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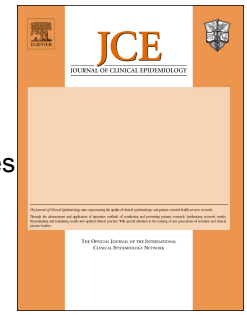

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Reporting Quality and Statistical Analysis of Published Dose-response Meta-Analyses was Suboptimal: a Cross-sectional Literature Survey

Qingqing Jiang[a,1], Qiaoyan Liu[b,c,1], Fan Chen[a], Xiantao Zeng[d,e,f] , Fujian Song[g], Zuxun Lu[a,*], Shiyi Cao[a,*]

[a]School of Public Health, Tongji Medical College, Huazhong University of Science and Technology, Wuhan, China

[b]China Rehabilitation Science Institute, Beijing, China

[c]Research Institute of Rehabilitation Information, China Rehabilitation Research Center, Beijing, China

[d]Center for Evidence-Based and Translational Medicine, Zhongnan Hospital of Wuhan University, Wuhan, China

[e]Department of Evidence-Based Medicine and Clinical Epidemiology, the Second Clinical College of Wuhan University, Wuhan, China

[f]Center for Evidence-Based and Translational Medicine, Wuhan University, Wuhan, China

[g]Norwich Medical School, Faculty of Medicine and Health Science, University of East Anglia, Norwich, United Kingdom.

[1]These authors contributed equally to this work

[*] Corresponding author:

Cao Shiyi: caoshiyi@hust.edu.cn

Lu Zuxun: zuxunlu@yahoo.com

Address: No. 13 Hangkong Road, Wuhan 430030, China

Abstract

Objective To investigate the characteristics, methodological quality, and reporting of statistical analyses of published dose-response meta-analyses (DRMAs).

Study Design and Setting We searched PubMed to identify DRMAs published in 2017. The reporting characteristics and methodological qualities were assessed by the PRISMA (27 items) and AMSTAR (11 items) respectively. We also summarized the reporting of statistical analyses of included DRMAs.

Results We identified 93 DRMAs, most of which (59/93) were conducted by Chinese researchers, the main outcome was the incidence of cancers. Of the PRISMA and AMSTAR items, twenty and five were well complied (80% or more) respectively. The compliance rates of several PRISMA checklist items, such as structured summary, objectives, protocol and registration, and funding, were less than 50%. There were no criteria to estimate the doses for the open-ended intervals of exposure or intervention doses. When the restricted cubic splines were used to fit nonlinear dose-response relationships, there were also no criteria to determine the fixed knots.

Conclusion The adherence to the methodological items of reporting guidelines and statistical analysis of published DRMAs were suboptimal. Development of reporting guidelines to assist authors in writing and readers in critically appraising the reports of DRMAs is timely.

Keywords: Dose-response meta-analyses; Methodological quality; Reporting characteristics; Statistical analysis; PRISMA; AMSTAR

1. Introduction

An increasing number of dose-response meta-analyses (DRMAs) have been published over the past several years[1]. When we research on observed associations between exposure and outcome, dose-response relationship is an important factors affecting the convincingness of clinical epidemiological evidence [2]. DRMAs were able to yield more precise estimates of putative dose-response effects when dose-specific findings from different studies on the same subjects were reported.

Generally, dose-response relationship may be linear or non-linear. Linear dose-response analyses are performed by fitting generalized least squares for trend (GLST)[3] model. There are generally three types of functions for fitting the nonlinear dose-response relationship: restricted cubic splines, natural quadratic function, and the fractional polynomials [4, 5]. The most common nonlinear function is the restricted cubic splines with 3 or 4 knots inserted in the data distribution.

Although DRMAs was a type of meta-analyses quantitatively synthesizing results of multiple original studies, the statistical analysis of DRMAs may be particularly different from traditional meta-analyses [6-11]. A comprehensive appraisal evaluating the reporting characteristics, methodological quality, and statistical analysis of published DRMAs is imperative but reporting guidelines for DRMAs is lacking. Recently, Xu et al. [12, 13] assessed 529 DRMAs published from January 2011 to July 2017 , using the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-analyses)[14], MOOSE

(Meta-analysis of Observational Studies in Epidemiology)[15], and AMSTAR (A Measurement Tool to Assess Systematic Reviews)[16]. However, currently there are no studies that have assessed the reported statistical analysis of DRMAs. The availability of such information is also critical for the development of reporting guidance for DRMAs, because it is possible that the reporting quality of DRMAs might be improved over time [17].

