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**Title Page**

# Does high carbohydrate intake lead to increased risk of obesity? A systematic review and meta-analysis

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**Abstract**

Objectives: The present study aimed to test the association between high versus low carbohydrate diets and obesity, and secondly, to test the link between total carbohydrate intake (as a percentage of total energy intake) and obesity.

Design, setting and participants: systematic review and meta-analysis. We sought literature databases for observational studies from the general population across the globe.

Primary outcome measures: obesity.

Primary exposure measures: high carbohydrate intake.

Results: The study identified 22 articles that fulfilled the inclusion and exclusion criteria and quantified an association between carbohydrate intake and obesity. The first pooled strata (high carbohydrate versus a low carbohydrate intake) suggested a weak increased risk of obesity. The second pooled strata (increasing percentage of total carbohydrate intake in daily diet) showed a weak decreased risk of obesity. Both these pooled strata estimates were however not statistically significant.

Conclusions: On the basis of the current study, it cannot be concluded that a high carbohydrate diet or increased percentage of total energy intake in the form of carbohydrates increases the odds of obesity. A central limitation of the study was the non-standard classification of dietary intake across the studies, as well as confounders like total energy intake, activity levels, age and gender. Further studies are needed that specifically classify refined versus unrefined carbohydrate intake, as well as studies that investigate the relationship between high fat, high unrefined carbohydrate-sugar diets.

**Registration number** PROSPERO CRD42015023257

**Keywords:** high carbohydrate intake, obesity, analytical, observational

**Strengths and limitations:**

- Systematic review of observational studies across LMIC and HIC countries and first to explore this angle as far as we are aware.
- The scarcity of studies and/or data that either measured obesity risk versus total carbohydrate intake or alternatively measured obesity risk on the basis of a high versus low carbohydrate intake is a limitation.
- The non- standardized instruments for total dietary and total carbohydrate intake across studies is a further limitation.
- The heterogeneity in the classification of dietary carbohydrate and variation is staple carbohydrates is especially emphasized across different countries, developed versus developing scenarios and socio-economic changes over the last three decades.
- Studies with high heterogeneity and varying design and measurement quality may limit the quality of evidence from this study.

**Introduction**

Global estimates in 2005 indicated 937 million people were overweight and 328 million were obese [1]. In 2010, an estimated 3.4 million deaths, 3.9% of years of life lost, and 3.8% of disability-adjusted life-years worldwide, were attributed to overweight and obesity [2]. The rate of change of obesity in this global study indicated significant increases in both men and women. In men the proportion of adults with a body mass index (BMI) of 25 or greater increased from 28.8% in 1980 to 36.9% in 2013 and for women increased from 29.8% to 38.0%. These increases occurred in both developed and developing countries. In addition, significant increases in obesity were also recorded among children and adolescents in developed countries that indicated 23.8% of boys were either overweight or obese and 22.6% of girls. Overweight and obesity is also increasing in children and adolescents in developing countries and has risen from 8.1% in 1980 to 12.9% in 2013 for boys and from 8.4% to 13.4% for girls [2]. The relationship between dietary intake, and specifically the role of carbohydrates and obesity at a population level, is also unclear.

The etiology of obesity increasingly reflects excessive calorie intake matched with higher levels of sedentary activity that occur in the face of a worldwide urban migration. In this scenario, traditional diets are often replaced with low cost energy dense foodstuffs produced by the industrialized food [3-5]. Body weight is ultimately determined by the interaction of genetic, environmental and psychosocial factors acting through the physiological mediators of energy intake and energy expenditure [6-8]. Nevertheless, carbohydrates have been linked to disease for many decades [9] and more recently with an epidemic of type 2 diabetes [10]. Although there is no consistent evidence that carbohydrates have driven the current levels of global obesity, carbohydrates form a major component of most national diets [11].

The objective of this systematic review/meta-analysis is to investigate the relationship between carbohydrate intake and obesity. More specifically, the first question is whether a high versus low carbohydrate diet is a risk factor for obesity and secondly, whether total carbohydrate intake is a risk factor related to obesity?

## Materials and Methods

*Registration of protocol with PROSPERO*

In accordance with the guidelines, the systematic review protocol was registered with the International Prospective Register of Systematic Reviews (PROSPERO) on 8 June 2015 (registration number CRD42015023257). The protocol was also formally peer reviewed and published in BMJ Open. Carbohydrate intake, obesity, metabolic syndrome and cancer risk? A two-part systematic review and meta-analysis protocol to estimate attributability [12].

This systematic review was aligned to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines to ensure all necessary steps have been followed (see Appendix 1).

*Data sources and searches*

We used the MEDLINE online database, EMBASE, Web of Science and the Cochrane Database of Systematic Reviews to identify selected studies that evaluated the determinants of obesity including the effect of high versus low carbohydrate diets, as well as the percentage of carbohydrates in total dietary intake. Studies published between 1 January 1980 and 31 December 2016 were included. In addition, web based studies that were unpublished (e.g. reports or unpublished theses) were evaluated using research engines like Google Scholar. The following keywords or medical subject headings on MEDLINE were used: ("Diet or low-carbohydrate diet or low sugar diet or diet, carbohydrate restricted or complex carbohydrates or refined carbohydrates or sugar or sugar sweetened beverages or fat or dietary fibre or protein intake or total carbohydrate intake or total calorie intake) AND ("body mass index" or "BMI" or "waist circumference" or "obesity" or "blood glucose" or "fat mass" or "free fat mass").

*Study screening and selection*

We included studies examining healthy adults (18 years or older). We also included studies on people who were overweight or obese, but otherwise excluded (after evaluation) studies of populations restricted to specific diseases, conditions, or metabolic disorders. Of specific interest were general population studies that investigated the prevalence of obesity in relation to detailed dietary intake [11]. Studies quantifying dietary intake in terms of total carbohydrate intake as a percentage of total energy, and high vs low carbohydrate intake in relation to the odds of obesity, were included.

Two authors (KS, BS) independently screened study titles and abstracts for potential eligibility. Screening questions were developed and pilot-tested with a subset of records before implementation. Full texts of potentially eligible studies were retrieved and the two authors independently applied inclusion/exclusion criteria to identify appropriate studies in this review. Disagreement was assessed using the Kappa statistic and was resolved through discussion and a third arbitrator. We developed a summary table with characteristics of included studies. Reasons for exclusion of studies were documented.

*Appraisal of the quality of included studies*

Three reviewers (KS, CS, TM) were content experts and one reviewer was an experienced biostatistician and epidemiologist (BS). The contents experts only assessed potential publications with respect to the appropriateness of the research questions being tested. The biostatistician only evaluated the appropriateness of the individual study methods employed to ensure that an odds ratio was developed to assess the relationship between carbohydrate intake and the risk of obesity.

(BS, KS) also evaluated studies for quality and bias using an adapted version of the Risk of Bias Tool for Prevalence Studies developed by Hoy et al [13]. Assessment of the risk of selection and attrition bias used the Cochrane guidelines available in Review Manager V.5.3 (http://tech.cochrane.org/revman). Furthermore, the reporting quality of each study was assessed using the STROBE checklist [14].

**Inclusion and exclusion criteria**

We included cross-sectional, case–control or cohort studies assessing risk factors for obesity including dietary carbohydrate intake (carbohydrate % intake of total energy and high vs low carbohydrate intake). Case series or case reports without controls were excluded. We excluded studies assessing restricted dietary interventions as our primary objective was to assess reported carbohydrate intake and measured obesity in normal diet. Studies not performed in human participants were excluded, as were studies lacking primary data and/or explicit method description. Studies with major ethical issues were also excluded. The classification of obesity was based on BMI or visceral obesity (waist circumference). We considered both published and unpublished studies. No language restriction was applied.

*Data extraction and management*

Feedback was solicited from the research team regarding the draft list of data variables for extraction. Data extraction forms were developed and pilot-tested in Distiller SR. One person (BS) extracted all the information. A second person (KS) verified 20% of studies for general characteristics information and 100% of studies regarding outcome data. Disagreements were resolved by consensus or by a third team member. Information on the descriptive and quantitative characteristics of studies included the following: Publication details (e.g. year of publication, language, publication status) , Characteristics of study (e.g. study design, methods, country, setting, sample size, number of centres [if applicable], duration of follow-up, source of funding), Characteristics of population (e.g. age, gender, ethnicity, co-interventions, information regarding respondent bias or representativeness of the included population), Details about the exposure (e.g. type of diet , percentage of total calories obtained from carbohydrate consumption, method of assessing carbohydrate consumption; type of educational or other interventions and description, type of professional delivering intervention). Following extraction of data we noted the need to stratify the studies in two exposure strata, namely:

- High vs low carbohydrate intake;
- Total Carbohydrate percentage intake of total energy.

***Data synthesis/analysis***

Data were analyzed using a random-effect meta-analysis model and incorporating a restricted maximum-likelihood (REML) variance estimator. Effect measures were presented as odds ratios (OR) with 95% confidence intervals (CI). All analyses were performed using R software version 3.2.0 or later (R Core Team (2015). R: A language and environment for statistical computing. R Foundation for Statistical Computing, Vienna, Austria.URL http://www.R-project.org/). The following packages were of R software were utilized for the meta-analyses: 'meta' version 4.2-0 (General Package for Meta-Analysis) and 'metafor' version 1.9-7 (A comprehensive collection of functions for conducting meta-analyses in). Recent GRADE guidelines were utilized for preparing summary tables for the primary outcomes [15 16].

*Heterogeneity*

We assessed statistical heterogeneity in our meta-analysis using the $I^2$ statistic. If the $I^2$ was greater than 50% we regarded this as substantial heterogeneity.

*Publication bias*

We investigated publication bias using funnel plots and Egger`s test [17] . In cases where asymmetry was present based on visual assessment, we performed exploratory analyses to investigate and adjust this using trim and/or fill analysis [18].

*Sensitivity analysis*

To further identify potential sources of heterogeneity, we performed the following subgroup analysis by type of carbohydrate intake i.e. high vs low classification compared to carbohydrate % intake of total energy.

**Results**

Of 2665 retrieved citations, 200 articles were selected following abstract screening, following which 22 articles met the inclusion criteria. Figure 1 shows our search and selection process. There was high agreement between articles selected based on abstract screening between the two reviewers (96.12% agreement between two independent raters, *Kappa statistic = 0.633, p<0.001). Figure 2 shows that all but one of the eligible and selected articles were published since 2000. There were a few large studies in early 2000's, a decrease in sample size of studies in mid-2000 period and then increase in sample size from 2009.

