44, $P_{quadratic}$=0.06). We chose 10 studies of testicular cancer [24-33] and the relationship between testicular cancer and BW satisfied the non-linear model (X^2= 236.7, P< 0.001) and quadratic model (X^2=235.3, P< 0.001). The fitting effect of the non-linear model was better, and the percentiles of three knots were 25th, 55th, 85th. Taking 3000g BW as the reference dose, the dose-response curve showed a U-shape. The slope decreased before 3000g and increased above 3000g. (Figure 2) The RRs (95% CIs) of testicular cancer risk were 1.12 (1.09-1.14), 1.05 (1.04-1.06), 1.00 (1.00-1.00) and 1.02 (0.96-1.10) for 1.0, 2.0, 3.0, and 4.0 kg, respectively. Yet the simulation of the linear model was not statistically significant. ($P_{linearity}$=0.15) Other types of cancer including ovarian

cancer, colorectal cancer, endometrial cancer and prostate cancer were not dose relative to BW. Both linear model and no-linear model were not statistically significant.

We conducted the sensitivity analysis and Egger's test (P_{breast}=0.40; $P_{colorectal}$=0.31; $P_{endometrial}$=0.68; $P_{ovarian}$=0.41; $P_{prostate}$=0.59; $P_{testicular}$=0.75) of all included articles to assess the heterogeneity between articles, all of them pass the tests. The sensitivity analysis plots and funnel plots were showed in figure S8-figure S19.

3. Mendelian randomization analysis

3.1 Power calculation and F statistics

We calculated the power values and F statistics of included GWAS studies to evaluate whether our sample size was enough to explore the causal effect between BW and cancer risk. According to the previous articles and our meta-analysis reporting the odds ratio (OR) of each cancer[52] and the interpretation of instrumental variables to BW, our study had an adequate statistical power (>80%) for statistical calculation. Our F statistics were range from 4802.59 to 81695.06 which meant that there was no evidence of weak instrument bias in our MR study. (Table 1)

3.2 MR estimates for the causal effects of BW on cancer risk.

The result of the IVW showed us that high BW can reduce the risk of invasive mucinous ovarian cancer (OR: 0.62; 95%CI: 0.39-0.97). However, the relationship between BW and ovarian cancer overall or endometrioid ovarian cancer was not significant (OR: 0.97; 95%CI: 0.69-1.38). Other cancers subsumed in our study were found to be unrelated to BW, including Lung cancer overall (OR:1.31; 95%CI: 0.92-1.69), Lung adenocarcinoma (OR: 1.14; 95%CI: 0.92-1.36); Squamous cell lung cancer (OR: 1.01; 95%CI: 0.72-1.30), Breast cancer overall (OR: 0.94; 95%CI: 0.80-1.11), ER-positive breast cancer (OR: 0.95; 95%CI: 0.80-1.11), ER-negative breast cancer (OR: 0.95; 95%CI: 0.76-1.17), Colorectal cancer(OR: 1.00; 95%CI: 0.99-1.00), Endometrial (OR: 0.99; 95%CI: 0.99-1.00), Malignant melanoma (OR: 1.00; 95%CI: 1.00-1.00), Prostate cancer(OR: 0.99; 95%CI: 0.98-1.01). (Table 2)

All types of cancers were tested for heterogeneity and pleiotropy analysis to ensure the reliability of our results. The MR-Egger regression is very close to 0 ($p>0.05$) and the results of MR-PRESSO were not statistically significant ($p>0.05$) which indicated that there was weak horizontal pleiotropy between BW and cancers. Besides, our outcomes of the Q test ($p<0.05$) and I^2 test ($I^2<25\%$) illustrated that the existence of heterogeneity is insignificant. And the leave-one-out sensitivity analysis showed that the effect of each SNP on the results was consistent. (Table S13 - Table S14, Figure S26- Figure S38)

Discussion

Main Findings

The meta-analysis suggested that higher BW was relative to the risk of many cancers including breast cancer, testicular cancer, colorectal cancer, prostate cancer, ovarian cancer while higher BW was the protective factor of endometrial cancer. But only breast cancer and testicular cancer had a non-linear relationship with BW. With the increase of BW, the slope of the dose-response curve of breast cancer increased. For testicular cancer, the slope increased before 3000g and decreased above 3000g. Our results were consistent with the conclusions of most previous articles. Current meta-analyses of BW and breast cancer reported that higher BW was relative to breast cancer[53-55]. Some found that the relationship was linear[53, 55] but some indicated that it was nonlinear[54]. One meta-analysis also found a U-shaped distribution between BW and subsequent risk for testicular cancer, but the risk of corresponding BW group was not specifically reported[56]. While another meta-analysis showed that there was no significant correlation in high BW [57].

Strengths

Our study has several advantages. Firstly, it's the first study to systematically elucidated the relationship between BW and the risk of multiple cancers by combining dose-response meta-analysis and mendelian

randomization analysis. In dose-response meta-analysis, we synthesized several articles to calculate the pooled RR and the changing trend of cancer risk with the increase of dose. In Mendelian randomization analysis, it could avoid the interference of confounding factors to calculate the effect value from the causal level. Secondly, when we collected studies in dose-response meta-analysis, we calculated the missing data of some studies instead of excluding them which made more articles were included in our study. Thirdly, we used three models for dose-response curve fitting to explore the optimal dose-response relationship. We changed the percentage of three nodes in the restricted cubic spline model according to different cancers data to ensure the accuracy of the fitting effect. Fourthly, we chose the newest GWAS studies of BW and cancers based on a large consortium which provided enough sample size to perform statistical calculations. And according to the power value and F statistic, we ensured that under the current sample size and genetic variation interpretation our MR result was statistically persuasive.