Therefore, we conducted a methodological review of DRMAs published in 2017, to summarize their characteristics and methodological quality based on the AMSTAR (11 items) and the PRISMA (27 items) respectively. And to investigate the key statistical analysis reported in recently published DRMAs.

2. Methods

2.1. Eligibility criteria

We included meta-analyses that explicitly combined dose-response estimates from multiple original studies on the same subjects and reported the results of dose-response analyses. Brief reports (i.e. a short demonstration of research results), letter, and conference abstracts were excluded since such type of publication contained limited information of reporting items.

2.2. Literature Search

We searched PubMed to identify DRMAs published from January 1st, 2017 to December 31st, 2017, using the following search strategy: ((meta-analysis [Title/Abstract]) AND dose-response [Title/Abstract]) AND ("2017/1/1"[Date - Publication]: "2017/12/31"[Date - Publication])

2.3. Study selection

Literature search records were imported into the literature management software of ENDNOTE X7. Two independent reviewers (QJ and QL) examined the title and abstract of retrieved records to identify potentially relevant DRMAs according to the eligibility criteria. Then, full-text versions of all potentially relevant DRMAs were obtained to further confirm the eligibility. By systematic sampling, renumbered all articles: 001, 002, ... 186 and divided into 93 groups of 2 numbers each. Randomly selected a number “t” in the first part 001, 002, and then selected all “t + 2k” (k = 0, 1, 2, ... 92) to obtain a sample with a capacity of 93. Disagreements between the two reviewers were resolved by discussing with a third reviewer (SC).

2.4. Data extraction

We collected data from included DRMAs on general characteristics, including countries of corresponding author, categories of study outcome, database searched, the key reporting (PRISMA) and methodological (AMSTAR) components, and specific items about the statistical analyses of dose-response effects. A standard data abstraction form was created using Microsoft Excel 2013 (Microsoft Corp, Redmond, WA, www.microsoft.com) .Two investigators (QJ, QL) independently extracted the data. Any disagreements were resolved by discussion.

2.5. Data analyses

General characteristics of included DRMAs were summarized descriptively. Since no specific reporting guidelines for DRMAs were available, we assessed the reporting and

methodology quality according to PRISMA and AMSTAR. We used the AMSTAR [16]to assess the methodological quality of the include DRMAs. The PRISMA statement is a checklist of 27 items that are recommended to be included in systematic reviews and meta-analyses to ensure that published reports contain all relevant information[14]. Each PRISMA item was rated with a ‘‘yes’’ or ‘‘no’’ response. A ‘‘yes’’ response means that the item was reported, and a ‘‘no’’ response means that the item was not reported. The AMSTAR tool is an 11-item questionnaire that is used to determine the methodological of systematic reviews and meta-analyses[16]. The original tool had four responses with each item, ‘‘yes,’’ ‘‘no,’’ ‘‘cannot answer,’’ or ‘‘not applicable’’. As we included only meta-analyses, every item was applicable. A ‘‘yes’’ response means that the item is fulfilled, a “no’’ response means that the item is not fulfilled, and a ‘‘cannot answer’’ response means that it is inconclusive as to whether the item is fulfilled. In this study, we assigned “1” to “yes” response, and “0”to “no” or “cannot answer” response for each of the PRISMA and AMSTAR items. Therefore, every included DRMA has an overall PRISMA counts rated out of a maximum point of 27, and every included DRMA has an overall AMSTAR counts rated out of a maximum point of 11.

We calculated the adherence rates of individual AMSTAR and PRISMA items and showed results in figures. The calculation formula was as follows: adherence rate of an item = (the number of articles with a “yes” response to the item/ the total number of articles)*100%. The AMSTAR and PRISMA counts of each article were also calculated.

To investigate the statistical analyses process of the included DRMAs, we descriptively summarized the methods of confirming dose, the methods used to estimate dose-response

effects, and knots used when restricted cubic splines were employed.

3. Results

3.1. Literature search

Initial literature search retrieved 292 citations. After removing duplicates and the title/abstracts screening, 248 publications were collected for the full text screening. We excluded articles that did not explicitly combine dose estimates from multiple original studies on the same subjects, or did not report results of dose-response analyses. Finally, through a round of systematic sampling, 93 citations were included (Fig. 1).