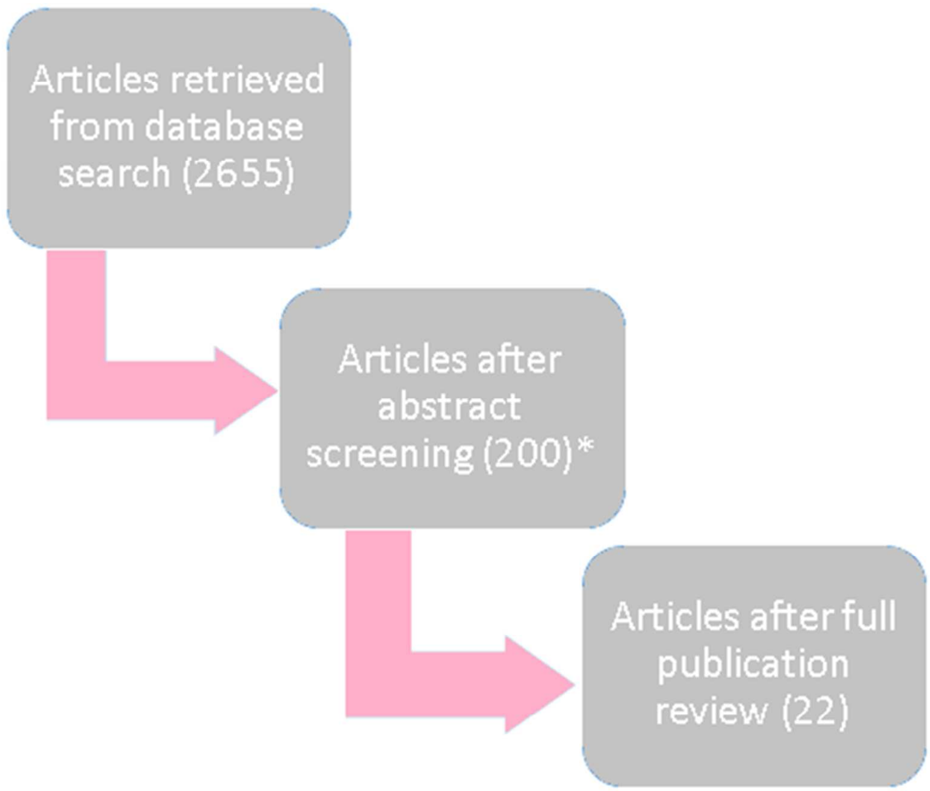


Figure 1: PRISMA flow diagram for study selection following search and selection process

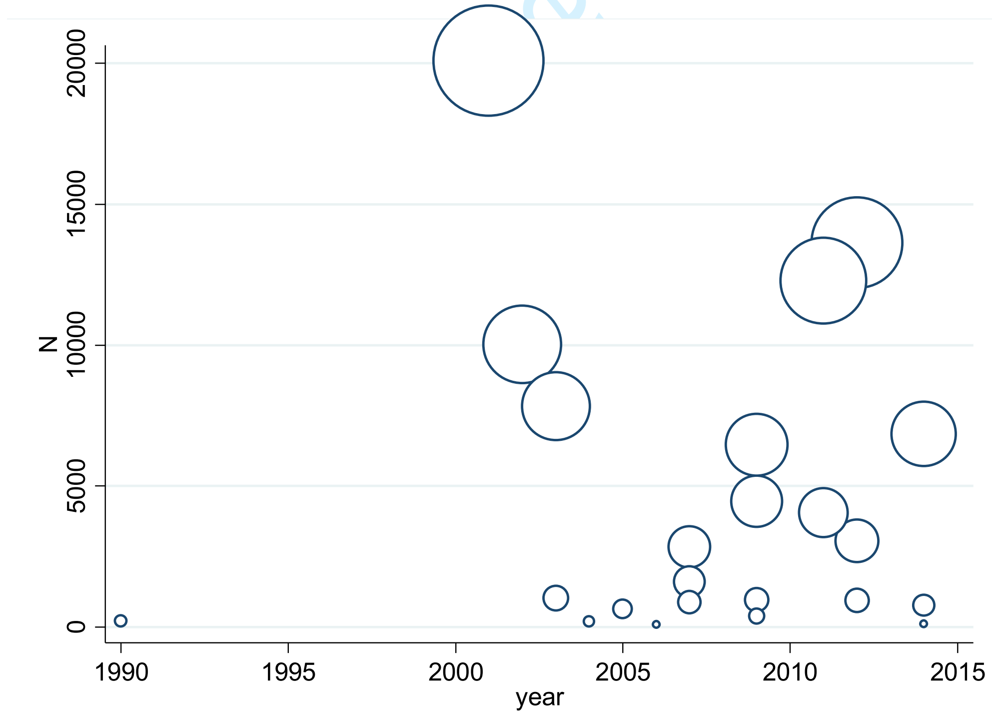


Figure 2: Study sample size by year (combined strata)

The odds ratios of becoming obese based on carbohydrate intake were tested using two strata of data (Table 1). Stratum one was based on high vs low classification of carbohydrate intake while stratum two assessed carbohydrate % intake of total energy. In stratum one, 13 adult based studies showed a non-significant pooled odds ratio of 1.043 (95%CI: 0.933-1.154) indicating a slight positive relationship between high carbohydrate intake and obesity (Figure 3). Within this stratum, eight studies showed an increased risk of obesity and five studies a reduced risk of obesity. Of the eight studies showing an increased risk, four Korean based studies, making up 51.92% of the total pooled sample, showed an increased risk of obesity related to high carbohydrate diets (id 420, 2616), a high carbohydrate rice based diet (1206) and a high carbohydrate refined grains based diet (2226). Two studies in the South Western United states showed contrasting odds in the risk of obesity across two ethnic groups. In these two studies, Hispanic females indicated a reduced risk of obesity in relation to a high carbohydrate diet, whereas white females indicated an increased risk of obesity. The highest odds of increased obesity were indicated in a Sri Lankan study involving high levels of inactivity, as well as a high carbohydrate intake.

In Stratum two, 11 adult based studies investigated the relationship between total calorie intake of carbohydrates and the odds of obesity. Six studies showed a reduced risk and five an increased risk (Figure 4), once more with a non-significant pooled odds ratio of 0.984 (95% CI: 0.926-1.042), in opposite direction to results observed for stratum one (Table 1). One study, involving multiple surveys of a multi-ethnic Hawaiian population (id 1480), making up 66% of the total pooled sample, indicated a 7.7% increased risk of obesity in response to a higher percentage of total carbohydrate intake. Conversely, the three US based National Health and Nutrition Examination Surveys (NHANES), making up 15.71 % of the total pooled sample indicated no increased risk (id 130, 130) or a reduced risk of obesity (id 2591).

The results of the meta-analyses by strata both suggested prominent heterogeneity across individual studies (Stratum one $I^2$ = 85.4%; Stratum two $I^2$ = 86.1%). Possible reasons for this are discussed under the limitations section.

**Table 1: Odds of developing obesity as a result of high carbohydrate diet**

| Strata | Id | Title | Exposure measured | Odds ratio | Lower bound | Upper bound | Sample size |
|---|---|---|---|---|---|---|---|
| 1 | 27 | Association of macronutrient intake patterns and overweight patterns in a population-based random sample of adult males in France. | Quartile 4 vs 1 (CHD per day) | 0.50 | 0.25 | 0.97 | 966 |
| 1 | 279 | A comparison of low-carbohydrate vs. high-carbohydrate diets: energy restriction, nutrient quality and correlation to body mass index. US adults | Above 55% calories (High) vs 0% to 30% calories (Very low) | 0.72 | 0.62 | 0.84 | 10014 |
| 1 | 420 | Characteristics of diet patterns in metabolically obese, normal weight adults (Korean National Health and Nutrition Examination Survey III, 2005). | Quartile 4 vs 1 (CHD per day) | 1.66 | 1.13 | 2.43 | 3050 |
| 1 | 1080 | Diet and overweight and obesity in populations of African origin: Cameroon, Jamaica and the UK. | Tertiale 3 vs 1 for CHD intake | 0.31 | 0.06 | 1.50 | 2842 |
| 1 | 1206 | A rice-based traditional dietary pattern is associated with obesity in Korean adults. | Tertiale 3 vs 1 for white Rice and Kimchi | 1.19 | 1.09 | 1.33 | 13618 |

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|---|---|---|---|---|---|---|---|
| 1 | 1364 | Dietary patterns of Hispanic elders are associated with acculturation and obesity. | Rice dietary pattern | 1.05 | 1.02 | 1.09 | 1030 |
| 1 | 1526 | [Overweight and obesity in Shanghai adults and their associations with dietary patterns]. | Staple food and vegetables higher obesity (Q4 vs Q1 higher proportion carb intake) | 1.28 | 1.00 | 1.64 | 768 |
| 1 | 1532 | Carbohydrate intake and overweight and obesity among healthy Canadian adults. | Quartiles of carbohydrate intake compared to the lowest intake category (Q4 vs Q1) | 0.6 | 0.42 | 0.85 | 4451 |
| 1 | 1634 | Diet composition and risk of overweight and obesity in women living in the southwestern United States. | High vs Low: Carbohydrate (% energy) - Non-Hispanic White | 1.48 | 0.83 | 2.63 | 1599 |
| 1 | 1634 | Diet composition and risk of overweight and obesity in women living in the southwestern United States. | High vs Low: Carbohydrate (% energy) – Hispanic | 0.57 | 0.21 | 1.54 | 871 |
| 1 | 1923 | High carbohydrate diet and physical inactivity associated with central obesity among premenopausal housewives in Sri Lanka. | Percent of energy from carbohydrate: high (>=70%) | 6.26 | 2.11 | 18.57 | 100 |
| 1 | 2226 | Carbohydrate intake and refined-grain consumption are associated with metabolic syndrome in the Korean adult population. | Energy from CHD (Q5 vs Q1) | 1.46 | 1.07 | 2.01 | 6845 |
| 1 | 2616 | Association between dietary carbohydrate, glycaemic index, glycaemic load, and the prevalence of obesity in Korean men and women. | Q4 vs Q1 carbohydrate intake | 1.12 | 0.60 | 2.21 | 933 |
| | | | | | | | |
| 2 | 130 | Trends in carbohydrate, fat, and protein intakes and association with energy intake in normal-weight, overweight, and obese US adults: 1971-2006. | Carbohydrate intake (% of energy)- NHANES I | 0.99 | 0.95 | 1.04 | 12276 |
| 2 | 130 | Trends in carbohydrate, fat, and protein intakes and association with energy intake in normal-weight, overweight, and obese US adults: 1971-2006. | Carbohydrate intake (% of energy)- NHANES 2005/2006 | 0.99 | 0.95 | 1.03 | 4057 |
| 2 | 782 | Adiposity and dietary intake in cardiovascular risk in an obese population from a Mediterranean area. | Carbohydrate intake (% of energy) | 0.71 | 0.25 | 2.07 | 193 |
| 2 | 930 | Are school employees role models of healthful eating? Dietary intake results from the ACTION worksite wellness trial, US adults | Carbohydrate intake (% of energy) | 0.83 | 0.54 | 1.29 | 373 |
| 2 | 1297 | Diet composition and obesity among Canadian adults. | Carbohydrate intake (% of energy) | 1.02 | 0.98 | 1.07 | 6454 |

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| 2 | 1410 | Diet variety based on macronutrient intake and its relationship with body mass index. US adults | Carbohydrate DVS | 1.42 | 0.85 | 2.36 | 74 |
| 2 | 1426 | Association between dietary carbohydrates and body weight. US adults | Daily dietary glycaemic index vs BMI continuous | 2.117 | 1.23 | 3.67 | 641 |
| 2 | 1480 | Dietary determinants of overweight and obesity in a multi-ethnic adult Hawaiian population. | Carbohydrate (1 g/100 kcal) | 1.08 | 1.04 | 1.12 | 101699 |
| 2 | 1557 | Diet composition, energy intake, and exercise in relation to body fat in men and women. US adults | Lean vs obese subjects and energy derived from carbohydrates | 0.87 | 0.67 | 1.13 | 216 |
| 2 | 1587 | Diet culture and obesity in northern Africa. | Carbohydrate mean daily energy intake | 1.07 | 1.05 | 1.09 | 20080 |
| 2 | 2591 | Carbohydrate intake is associated with diet quality and risk factors for cardiovascular disease in U.S. adults: NHANES III. | Carbohydrate intakes (% of energy) | 0.39 | 0.24 | 0.64 | 7828 |