Limitations

Yet there are still some limitations in our study. Firstly, when we gathered data on BW with the risk of breast cancer, we found moderate heterogeneity among articles (I^2=48%). But in the sensitivity analyses by removing one study at a time, we did not observe obvious fluctuation of the result, with a range from 1.08 (95% CI, 1.02-1.15) to 1.13 (95% CI, 1.06-1.19). In addition, except for breast cancer and testicular cancer, studies included in other cancers were fewer so it may increase publication bias. But all of them passed the Egger's test ($P_{ovarian}$=0.41, $P_{colorectal}$=0.31, $P_{endometrial}$=0.68, $P_{prostate}$=0.59). Secondly, most of our research articles came from high-income countries especially for the Mendelian randomization analysis which the population was all from Europe. It may limit the generalization of the results. Therefore, it should be considered carefully when applied the results.

Interpretation

Several studies had shown that high BW was related to the increase of intrauterine estrogen [58, 59]. Significantly, excessive intrauterine estrogen exposure was often considered as the pathogenesis of both breast cancer and testicular cancer [60, 61]. In the process of individual growth, the development of the mammary gland and testis was regulated by estrogen. Trichopoulos et al. early reported that breast cancer may originate from the uterus in 1990[62]. The study suggested that prenatal exposure to estrogen is the highest at any other time in a woman's life. After 4 weeks of pregnancy, most estrogens in the maternal body were produced by the placenta that was significantly higher than before pregnancy which estrogen was produced by the ovary [63]. One study also found that the occurrence of breast cancer may be due to the imbalance of the self-renewal function of normal stem cells. Estrogen could promote cell proliferation, which also made it a cancer promoter, thus affecting cell growth and mutation [64, 65]. During the fetal period, excessive estrogen can inhibit the secretion of Miller inhibitory substance (MIS) and the development of Leydig cells which produced testosterone, thereby affecting the development of testicles and then promoting the incidence rate of testicular cancer[61]. On the other hand, intrauterine growth retardation (IUGR) may lead to a lower BW which is associated with cryptorchidism and maldescended testis [66, 67]. Both of them were considered to be risk factors for testicular cancer[68]. Therefore, low BW also increases the risk of testicular cancer.

However, in our two-sample MR, we provided no evidence to support the association between BW and cancer which meant that BW may not affect tumorigenesis as an independent factor. We only found that BW had a casual effect of invasive mucinous ovarian cancer. But the incidence rate of this subtype of ovarian cancer was very low[69], and most of them were metastatic cancer. These positive results did not affect the total conclusion of the irrelevant relationship between BW and ovarian cancer. Due to the lack of corresponding GWAS articles, we did not analyze the causal relationship between testicular cancer and BW.

Our MR analysis contradicted the traditional observational results. The MR analysis used single nucleotide polymorphisms (SNPs) relative to the exposure to infer a causal relationship between the exposure and the outcome. Compared with an observational study, it could avoid potential confounding and reverse causality. In addition, our MR results showed consistency when using different MR methods and the sensitivity analysis under sufficient statistical power. Therefore, we were sure that our MR results can better illustrate the

relationship between BW and cancer.

There were some reasons to explain the contradiction between meta-analysis and MR analysis. Firstly, BW was correlated with other characteristics such as birth length, body mass index, menarche age and so on which would also affect the risk of cancers. One newest meta-analysis of BW and cancer risk found that after adjusting the potential confounding factors the relationship was null or weak[52]. Silva et al. reassessed the relationship between birth size and breast cancer risk from 32 studies and found that birth length is the strongest independent indicator of breast cancer risk. After adjusting for birth length, the association with BW disappeared[70]. Meanwhile, as mentioned above, low BW may be caused by fetal intrauterine dysplasia which was also the risk factor of cryptorchidism [66, 67]. All suggested that BW may not be a direct factor in the occurrence of testicular cancer. Secondly, compared with genetic factors, BW is more affected by maternal nutrition and hormones. The growth of the fetus depends on the nutrition provided by the mother through the placenta. As the report of Horikoshi M et al.[45], the genes they identified associated with BW could only explained 15% of the weight variation. Therefore, the increase of BW may be related to the risk of cancer through other non genetic factors. But so far, It is difficult to distinguish the role of genetic and non genetic factors in the relationship between BW and the developing of cancers. What's more, Horikoshi M et al. excluded individuals with extreme BW when collecting the data which we thought to be relative to cancer risk. To some extent, we lacked genetic variation for extreme BW that may affect the results.

Conclusion

In conclusion, the meta-analysis suggested that a higher BW was relative to a higher risk of overall cancer. And BW had a dose-response relationship with breast cancer and testicular cancer. Meanwhile, our MR analysis found that there was no obvious casual association between BW and overall cancer. This suggested that BW was not an direct factor in cancer prevention. It's still a long way to go and more researches are needed to explore the potential mechanism between BW and the risk of cancers.

Disclosure of Interests

None.

Contribution to Authorship

CC and CXY were responsible for data acquisition and data analysis. SJN and AYR contributed to the quality assessment of included studies. CC, CXY and WDH accessed and verified the data. WHT, WCQ , ZR, LCC and LWH supervised the project and provided help at all stages. All authors contributed to the writing of the manuscript and critically reviewed and approved the final manuscript.

Acknowledgements

We thank all the consortia who make data publicly available for us to obtain in our study.

Funding

None.

Data sharing

All data collected for this study, including data extraction tables and the statistical analysis, will be available from the publication date.

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