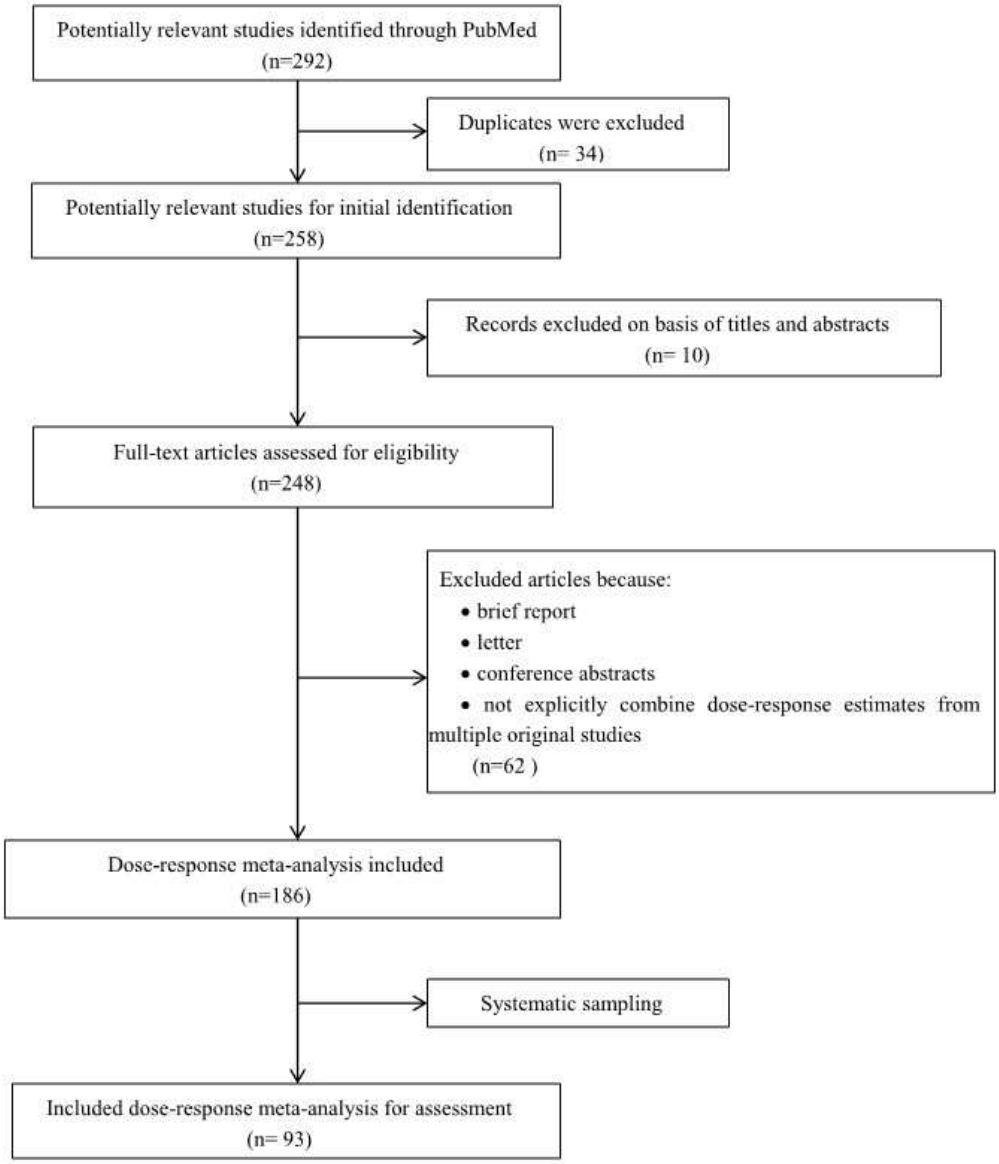

Fig.1 The Flow chart of literature selection.

3.2. General characteristics of included DRMAs

China was the most common country in which the included DRMAs were conducted (59/93, 63.4%), followed by Germany (6/93, 6.5%) and Italy (5/93, 5.4%) (Fig.2). Cancer (31/93, 33.3%) was the most common disease outcome in the included DRMAs (Fig.3). PubMed/MEDLINE was the most common single database search, accounting for 98%, and it

was frequently combined with a search of EMBASE (64/93, 68.8%). The details of databases searched are shown in Table 1.