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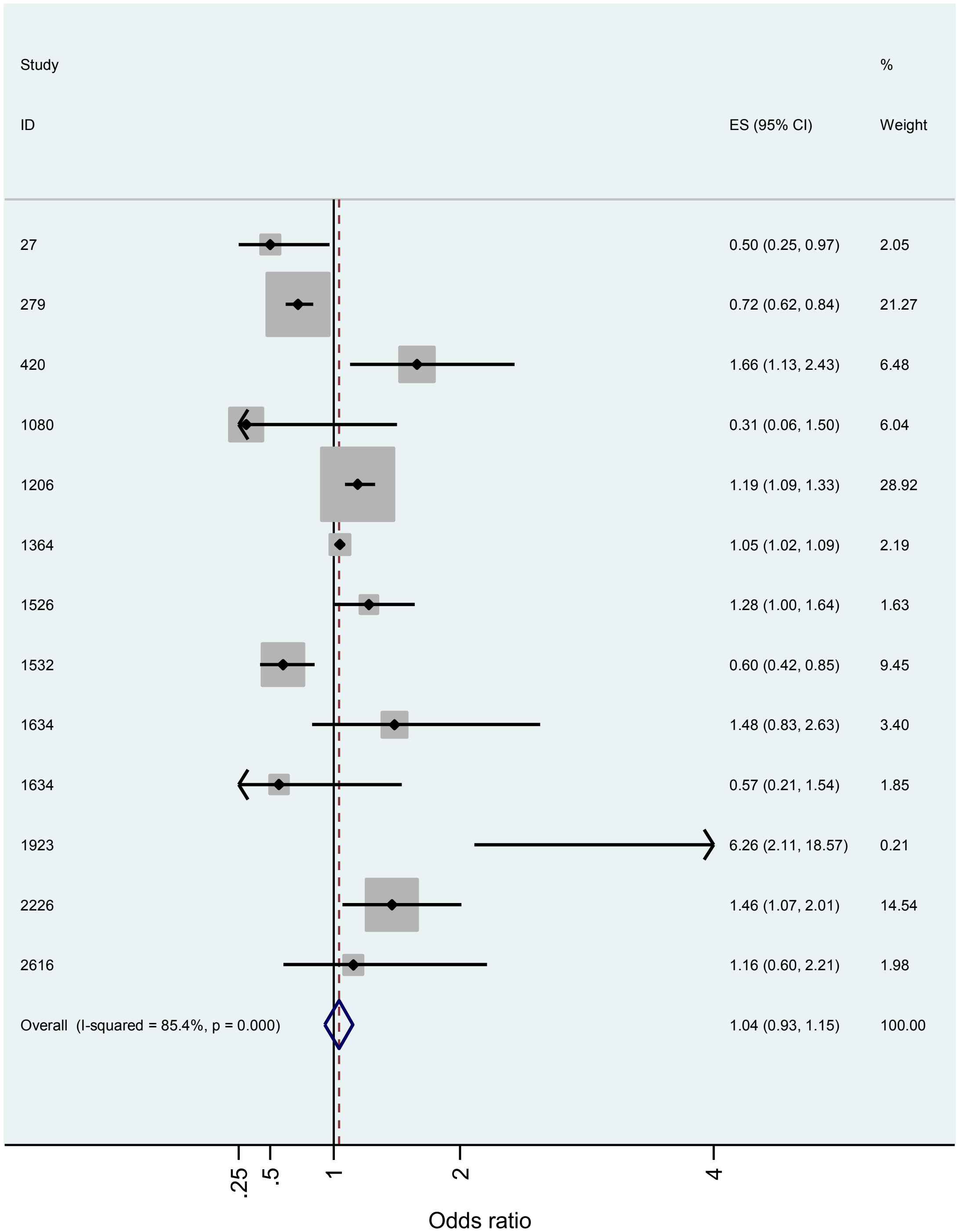


**Figure 3:** Forest plot of association between high vs low carbohydrate intake and obesity

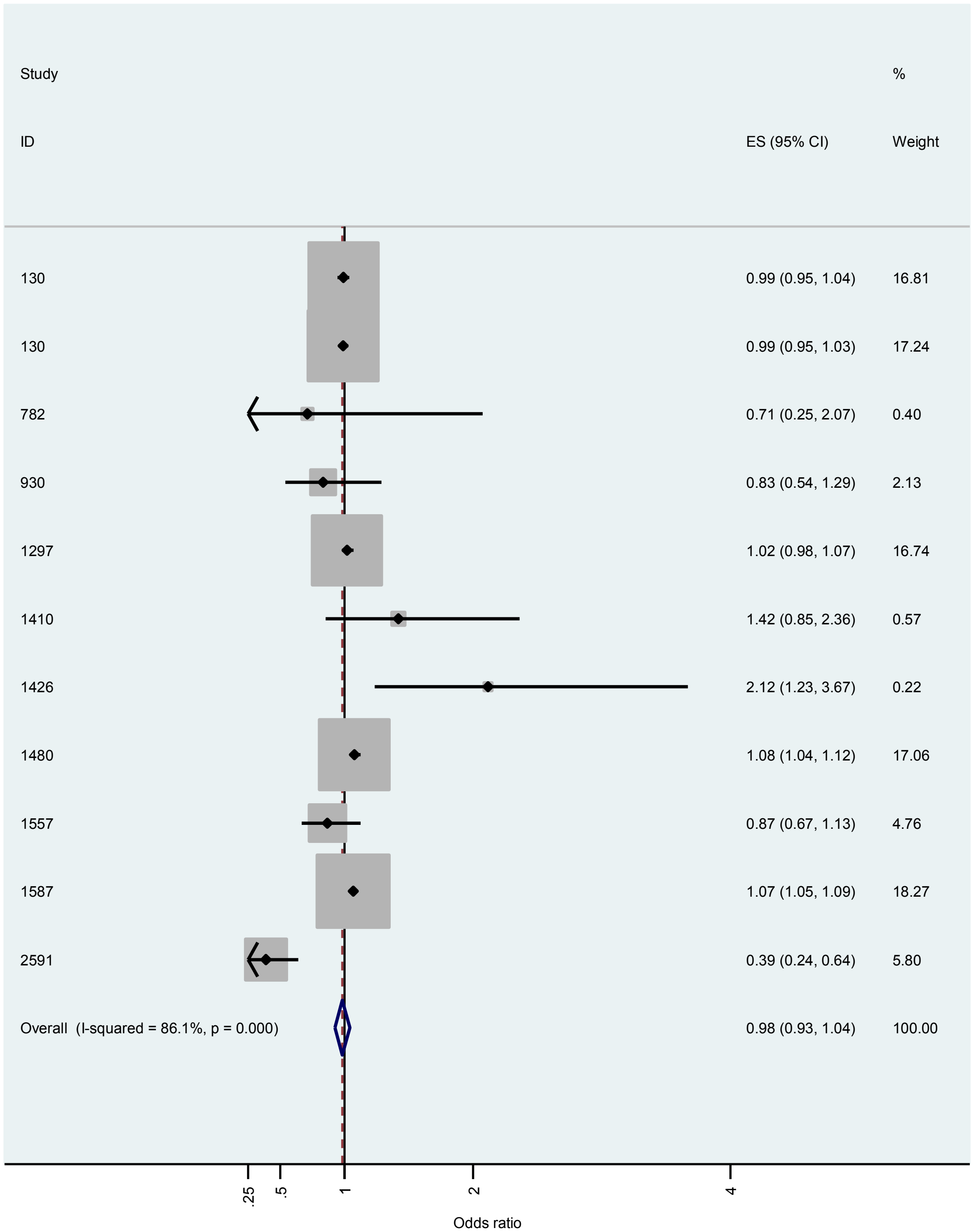


**Figure 4:** Forest plot of association between % carbohydrate intake of total energy and obesity

Publication bias: the p-values from the Egger test for publication bias by strata both suggested no significant publication bias (Strata one p-value=0.691; Strata two p-value=0.199). A visualisation based on funnel plots (Figure 5) confirmed a likely lack of potential publication bias.

Strata 1 Strata 2

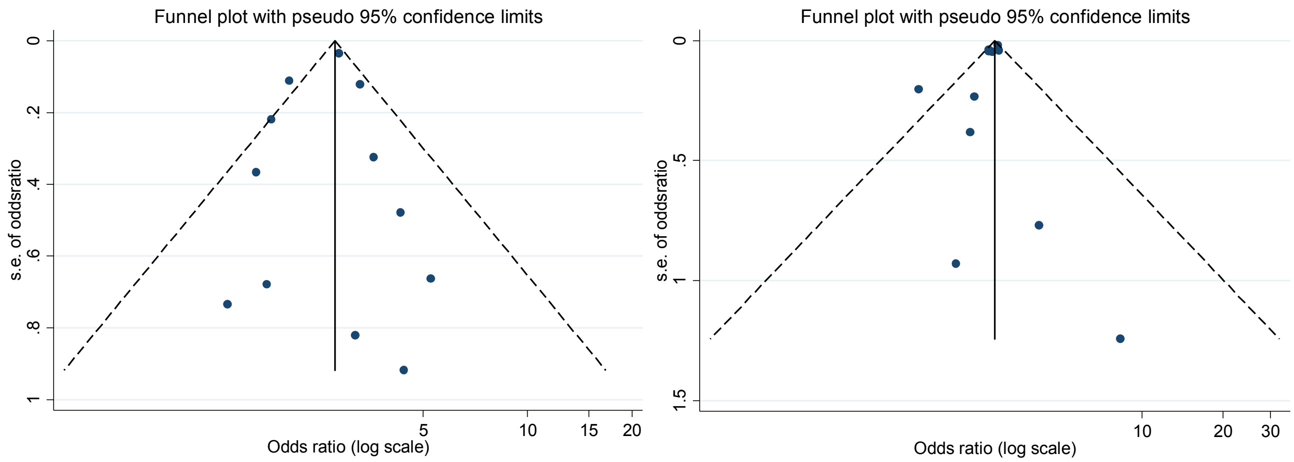


Figure 5: Funnel plots for assessment of publication bias by strata

## Discussion

The literature, as well as the results of this study, suggest a conflicting association between the proportions of energy consumed as carbohydrate and obesity propensity and reinforces the dominance of the total energy intake/expenditure paradigm as the primary driver of body weight, modulated by an interaction of genetic, environmental and psychosocial factors [6-8]. Notwithstanding the results of our systematic meta review that suggest no significant evidence of a relationship between total carbohydrate intake and body weight, other studies have indicated that dietary carbohydrates have been shown to be associated with weight gain [19] and specific carbohydrates, like sugar sweetened beverages, are positively associated with weight gain and obesity [11 20].

The results of a number of systematic reviews, investigating high versus low carbohydrate restricted calorie diets, are interesting. In terms of achieving weight loss on a restricted calorie diet, both high fat - low carbohydrate and low fat - high carbohydrate diets were equally effective albeit there were differences in serum lipid profiles [21-23] . Low carbohydrate restricted calorie diets (high fat) have shown that they induce at least the same level (or more) of weight loss than their low fat (high carbohydrate) counterpart diets [1 24 25]. Low carbohydrate diets also substantially reduce body weight , BMI, abdominal circumference, systolic and diastolic BP and triglycerides, as well as fasting glucose, glycated haemoglobin (HbA1c), plasma insulin and plasma C-reactive protein, as well as increasing HDL [26]. From a physiological perspective, low carbohydrate diets may decrease calorie intake because they increase demands on protein and amino acid turnover for gluconeogenesis which has a high energy cost. Alternatively, low carbohydrate diets may induce weight loss due to reducing insulin concentrations, thus promoting free fatty acid mobilization from body fat storage [27].

The linkage between carbohydrates and obesity continues to be an intense debate with no clear resolution at this stage. A major issue that needs to be addressed is whether the opposing roles of carbohydrates in disease is paralleled by their role in obesity. The good and bad role of refined versus unrefined carbohydrates is well documented in disease [28]. Refined carbohydrates and sugars have long been labelled as the cause of “saccharine disease” involving a wide variety of vascular disorders [9], metabolic syndrome and type 2 diabetes [29], cardiovascular and kidney disease [30]. Conversely, the protective role of unrefined carbohydrates is reflected in a reduction in cardiovascular disease [28 31], certain cancers and ulcerative colitis [32]. Interestingly, a recent projection of longevity in 35 industrialized countries reflects that carbohydrates are an integral aspect of the diets of the four leading countries [33-35]. The opposing roles of dietary carbohydrates and obesity is also supported in the literature that demonstrates bad carbohydrates (unrefined carbohydrates and sugar) promote obesity whilst unrefined carbohydrates may have the opposite effect [7 11 36]. However, the same evidence of good and bad carbohydrates in obesity is far from conclusive.

Many limitations persist to establish whether there is a direct link between high carbohydrate intake and obesity. Firstly, the non-standard nature of dietary records used across different settings make it difficult to compare the results in a meta study [37 38]. This is further compounded by the type and nature of staple carbohydrates being consumed in different countries/population groups. A further factor involves multiple confounding influences that are nuanced across different populations as well as age, gender and ethnic groups [6 39 40].

A further limitation of our study was the concentration of a few countries in the two strata. In the first stratum, the weighting of the pooled sample was largely made up of South Korean and United States data. In the second stratum, the pooled sample was influenced by a large sample resulting from multiple surveys of a multi-ethnic Hawaiian population. A further limitation was the heterogeneity across studies as evidenced by the large $I^2$ statistics. This was potentially due to the heterogeneity in the classification of dietary intake across the studies.

## Conclusion

Based on our findings it cannot be concluded that a high carbohydrate diet or increased percentage of total energy intake in the form of carbohydrates increases the odds of being obese. Further studies are needed that specifically classify refined versus unrefined carbohydrate intake, as well as studies that investigate the relationship between high fat, high unrefined carbohydrates-sugar diets.

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## Author contributions

KS, BS, TM, CS contributed to the conception and design of the systematic literature review, the collection and screening of publications. KS, BS contributed to the analysis and interpretation of the findings. KS, BS drafted the manuscript. TM, CS reviewed and provided input to revise the manuscript. All authors gave final approval for submission.

## Competing interests

The author(s) declare that they have no competing interests.

## Funding

Not applicable.

## Role of funder

The funders had no role in study design, data collection and analysis, decision to publish, or preparation of the manuscript

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41. Moher D, Liberati A, Tetzlaff J, et al. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. International journal of surgery 2010;**8**(5):336-41

**Appendix 1:** PRISMA (preferred reporting items for systematic review and meta-analysis) checklist [41]

| Section/topic | # | Checklist item | Reported on page # |
|---|---|---|---|
| **TITLE** | | | |
| Title | 1 | Identify the report as a systematic review, meta-analysis, or both. | 1 |
| **ABSTRACT** | | | |
| Structured summary | 2 | Provide a structured summary including, as applicable: background; objectives; data sources; study eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number. | 2 |
| **INTRODUCTION** | | | |
| Rationale | 3 | Describe the rationale for the review in the context of what is already known. | 2-3 |
| Objectives | 4 | Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS). | 3 |
| **METHODS** | | | |
| Protocol and registration | 5 | Indicate if a review protocol exists, if and where it can be accessed (e.g., Web address), and, if available, provide registration information including registration number. | 2, 3 |
| Eligibility criteria | 6 | Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale. | 4 |
| Information sources | 7 | Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched. | 3 |
| Search | 8 | Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated. | 3 |
| Study selection | 9 | State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis). | 4 |
| Data collection process | 10 | Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators. | 4-5 |
| Data items | 11 | List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made. | 4-5 |
| Risk of bias in individual studies | 12 | Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis. | 4 |

| | | | |
|---|---|---|---|
| Summary measures | 13 | State the principal summary measures (e.g., risk ratio, difference in means). | 5 |
| Synthesis of results | 14 | Describe the methods of handling data and combining results of studies, if done, including measures of consistency (e.g., $I^2$) for each meta-analysis. | 5 |

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BMJ Open

# Does high carbohydrate intake lead to increased risk of obesity? A systematic review and meta-analysis

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| | |

**Title Page**

# Does high carbohydrate intake lead to increased risk of obesity? A systematic review and meta-analysis

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**Abstract**

Objectives: The present study aimed to test the association between high versus low carbohydrate diets and obesity, and secondly, to test the link between total carbohydrate intake (as a percentage of total energy intake) and obesity.

Setting, participants and outcome measures: We sought MEDLINE, PubMed and google scholar for observation studies published between January 1990 and December 2016 assessing an association between obesity and high carbohydrate intake. Two independent reviewers selected candidate studies, extracted data and assessed study quality.

Results: The study identified 22 articles that fulfilled the inclusion and exclusion criteria and quantified an association between carbohydrate intake and obesity. The first pooled strata (high carbohydrate versus a low carbohydrate intake) suggested a weak increased risk of obesity. The second pooled strata (increasing percentage of total carbohydrate intake in daily diet) showed a weak decreased risk of obesity. Both these pooled strata estimates were however not statistically significant.

Conclusions: On the basis of the current study, it cannot be concluded that a high carbohydrate diet or increased percentage of total energy intake in the form of carbohydrates increases the odds of obesity. A central limitation of the study was the non-standard classification of dietary intake across the studies, as well as confounders like total energy intake, activity levels, age and gender. Further studies are needed that specifically classify refined versus unrefined carbohydrate intake, as well as studies that investigate the relationship between high fat, high unrefined carbohydrate-sugar diets.

**Registration number** PROSPERO CRD42015023257

**Keywords:** high carbohydrate intake, obesity, analytical, observational

**Strengths and limitations:**

- Systematic review of observational studies across LMIC and HIC countries and first to explore this angle as far as we are aware.
- The scarcity of studies and/or data that either measured obesity risk versus total carbohydrate intake or alternatively measured obesity risk on the basis of a high versus low carbohydrate intake is a limitation.
- The non- standardized instruments for total dietary and total carbohydrate intake across studies is a further limitation.
- The heterogeneity in the classification of dietary carbohydrate and variation is staple carbohydrates is especially emphasized across different countries, developed versus developing scenarios and socio-economic changes over the last three decades.
- Studies with high heterogeneity and varying design and measurement quality may limit the quality of evidence from this study.

**Introduction**

Global estimates in 2005 indicated 937 million people were overweight and 328 million were obese [1]. In 2010, an estimated 3.4 million deaths, 3.9% of years of life lost, and 3.8% of disability-adjusted life-years worldwide, were attributed to overweight and obesity [2]. The rate of change of obesity in this global study indicated significant increases in both men and women. In men the proportion of adults with a body mass index (BMI) of 25 or greater increased from 28.8% in 1980 to 36.9% in 2013 and for women increased from 29.8% to 38.0%. These increases occurred in both developed and developing countries. In addition, significant increases in obesity were also recorded among children and adolescents in developed countries that indicated 23.8% of boys were either overweight or obese and 22.6% of girls. Overweight and obesity is also increasing in children and adolescents in developing countries and has risen from 8.1% in 1980 to 12.9% in 2013 for boys and from 8.4% to 13.4% for girls [2]. The relationship between dietary intake, and specifically the role of carbohydrates and obesity at a population level, is also unclear.

The etiology of obesity increasingly reflects excessive calorie intake matched with higher levels of sedentary activity that occur in the face of a worldwide urban migration. In this scenario, traditional diets are often replaced with low cost energy dense foodstuffs produced by the industrialized food [3-5]. Body weight is ultimately determined by the interaction of genetic, environmental and psychosocial factors acting through the physiological mediators of energy intake and energy expenditure [6-8]. Nevertheless, carbohydrates have been linked to disease for many decades [9] and more recently with an epidemic of type 2 diabetes [10]. Although there is no consistent evidence that carbohydrates have driven the current levels of global obesity, carbohydrates form a major component of most national diets [11].

The objective of this systematic review/meta-analysis is to investigate the relationship between carbohydrate intake and obesity. More specifically, the first question is whether a high versus low carbohydrate diet is a risk factor for obesity and secondly, whether total carbohydrate intake is a risk factor related to obesity?

**Materials and Methods**

*Registration of protocol with PROSPERO*

In accordance with the guidelines, the systematic review protocol was registered with the International Prospective Register of Systematic Reviews (PROSPERO) on 8 June 2015 (registration number CRD42015023257). The protocol was also formally peer reviewed and published in BMJ Open. Carbohydrate intake, obesity, metabolic syndrome and cancer risk? A two-part systematic review and meta-analysis protocol to estimate attributability [12].

This systematic review was aligned to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines to ensure all necessary steps have been followed (see Supplementary Table 1).

*Data sources and searches*

We used MEDLINE/PubMed and google scholar to identify suitable studies that evaluated the determinants of obesity including the effect of high versus low carbohydrate diets, as well as the percentage of carbohydrates in total dietary intake. Studies published between 1 January 1980 and 31 December 2016 were included. In addition, web based studies that were unpublished (e.g. reports or unpublished theses) were evaluated using research engines like Google Scholar. The following keywords or medical subject headings on MEDLINE/PubMed and Google Scholar were used:
("carbohydrate" OR "low carbohydrate" OR "low carb" OR "high carbohydrate" OR "high carb") AND ("composition" OR "diet" OR "dietary" OR "intake" OR "determinant") AND ("obesity" OR "obese") AND ("attributable" OR "odds" OR "risk" OR "hazard" OR "prevalence")

*Study screening and selection*

We included studies examining healthy adults (18 years or older). We also included studies on people who were overweight or obese, but otherwise excluded (after evaluation) studies of populations restricted to specific diseases, conditions, or metabolic disorders. Of specific interest were general population studies that investigated the prevalence of obesity in relation to detailed dietary intake [11]. Studies quantifying dietary intake in terms of total carbohydrate intake as a percentage of total energy, and high vs low carbohydrate intake in relation to the odds of obesity, were included.

Two authors (KS, BS) independently screened study titles and abstracts for potential eligibility. Screening questions were developed and pilot-tested with a subset of records before implementation. Full texts of potentially eligible studies were retrieved and the two authors independently applied inclusion/exclusion criteria to identify appropriate studies in this review. Disagreement was assessed using the Kappa statistic and was resolved through discussion and a third arbitrator. We developed a summary table with characteristics of included studies. Reasons for exclusion of studies were documented.

*Appraisal of the quality of included studies*

Three reviewers (KS, CS, TM) were content experts and one reviewer was an experienced biostatistician and epidemiologist (BS). The contents experts only assessed potential publications with respect to the appropriateness of the research questions being tested. The biostatistician only evaluated the appropriateness of the individual study methods employed to ensure that an odds ratio was developed to assess the relationship between carbohydrate intake and the risk of obesity.

(BS, KS) also evaluated studies for quality and bias using an adapted version of the Risk of Bias Tool for Prevalence Studies developed by Hoy et al [13]. The tool has 9 indicators to assess risk of bias which include the representativeness of sample, sampling frame, random selection, nonresponse bias, direct informant, and reliability/validity of the instrument(s). We dichotomised the quality appraisal for each item on the Hoy scale as "low risk" i.e. 0 or "high risk" i.e. 1. We further classified a response rate <80% with no assessment of responders vs non-responders as high risk in our assessment of the non-response indicator. If the selected text of the manuscript was unclear with regards to s specific indicator, when then assigned a high risk of bias. A study was considered to have a high overall risk of bias if ≤3 criteria were met, moderate risk of bias if 4 to 6 criteria were met, and low risk of bias if studies met 7 to 9 criteria. The detailed assessment of risk of bias for the selected 22 studies are presented in Supplementary Table 2. Only one study was scored as having a high risk of bias, 7 scored a medium risk of bias and the majority (n=14) were scored as low risk of bias. The potential of non-response bias appeared high based on the 80% minimum response rate cut-off. The sampling frame and strategy were the next least fulfilled criteria based on the bias criteria indicators on the Hoy instrument (Figure 1).