3.3. Reporting quality based on PRISMA

The highest and lowest scores for a single article based on PRISMA were 26 and 17, and the average score and corresponding standard deviation were 22.83 and 1.96. About half of PRISMA items (13/27, 48.2%) were reported in the included DRMAs. 48.4% of DRMAs provided a structured summary and only 6.5% provided an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS). 48.4% of DRMAs provided registration information on review protocols. 52.7% of DRMAs described methods used for assessing risk of bias of individual studies and 75.3% considered impact of possible risk of bias on the cumulative evidence (e.g., publication bias, selective reporting, and so on). In addition, 36.6% of DRMAs described sources of funding for the systematic review and other support. The percentages of adequately reported individual PRISMA items are shown in Fig. 4.

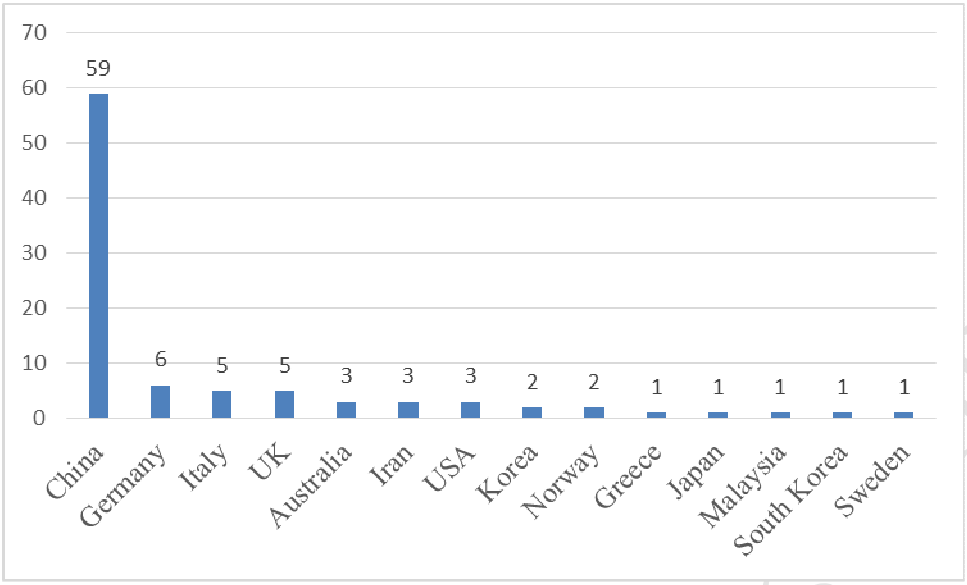

Fig.2. Countries of included dose-response meta-analyses.

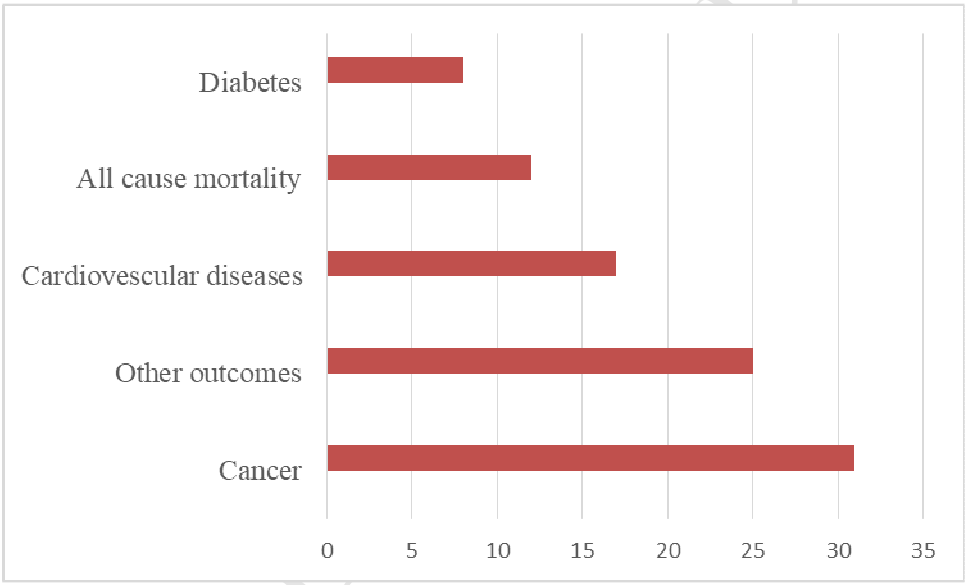

Fig.3. Categories of outcome of included dose-response meta-analyses.