**Inclusion and exclusion criteria**

We included cross-sectional, case–control or cohort studies assessing risk factors for obesity including dietary carbohydrate intake (carbohydrate % intake of total energy and high vs low carbohydrate intake). Case series or case reports without controls were excluded. We excluded studies assessing restricted dietary interventions as our primary objective was to assess reported carbohydrate intake and measured obesity in normal diet. Studies not performed in human participants were excluded, as were studies lacking primary data and/or explicit method description. Studies with major ethical issues were also excluded. The classification of obesity was based on BMI or visceral obesity (waist circumference). We considered both published and unpublished studies. No language restriction was applied.

*Data extraction and management*

Feedback was solicited from the research team regarding the draft list of data variables for extraction. Data extraction forms were developed and pilot-tested in Distiller SR. One person (BS) extracted all the information. A second person (KS) verified 20% of studies for general characteristics information and 100% of studies regarding outcome data. Disagreements were resolved by consensus or by a third team member. Information on the descriptive and quantitative characteristics of studies included the following: Publication details (e.g. year of publication, language, publication status) , Characteristics of study (e.g. study design, methods, country, setting, sample size, number of centres [if applicable], duration of follow-up, source of funding), Characteristics of population (e.g. age, gender, ethnicity, co-interventions, information regarding respondent bias or representativeness of the included population), Details about the exposure (e.g. type of diet , percentage of total calories obtained from carbohydrate consumption, method of assessing carbohydrate consumption; type of educational or other interventions and description, type of professional delivering intervention). Following extraction of data we noted the need to stratify the studies in two exposure strata, namely:

- High vs low carbohydrate intake;
- Total Carbohydrate percentage intake of total energy.

***Data synthesis/analysis***

Data were analyzed using a random-effect meta-analysis model and incorporating a restricted maximum-likelihood (REML) variance estimator. Effect measures were presented as odds ratios (OR) with 95% confidence intervals (CI). All analyses were performed using R software version 3.2.0 or later (R Core Team (2015). R: A language and environment for statistical computing. R Foundation for Statistical Computing, Vienna, Austria.URL http://www.R-project.org/). The following packages were of R software were utilized for the meta-analyses: 'meta' version 4.2-0 (General Package for Meta-Analysis) and 'metafor' version 1.9-7 (A comprehensive collection of functions for conducting meta-analyses in). Recent GRADE guidelines were utilized for preparing summary tables for the primary outcomes [14 15].

*Heterogeneity*

We assessed statistical heterogeneity in our meta-analysis using the $I^2$ statistic. If the $I^2$ was greater than 50% we regarded this as substantial heterogeneity.

*Publication bias*

We investigated publication bias using funnel plots and Egger`s test [16] . In cases where asymmetry was present based on visual assessment, we performed exploratory analyses to investigate and adjust this using trim and/or fill analysis [17].

*Sensitivity analysis*

To further identify potential sources of heterogeneity, we performed the following subgroup analysis by type of carbohydrate intake i.e. high vs low classification compared to carbohydrate % intake of total energy.

**Results**

Of 2665 retrieved citations, 200 articles were selected following abstract screening, following which 22 articles met the inclusion criteria. Figure 2 shows our search and selection/exclusion process. There was high agreement between articles selected based on abstract screening between the two reviewers (96.12% agreement between two independent raters, *Kappa statistic = 0.633, p<0.001). Figure 3 shows that all but one of the eligible and selected articles were published since 2000. There were a few large studies in early 2000's, a decrease in sample size of studies in mid-2000 period and then increase in sample size from 2009.

The odds ratios of becoming obese based on carbohydrate intake were tested using two strata of data (Table 1). Stratum one was based on high vs low classification of carbohydrate intake while stratum two assessed carbohydrate % intake of total energy. In stratum one, 13 adult based studies showed a non-significant pooled odds ratio of 1.043 (95%CI: 0.933-1.154) indicating a slight positive relationship between high carbohydrate intake and obesity (Figure 4). Within this stratum, eight studies showed an increased risk of obesity and five studies a reduced risk of obesity. Of the eight studies showing an increased risk, four Korean based studies, making up 51.92% of the total pooled sample, showed an increased risk of obesity related to high carbohydrate diets (id 420, 2616), a high carbohydrate rice based diet (1206) and a high carbohydrate refined grains based diet (2226). Two studies in the South Western United states showed contrasting odds in the risk of obesity across two ethnic groups. In these two studies, Hispanic females indicated a reduced risk of obesity in relation to a high carbohydrate diet, whereas white females indicated an increased risk of obesity. The highest odds of increased obesity were indicated in a Sri Lankan study involving high levels of inactivity, as well as a high carbohydrate intake.

In Stratum two, 11 adult based studies investigated the relationship between total calorie intake of carbohydrates and the odds of obesity. Six studies showed a reduced risk and five an increased risk (Figure 5), once more with a non-significant pooled odds ratio of 0.984 (95% CI: 0.926-1.042), in opposite direction to results observed for stratum one (Table 1). One study, involving multiple surveys of a multi-ethnic Hawaiian population (id 1480), making up 66% of the total pooled sample, indicated a 7.7% increased risk of obesity in response to a higher percentage of total carbohydrate intake. Conversely, the three US based National Health and Nutrition Examination Surveys (NHANES), making up 15.71 % of the total pooled sample indicated no increased risk (id 130, 130) or a reduced risk of obesity (id 2591).

The results of the meta-analyses by strata both suggested prominent heterogeneity across individual studies (Stratum one $I^2$ = 85.4%; Stratum two $I^2$ = 86.1%). Possible reasons for this are discussed under the limitations section.

**Table 1: Odds ratios (and log odds) for developing obesity as a result of high vs low carbohydrate diet (strata 1) or increasing carbohydrate intake percentage (strata 2)**

| Strata | Id | Study | Exposure measured | Odds ratio | 95% CI | | Log odds ratio | 95% CI | | Sample size |
|---|---|---|---|---|---|---|---|---|---|---|
| 1 | 27 | Ahluwalia N, Ferrières J, Dallongeville J, Simon C, Ducimetière P, Amouyel P, Arveiler D, Ruidavets JB. Association of macronutrient intake patterns with being overweight in a population-based random sample of men in France. Diabetes & metabolism. 2009 Apr 30;35(2):129-36. | Quartile 4 vs 1 (CHD per day) | 0.50 | 0.25 | 0.97 | -0.30 | -0.60 | -0.01 | 966 |
| 1 | 279 | Bowman SA, Spence JT. A comparison of low-carbohydrate vs. high-carbohydrate diets: energy restriction, nutrient quality and correlation to body mass index. Journal of the American College of Nutrition. 2002 Jun 1;21(3):268-74. | Above 55% calories (High) vs 0% to 30% calories (Very low) | 0.72 | 0.62 | 0.84 | -0.14 | -0.21 | -0.08 | 10014 |
| 1 | 420 | Choi J, Se-Young O, Lee D, Tak S, Hong M, Park SM, Cho B, Park M. Characteristics of diet patterns in metabolically obese, normal weight adults (Korean National Health and Nutrition Examination Survey III, 2005). Nutrition, Metabolism and Cardiovascular Diseases. 2012 Jul 31;22(7):567-74. | Quartile 4 vs 1 | 1.66 | 1.13 | 2.43 | 0.22 | 0.05 | 0.39 | 3050 |
| 1 | 1080 | Jackson M, Walker S, Cruickshank JK, Sharma S, Cade J, Mbanya JC, Younger N, Forrester TF, Wilks R. Diet and overweight and obesity in populations of African origin: Cameroon, Jamaica and the UK. Public health nutrition. 2007 Feb;10(2):122-30. | Tertiale 3 vs 1 for CHD intake | 0.31 | 0.06 | 1.50 | -0.51 | -1.22 | 0.18 | 2842 |
| 1 | 1206 | Kim J, Jo I, Joung H. A rice-based traditional dietary pattern is associated with obesity in Korean adults. Journal of the Academy of Nutrition and Dietetics. 2012 Feb 29;112(2):246-53. | Tertiale 3 vs 1 for white Rice and Kimchi | 1.19 | 1.09 | 1.33 | 0.08 | 0.04 | 0.12 | 13618 |
| 1 | 1364 | Lin H, Bermudez OI, Tucker KL. Dietary patterns of Hispanic elders are associated with acculturation and obesity. The Journal of nutrition. 2003 Nov 1;133(11):3651-7. | Rice dietary pattern | 1.05 | 1.02 | 1.09 | 0.02 | 0.01 | 0.04 | 1030 |
| 1 | 1526 | Meng P, Jia L, Gao X, Liao Z, Wu M, Li S, Chen B. Overweight and obesity in Shanghai adults and their associations with dietary patterns. Wei sheng yan jiu= Journal of hygiene research. 2014 Jul;43(4):567-72. | Staple food and vegetables higher obesity (Q4 vs Q1 higher proportion carb intake) | 1.28 | 1.00 | 1.64 | 0.11 | 0.00 | 0.22 | 768 |
| 1 | 1532 | Merchant AT, Vatanparast H, Barlas S, Dehghan M, Shah SM, De Koning L, Steck SE. Carbohydrate intake and overweight and obesity among healthy adults. Journal of the American Dietetic Association. 2009 Jul 31;109(7):1165-72. | Quartiles of carbohydrate intake compared to the lowest intake category (Q4 vs Q1) | 0.60 | 0.42 | 0.85 | -0.22 | -0.38 | -0.07 | 4451 |
| 1 | 1634 | Murtaugh, M. A., Herrick, J. S., Sweeney, C., Baumgartner, K. B., Guiliano, A. R., Byers, T., & Slattery, M. L. (2007). Diet composition and risk of overweight and obesity in women living in the southwestern United States. Journal of the American Dietetic Association, 107(8), 1311-1321 | High vs Low: Carbohydrate (% energy) - Non-Hispanic (White) | 1.48 | 0.83 | 2.63 | 0.17 | -0.08 | 0.42 | 1599 |
| 1 | 1634 | Murtaugh, M. A., Herrick, J. S., Sweeney, C., Baumgartner, K. B., Guiliano, A. R., Byers, T., & Slattery, M. L. (2007). Diet composition and risk of overweight and obesity in women living in the southwestern United States. Journal of the American Dietetic Association, 107(8), 1311-1321 | High vs Low: Carbohydrate (% energy) - Hispanic | 0.57 | 0.21 | 1.54 | -0.24 | -0.68 | 0.19 | 871 |
| 1 | 1923 | Rathnayake KM, Roopasingam T, Dibley MJ. High carbohydrate diet and physical inactivity associated with central obesity among premenopausal housewives in Sri Lanka. BMC research notes. 2014 Aug 23;7(1):564. | Percent of energy from carbohydrate: high (>=70%) | 6.26 | 2.11 | 18.57 | 0.80 | 0.32 | 1.27 | 100 |
| 1 | 2226 | Song, S., Lee, J. E., Song, W. O., Paik, H. Y., & Song, Y. (2014). Carbohydrate intake and refined-grain consumption are associated with metabolic syndrome in the | Energy from CHD (Q5 vs Q1) | 1.46 | 1.07 | 2.01 | 0.16 | 0.03 | 0.30 | 6845 |

| | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | | Korean adult population. Journal of the Academy of Nutrition and Dietetics, 114(1), 54-62 | | | | | | | | |
| 1 | 2616 | Youn, S., Woo, H. D., Cho, Y. A., Shin, A., Chang, N., & Kim, J. (2012). Association between dietary carbohydrate, glycemic index, glycemic load, and the prevalence of obesity in Korean men and women. Nutrition research, 32(3), 153-159 | Q4 vs Q1 carbohydrate intake | 1.16 | 0.60 | 2.21 | 0.06 | -0.22 | 0.35 | 933 |
| | | | | | | | | | | |
| 2 | 130 | Austin GL, Ogden LG, Hill JO. Trends in carbohydrate, fat, and protein intakes and association with energy intake in normal-weight, overweight, and obese individuals: 1971–2006. The American journal of clinical nutrition. 2011 Apr 1;93(4):836-43. | Carbohydrate intake (% of energy)- NHANES I | 0.99 | 0.95 | 1.04 | 0.00 | -0.02 | 0.02 | 12276 |
| 2 | 130 | Austin GL, Ogden LG, Hill JO. Trends in carbohydrate, fat, and protein intakes and association with energy intake in normal-weight, overweight, and obese individuals: 1971–2006. The American journal of clinical nutrition. 2011 Apr 1;93(4):836-43. | Carbohydrate intake (% of energy)- NHANES 2005/2006 | 0.99 | 0.95 | 1.03 | 0.00 | -0.02 | 0.01 | 4057 |
| 2 | 782 | Garaulet M, Marin C, Perez-Llamas F, Canteras M, Tebar FJ, Zamora S. Adiposity and dietary intake in cardiovascular risk in an obese population from a Mediterranean area. Journal of physiology and biochemistry. 2004 Mar 1;60(1):39-49. | Carbohydrate intake (% of energy) | 0.71 | 0.25 | 2.07 | -0.15 | -0.60 | 0.32 | 193 |
| 2 | 930 | Hartline-Grafton HL, Rose D, Johnson CC, Rice JC, Webber LS. Are school employees role models of healthful eating? Dietary intake results from the ACTION worksite wellness trial. Journal of the American Dietetic Association. 2009 Sep 30;109(9):1548-56. | Carbohydrate intake (% of energy) | 0.83 | 0.54 | 1.29 | -0.08 | -0.27 | 0.11 | 373 |
| 2 | 1297 | Langlois K, Garriguet D, Findlay L. Diet composition and obesity among Canadian adults. Health Reports. 2009 Dec 1;20(4):11. | Carbohydrate intake (% of energy) | 1.02 | 0.98 | 1.07 | 0.01 | -0.01 | 0.03 | 6454 |
| 2 | 1410 | Lyles III TE, Desmond R, Faulk LE, Henson S, Hubbert K, Heimburger DC, Ard JD. Diet variety based on macronutrient intake and its relationship with body mass index. Medscape General Medicine. 2006;8(3):39. | Carbohydrate DVS | 1.42 | 0.85 | 2.36 | 0.15 | -0.07 | 0.37 | 74 |
| 2 | 1426 | Ma Y, Olendzki B, Chiriboga D, Hebert JR, Li Y, Li W, Campbell M, Gendreau K, Ockene IS. Association between dietary carbohydrates and body weight. American journal of epidemiology. 2005 Feb 15;161(4):359-67. | Daily dietary glycemic index vs BMI continuous | 2.12 | 1.23 | 3.67 | 0.33 | 0.09 | 0.56 | 641 |
| 2 | 1480 | Maskarinec G, Takata Y, Pagano I, Carlin L, Goodman MT, Marchand L, Nomura AM, Wilkens LR, Kolonel LN. Trends and dietary determinants of overweight and obesity in a multiethnic population. Obesity. 2006 Apr 1;14(4):717-26. | Carbohydrate (1 g/100 kcal) | 1.08 | 1.04 | 1.12 | 0.03 | 0.02 | 0.05 | 101699 |
| 2 | 1557 | Miller WC, Lindeman AK, Wallace J, Niederpruem M. Diet composition, energy intake, and exercise in relation to body fat in men and women. The American journal of clinical nutrition. 1990 Sep 1;52(3):426-30. | Lean vs obese subjects and energy derived from carbohydrates | 0.87 | 0.67 | 1.13 | -0.06 | -0.18 | 0.05 | 216 |
| 2 | 1587 | Mokhtar N, Elati J, Chabir R, Bour A, Elkari K, Schlossman NP, Caballero B, Aguenaou H. Diet culture and obesity in northern Africa. The Journal of nutrition. 2001 Mar 1;131(3):887S-92S. | Carbohydrate mean daily energy intake | 1.07 | 1.05 | 1.09 | 0.03 | 0.02 | 0.04 | 20080 |
| 2 | 2591 | Yang, E. J., Chung, H. K., Kim, W. Y., Kerver, J. M., & Song, W. O. (2003). Carbohydrate intake is associated with diet quality and risk factors for cardiovascular disease in US adults: NHANES III. Journal of the American College of Nutrition, 22(1), 71-79 | Carbohydrate intakes (% of energy) | 0.39 | 0.24 | 0.64 | -0.41 | -0.62 | -0.19 | 7828 |

Publication bias: the p-values from the Egger test for publication bias by strata both suggested no significant publication bias (Strata one p-value=0.691; Strata two p-value=0.199). A visualisation based on funnel plots (Figure 6) confirmed a likely lack of potential publication bias.

**Discussion**

The results of this systematic review/meta-analysis study, suggest that a higher proportion of carbohydrates in unrestricted diets do not increase obesity levels. . Our paper, therefore, cannot contradict the assumption of the total energy intake/expenditure paradigm as the primary driver of body weight, modulated by an interaction of genetic, environmental and psychosocial factors [6-8]. Other studies, however, have indicated that certain dietary carbohydrates, like sugar sweetened beverages, have been shown to be positively associated with weight gain [18] [11 19].

The results of a number of systematic reviews, investigating high versus low carbohydrate restricted calorie diets, are interesting. In terms of achieving weight loss on a restricted calorie diet, both high fat - low carbohydrate and low fat - high carbohydrate diets were equally effective albeit there were differences in serum lipid profiles [20-22] . Low carbohydrate restricted calorie diets (high fat) have shown that they induce at least the same level (or more) of weight loss than their low fat (high carbohydrate) counterpart diets [1 23 24]. Low carbohydrate diets also substantially reduce body weight , BMI, abdominal circumference, systolic and diastolic BP and triglycerides, as well as fasting glucose, glycated haemoglobin (HbA1c), plasma insulin and plasma C-reactive protein, as well as increasing HDL [25]. From a physiological perspective, low carbohydrate diets may decrease calorie intake because they increase demands on protein and amino acid turnover for gluconeogenesis which has a high energy cost. Alternatively, low carbohydrate diets may induce weight loss due to reducing insulin concentrations, thus promoting free fatty acid mobilization from body fat storage [26]. Low carbohydrates diets are also related to weight loss because of increased levels of satiety thus positively re-enforcing reduced calorie intake [27 28].

The linkage between carbohydrates and obesity continues to be an intense debate with no clear resolution at this stage. A major issue that needs to be addressed is whether the opposing roles of carbohydrates in disease is paralleled by their role in obesity. The good and bad role of refined versus unrefined carbohydrates is well documented in disease [29-31]. Refined carbohydrates and sugars have long been labelled as the cause of “saccharine disease” involving a wide variety of vascular disorders [9], metabolic syndrome and type 2 diabetes [32], cardiovascular and kidney disease [33]. Conversely, the protective role of unrefined carbohydrates is reflected in a ‘ consistent, inverse association between dietary whole grains and the incidence of cardiovascular disease’ [29]. In general, moreover, pooled meta-analyses have indicated a protective effect from the consumption of coarse grains [34 35]. Interestingly, a recent projection of longevity in 35 industrialized countries reflects that carbohydrates are an integral aspect of the diets of the four leading countries [36-38]. The opposing roles of dietary carbohydrates and obesity is also supported in the literature that demonstrates bad carbohydrates (unrefined carbohydrates and sugar) promote obesity whilst unrefined carbohydrates may have the opposite effect [7 11 39]. However, the same evidence of good and bad carbohydrates in obesity is far from conclusive and the studies included in this paper provided insufficient evidence of the risk of obesity relating to different categories of carbohydrates as envisaged in our initial research protocol.

Many limitations persist to establish whether there is a direct link between high carbohydrate intake and obesity. Firstly, the non-standard nature of dietary records used across different settings make it difficult to compare the results in a meta study. In particular, the selected studies did not quantify different classes of carbohydrates [40 41]. . This is further complicated by significant changes in carbohydrate type and proportion in the same population groups over time [42]. Finally, multiple confounding influences are nuanced across different populations, as well as age, gender and different ethnic groups in the same population, as well as differences across the urban-rural divide [6 43 44].

A further limitation of our study was the concentration of a few countries in the two strata and the recognition that different populations/sub-populations consume varying proportions of different categories of carbohydrates in their daily diet [45]. This limitation is further nuanced by the nutrition transition experienced in industrializing countries in which higher a proportion of carbohydrates consumed consist of refined carbohydrates and sugars [46]. In the first stratum, the weighting of the pooled sample was largely made up of South Korean and United States data. In the second stratum, the pooled sample was influenced by a large sample resulting from multiple surveys of a multi-ethnic Hawaiian population. A further limitation was the heterogeneity across studies as evidenced by the large $I^2$ statistics. This was potentially due to the heterogeneity in the classification of dietary intake across the studies.

**Conclusion**

Based on our findings it cannot be concluded that a high carbohydrate diet, or increased percentage of total energy intake in the form of carbohydrates, increases the odds of being obese. Mounting evidence exists, however, to indicate that the obesity epidemic has occurred during the industrial food era that has promoted the increased intake of refined carbohydrates and sugars. Further studies are needed that specifically investigate obesity as a function of different carbohydrate groups including refined versus unrefined carbohydrate intake. In parallel, prospective studies are needed to ascertain the relationship between obesity and long term high fat, high unrefined carbohydrates-sugar diets. We, therefore, advise readers that the assumption that all carbohydrates are not linked to obesity, is potentially erroneous.

**Acknowledgements**
We would like to thank Professor Colleen Aldous and Professor Timothy Noakes for their input into the protocol which was designed for this study and previously published.

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**Author contributions**

KS, BS, TM, CS contributed to the conception and design of the systematic literature review, the collection and screening of publications. KS, BS contributed to the analysis and interpretation of the findings. KS, BS drafted the manuscript. TM, CS reviewed and provided input to revise the manuscript. All authors gave final approval for submission.

**Competing interests**
The author(s) declare that they have no competing interests.

**Funding**

Not applicable.

**Role of funder**

The funders had no role in study design, data collection and analysis, decision to publish, or preparation of the manuscript

**Data sharing statement**

All meta-data utilized in this analysis are provided in Table 1. No additional data available.

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**Figure legends**

**Figure 1:** Risk of bias assessment of the 9 indicators comparing the Hoy et al [13] instrument [light grey=low risk, medium grey: moderate risk, black: high risk].