Table 1. database searched

	Category	Frequency	Proportion (%)
Name of database searched	PubMed/Medline	91	97.85
	Embase	70	75.27
	Web of Science	38	40.86
	Cochrane library	23	24.73
	Scopus	11	11.83
	Ovid	8	8.6
	Google Scholar	8	8.6

Common combination of database searched	CNKI	7	7.53
	Wanfang	7	7.53
	Others	28	30.11
	PubMed/Medline + EMBASE	64	68.82
	PubMed/Medline + Web of Science	52	55.91
	PubMed/Medline + Embase + Web of Science	46	49.46
	PubMed/Medline + Embase + Cochrane Library	22	23.66
	PubMed/Medline + Embase + Google Scholar	19	20.43
	PubMed/Medline + Web of Science + Cochrane Library	16	17.2
	PubMed/Medline + Web of Science + CNKI + WANFANG	7	7.53

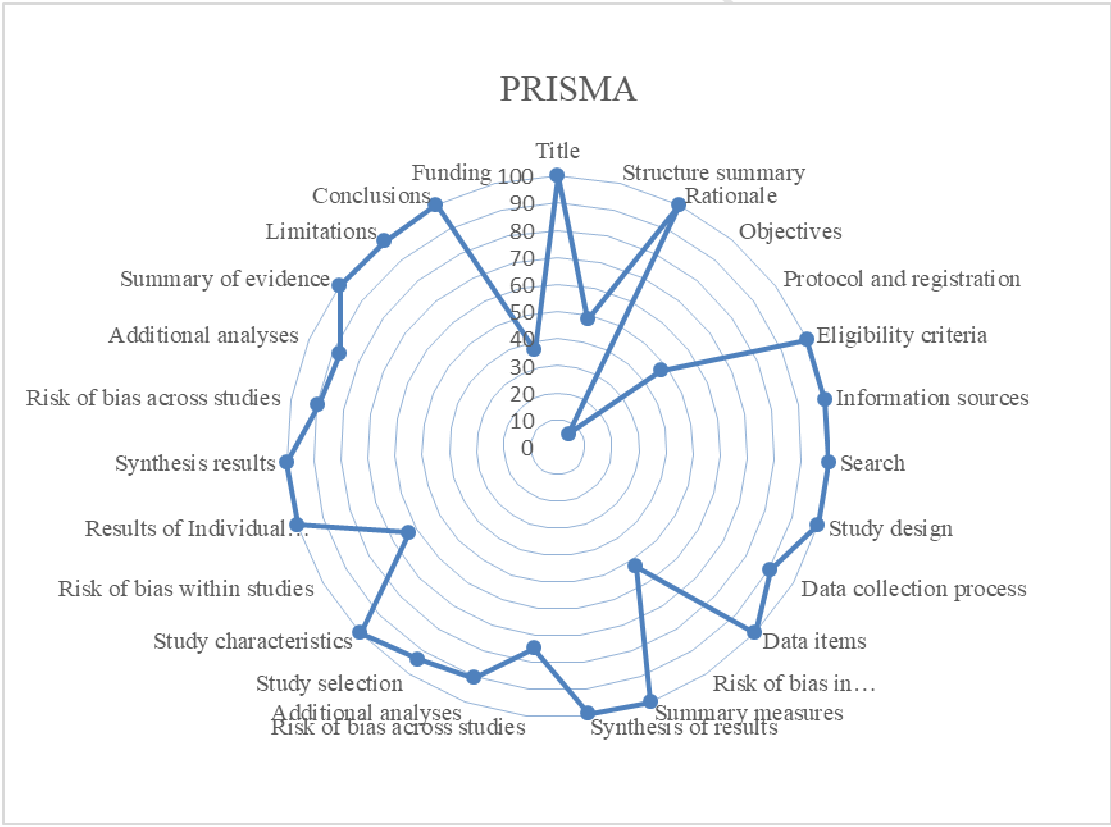

Fig.4. The percentage of adequately reported individual items based on PRISMA.