**Figure 2**: PRISMA flow diagram for study selection following search and selection/exclusion process

**Figure 3**: Study sample size by year (combined strata)

**Figure 4:** Forest plot of association (logs odds ratio) between high vs low carbohydrate intake and obesity

**Figure 5:** Forest plot of association (log odds ratio) between % carbohydrate intake of total energy and obesity

**Figure 6**: Funnel plots for assessment of publication bias by strata

**Supplementary Tables**

**Supplementary Table 1:** PRISMA (preferred reporting items for systematic review and meta-analysis) checklist [47]

**Supplementary Table 2:** Risk of bias among eligible studies (n=22)

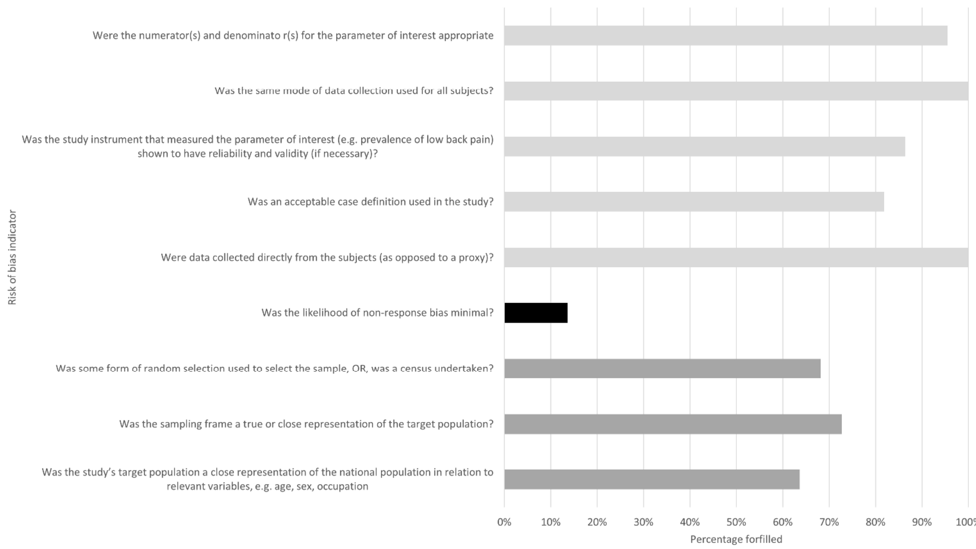


Figure 1: Risk of bias assessment of the 9 indicators comparing the Hoy et al [13] instrument [light grey=low risk, medium grey: moderate risk, black: high risk]

338x190mm (300 x 300 DPI)

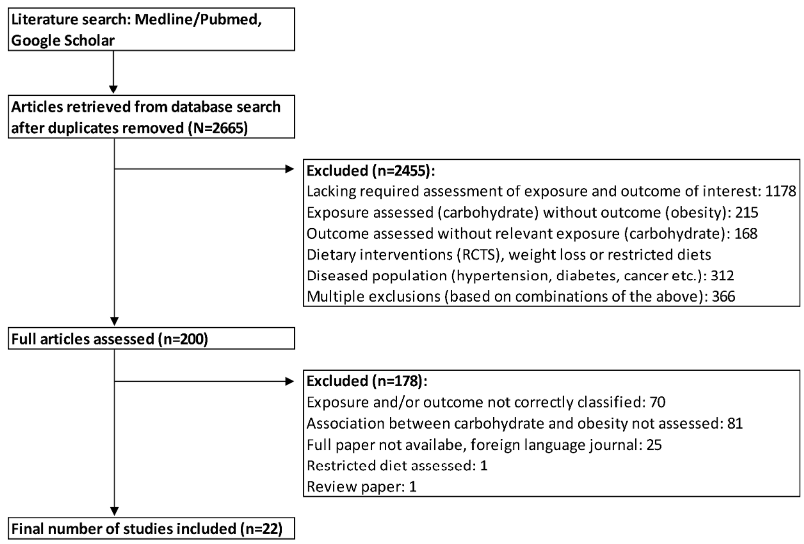


Figure 2: PRISMA flow diagram for study selection following search and selection/exclusion process

338x190mm (300 x 300 DPI)

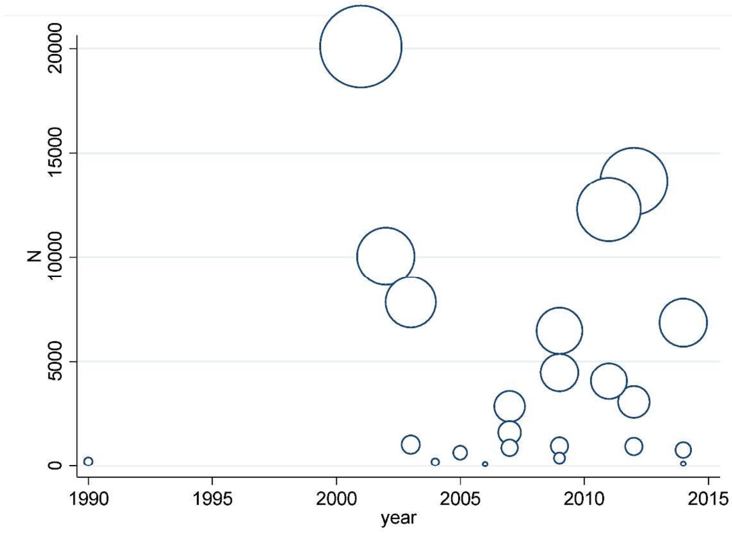


Figure 3: Study sample size by year (combined strata)

338x190mm (300 x 300 DPI)

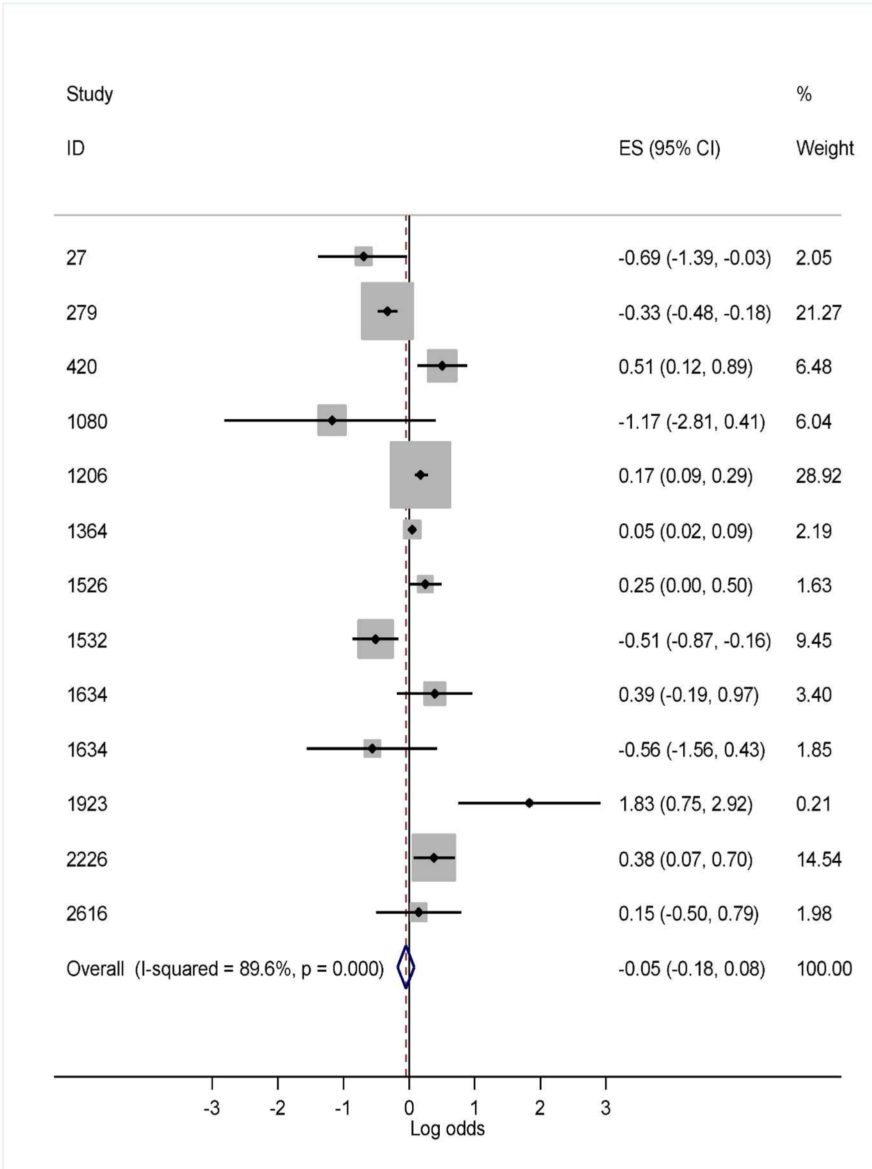


Figure 4: Forest plot of association (logs odds ratio) between high vs low carbohydrate intake and obesity

190x254mm (300 x 300 DPI)

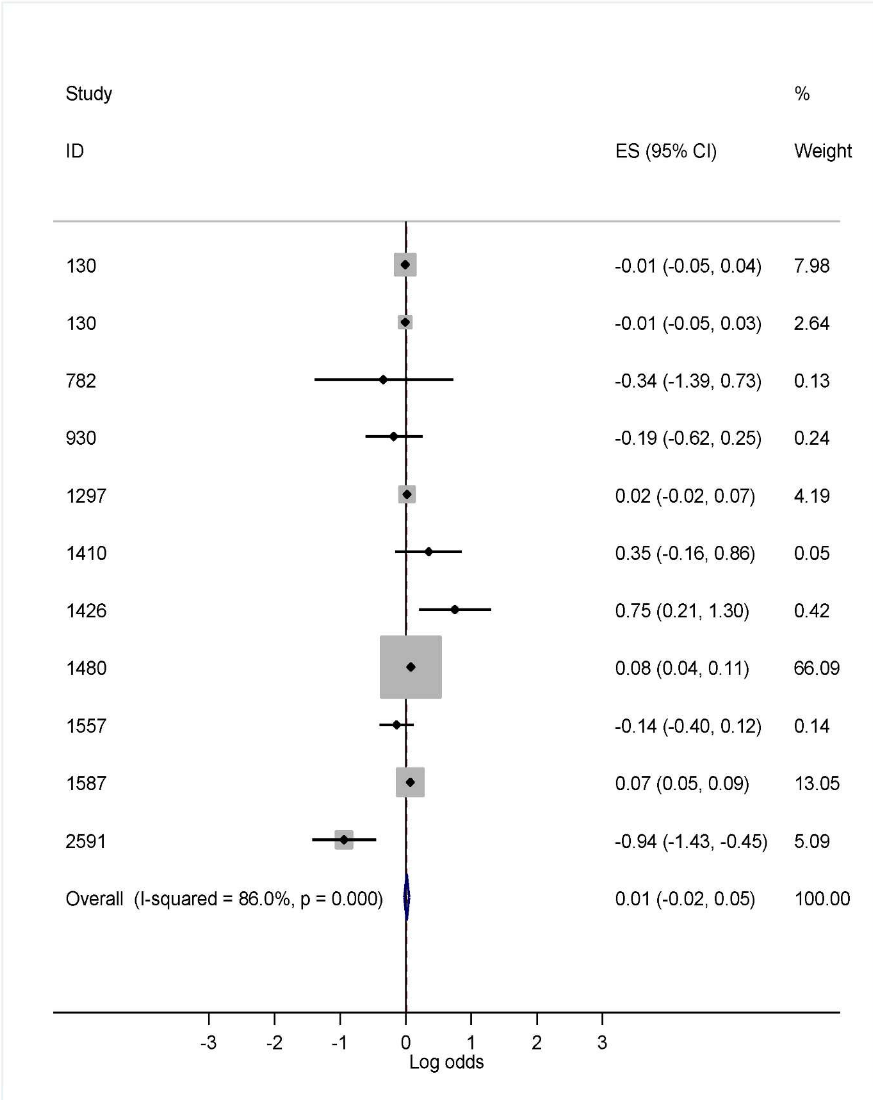


Figure 5: Forest plot of association (log odds ratio) between % carbohydrate intake of total energy and obesity

190x254mm (300 x 300 DPI)

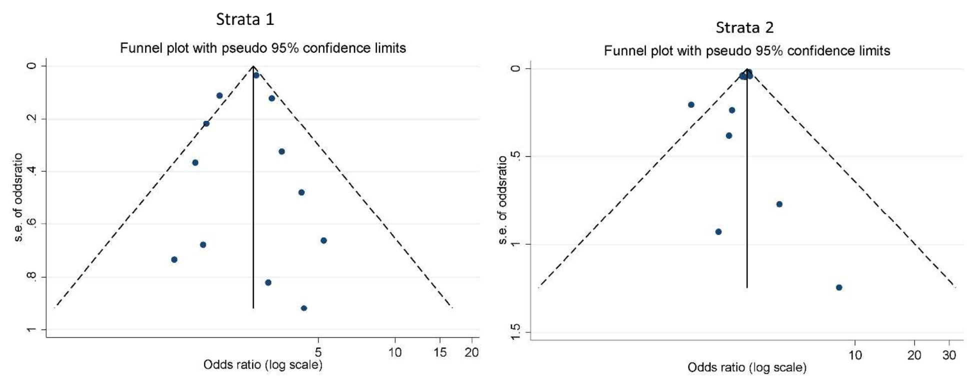


Figure 6: Funnel plots for assessment of publication bias by strata

338x190mm (300 x 300 DPI)

**Supplementary Table 1:** PRISMA (preferred reporting items for systematic review and meta-analysis) checklist [47]

| Section/topic | # | Checklist item | Reported on page # |
|---|---|---|---|
| **TITLE** | | | |
| Title | 1 | Identify the report as a systematic review, meta-analysis, or both. | 1 |
| **ABSTRACT** | | | |
| Structured summary | 2 | Provide a structured summary including, as applicable: background; objectives; data sources; study eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number. | 2 |
| **INTRODUCTION** | | | |
| Rationale | 3 | Describe the rationale for the review in the context of what is already known. | 2-3 |
| Objectives | 4 | Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS). | 3 |
| **METHODS** | | | |
| Protocol and registration | 5 | Indicate if a review protocol exists, if and where it can be accessed (e.g., Web address), and, if available, provide registration information including registration number. | 2, 3 |
| Eligibility criteria | 6 | Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale. | 4 |
| Information sources | 7 | Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched. | 3 |
| Search | 8 | Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated. | 3 |
| Study selection | 9 | State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis). | 4 |
| Data collection process | 10 | Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators. | 4-5 |
| Data items | 11 | List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made. | 4-5 |
| Risk of bias in individual studies | 12 | Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis. | 4 |

| | | | |
|---|---|---|---|
| Summary measures | 13 | State the principal summary measures (e.g., risk ratio, difference in means). | 5 |
| Synthesis of results | 14 | Describe the methods of handling data and combining results of studies, if done, including measures of consistency (e.g., $I^2$) for each meta-analysis. | 5 |

**Supplementary Table 2:** Risk of bias among eligible studies (n=22)

| | | Hoy et al item* | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **No.** | **Study** | **1** | **2** | **3** | **4** | **5** | **6** | **7** | **8** | **9** | **Total** | **10** |
| 1 | Ahluwalia N, Ferrières J, Dallongeville J, Simon C, Ducimetière P, Amouyel P, Arveiler D, Ruidavets JB. Association of macronutrient intake patterns with being overweight in a population-based random sample of men in France. Diabetes & metabolism. 2009 Apr 30;35(2):129-36. | 0 | 1 | 1 | 0 | 1 | 1 | 1 | 1 | 1 | 7 | Low |
| 2 | Austin GL, Ogden LG, Hill JO. Trends in carbohydrate, fat, and protein intakes and association with energy intake in normal-weight, overweight, and obese individuals: 1971–2006. The American journal of clinical nutrition. 2011 Apr 1;93(4):836-43. | 1 | 1 | 1 | 0 | 1 | 1 | 1 | 1 | 1 | 8 | Low |
| 3 | Bowman SA, Spence JT. A comparison of low-carbohydrate vs. high-carbohydrate diets: energy restriction, nutrient quality and correlation to body mass index. Journal of the American College of Nutrition. 2002 Jun 1;21(3):268-74. | 1 | 1 | 1 | 0 | 1 | 0 | 0 | 1 | 1 | 6 | Medium |
| 4 | Choi J, Se-Young O, Lee D, Tak S, Hong M, Park SM, Cho B, Park M. Characteristics of diet patterns in metabolically obese, normal weight adults (Korean National Health and Nutrition Examination Survey III, 2005). Nutrition, Metabolism and Cardiovascular Diseases. 2012 Jul 31;22(7):567-74. | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 9 | Low |
| 5 | Garaulet M, Marin C, Perez-Llamas F, Canteras M, Tebar FJ, Zamora S. Adiposity and dietary intake in cardiovascular risk in an obese population from a Mediterranean area. Journal of physiology and biochemistry. 2004 Mar 1;60(1):39-49. | 0 | 0 | 0 | 0 | 1 | 0 | 1 | 1 | 0 | 3 | High |
| 6 | Hartline-Grafton HL, Rose D, Johnson CC, Rice JC, Webber LS. Are school employees role models of healthful eating? Dietary intake results from the ACTION worksite wellness trial. Journal of the American Dietetic Association. 2009 Sep 30;109(9):1548-56. | 0 | 0 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 7 | Low |
| 7 | Jackson M, Walker S, Cruickshank JK, Sharma S, Cade J, Mbanya JC, Younger N, Forrester TF, Wilks R. Diet and overweight and obesity in populations of African origin: Cameroon, Jamaica and the UK. Public health nutrition. 2007 Feb;10(2):122-30. | 1 | 1 | 1 | 0 | 1 | 1 | 1 | 1 | 1 | 8 | Low |
| 8 | Kim J, Jo I, Joung H. A rice-based traditional dietary pattern is associated with obesity in Korean adults. Journal of the Academy of | 1 | 1 | 1 | 0 | 1 | 1 | 1 | 1 | 1 | 8 | Low |

| | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Nutrition and Dietetics. 2012 Feb 29;112(2):246-53. | | | | | | | | | | | |
| 9 | Langlois K, Garriguet D, Findlay L. Diet composition and obesity among Canadian adults. Health Reports. 2009 Dec 1;20(4):11. | 1 | 1 | 1 | 0 | 1 | 1 | 1 | 1 | 1 | 8 | Low |
| 10 | Lin H, Bermudez OI, Tucker KL. Dietary patterns of Hispanic elders are associated with acculturation and obesity. The Journal of nutrition. 2003 Nov 1;133(11):3651-7. | 0 | 1 | 0 | 0 | 1 | 1 | 1 | 1 | 1 | 6 | Medium |
| 11 | Lyles III TE, Desmond R, Faulk LE, Henson S, Hubbert K, Heimburger DC, Ard JD. Diet variety based on macronutrient intake and its relationship with body mass index. Medscape General Medicine. 2006;8(3):39. | 0 | 0 | 0 | 0 | 1 | 0 | 1 | 1 | 1 | 4 | Medium |
| 12 | Ma Y, Olendzki B, Chiriboga D, Hebert JR, Li Y, Li W, Campbell M, Gendreau K, Ockene IS. Association between dietary carbohydrates and body weight. American journal of epidemiology. 2005 Feb 15;161(4):359-67. | 1 | 0 | 0 | 0 | 1 | 1 | 1 | 1 | 1 | 6 | Medium |
| 13 | Maskarinec G, Takata Y, Pagano I, Carlin L, Goodman MT, Marchand L, Nomura AM, Wilkens LR, Kolonel LN. Trends and dietary determinants of overweight and obesity in a multiethnic population. Obesity. 2006 Apr 1;14(4):717-26. | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 9 | Low |
| 14 | Meng P, Jia L, Gao X, Liao Z, Wu M, Li S, Chen B. Overweight and obesity in Shanghai adults and their associations with dietary patterns. Wei sheng yan jiu= Journal of hygiene research. 2014 Jul;43(4):567-72. | 1 | 1 | 1 | 0 | 1 | 1 | 0 | 1 | 1 | 7 | Low |
| 15 | Merchant AT, Vatanparast H, Barlas S, Dehghan M, Shah SM, De Koning L, Steck SE. Carbohydrate intake and overweight and obesity among healthy adults. Journal of the American Dietetic Association. 2009 Jul 31;109(7):1165-72. | 1 | 1 | 1 | 0 | 1 | 0 | 1 | 1 | 1 | 7 | Low |
| 16 | Miller WC, Lindeman AK, Wallace J, Niederpruem M. Diet composition, energy intake, and exercise in relation to body fat in men and women. The American journal of clinical nutrition. 1990 Sep 1;52(3):426-30. | 1 | 0 | 0 | 0 | 1 | 1 | 1 | 1 | 1 | 6 | Medium |
| 17 | Mokhtar N, Elati J, Chabir R, Bour A, Elkari K, Schlossman NP, Caballero B, Aguenaou H. Diet culture and obesity in northern Africa. The Journal of nutrition. 2001 Mar 1;131(3):887S-92S. | 1 | 1 | 1 | 0 | 1 | 1 | 0 | 1 | 1 | 7 | Low |
| 18 | Murtaugh, M. A., Herrick, J. S., Sweeney, C., Baumgartner, K. B., Guiliano, A. R., Byers, T., & Slattery, M. L. (2007). Diet composition and risk of overweight and obesity in women living in the southwestern United | 0 | 1 | 1 | 0 | 1 | 1 | 1 | 1 | 1 | 7 | Low |

| | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | States. Journal of the American Dietetic Association, 107(8), 1311-1321 | | | | | | | | | | | |
| 19 | Rathnayake KM, Roopasingam T, Dibley MJ. High carbohydrate diet and physical inactivity associated with central obesity among premenopausal housewives in Sri Lanka. BMC research notes. 2014 Aug 23;7(1):564. | 0 | 0 | 0 | 0 | 1 | 1 | 1 | 1 | 1 | 5 | Medium |
| 20 | Song, S., Lee, J. E., Song, W. O., Paik, H. Y., & Song, Y. (2014). Carbohydrate intake and refined-grain consumption are associated with metabolic syndrome in the Korean adult population. Journal of the Academy of Nutrition and Dietetics, 114(1), 54-62 | 1 | 1 | 1 | 0 | 1 | 1 | 1 | 1 | 1 | 8 | Low |
| 21 | Yang, E. J., Chung, H. K., Kim, W. Y., Kerver, J. M., & Song, W. O. (2003). Carbohydrate intake is associated with diet quality and risk factors for cardiovascular disease in US adults: NHANES III. Journal of the American College of Nutrition, 22(1), 71-79 | 1 | 1 | 1 | 0 | 1 | 1 | 1 | 1 | 1 | 8 | Low |
| 22 | Youn, S., Woo, H. D., Cho, Y. A., Shin, A., Chang, N., & Kim, J. (2012). Association between dietary carbohydrate, glycemic index, glycemic load, and the prevalence of obesity in Korean men and women. Nutrition research, 32(3), 153-159 | 0 | 1 | 0 | 0 | 1 | 1 | 1 | 1 | 1 | 6 | Medium |

| * | **Hoy et al item description** |
|---|---|
| 1 | Was the study's target population a close representation of the national population in relation to relevant variables, e.g. age, sex, occupation |
| 2 | Was the sampling frame a true or close representation of the target population? |
| 3 | Was some form of random selection used to select the sample, OR, was a census undertaken? |
| 4 | Was the likelihood of non-response bias minimal? |
| 5 | Were data collected directly from the subjects (as opposed to a proxy)? |
| 6 | Was an acceptable case definition used in the study? |
| 7 | Was the study instrument that measured the parameter of interest (e.g. prevalence of low back pain) shown to have reliability and validity (if necessary)? |
| 8 | Was the same mode of data collection used for all subjects? |
| 9 | Were the numerator(s) and denominator(s) for the parameter of interest appropriate |
| 10 | Summary on the overall risk of study bias (0-3: high, 4-6: moderate, 7-9: low) |