3.4. Methodological quality based on AMSTAR

Fig. 5 shows the results of methodological quality assessment based on AMSTAR. The

highest and lowest AMSTAR scores were 11 and 5, and the average score and corresponding standard deviation were 8.40 and 1.60**.** Of the included DRMAs, 53.8% provided an “a priori” design, about one third did not perform a comprehensive literature search. Only 39.8% used the status of publications (i.e. grey literature) as an inclusion criterion. More than half of the included DRMAs considered the scientific quality and the conflict of interest in formulating conclusions, and assessed the likelihood of publication bias.

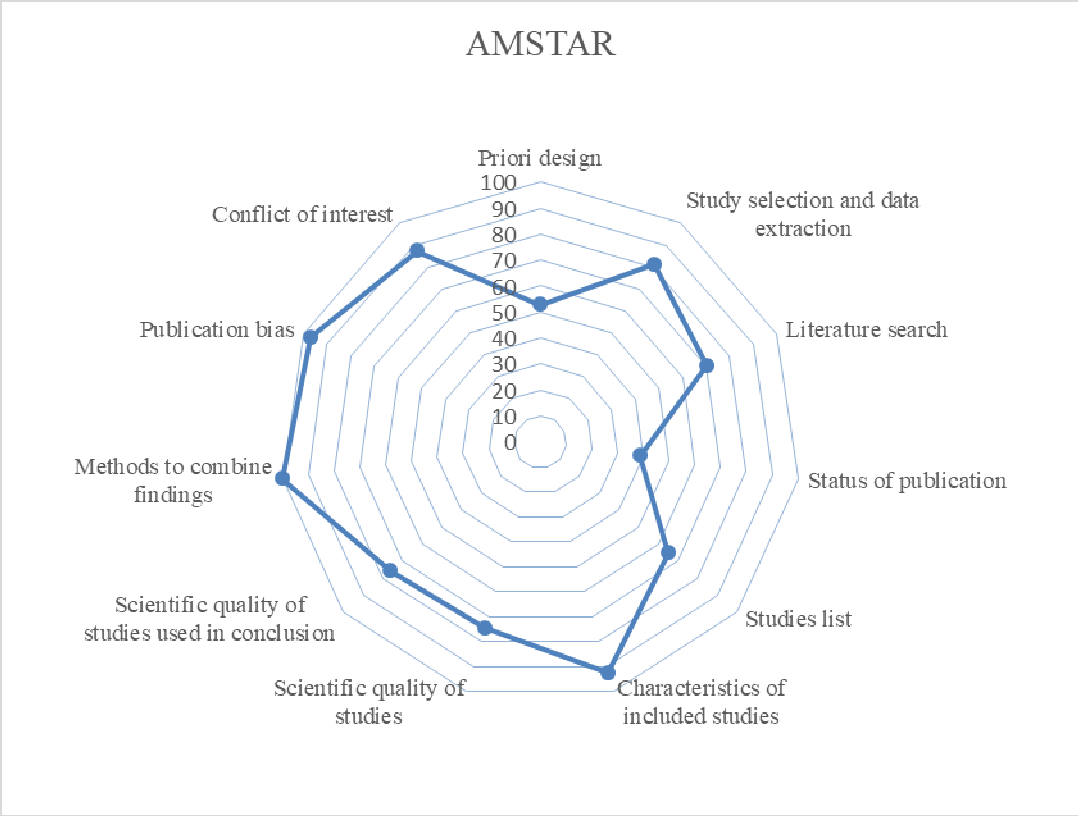

Fig.5. The percentage of adequately reported individual items by AMSTAR.

3.5. Statistical analysis of dose-response effects

The statistical reporting in dose-response meta-analysis is shown in Table 2. For the corresponding RR, approximately half of the included DRMAs (44/93, 47.3%) assigned the median or mean dose of exposure for each category. 57% of the included DRMAs used the

midpoint as the dose when studies reported the exposure by range. When the highest category was open-ended, the most common method (42/93, 45.2%) to assign the dose was the sum of the low end of the interval plus half of the width of the adjacent category. When the lowest category was open-ended, 38(40.9%) of the included DRMAs assumed the dose to be half of the high end of the interval, 14(15.1%) set the lowest boundary as zero, and 41(44.1%) did not mention the method used.

When it comes to dose-response assessment, 69.9% and 76.3% of the included DRMAs assessed linear and non-linear relationships respectively. Half of the included DRMAs used the restricted cubic splines with fixed knots to assess the potential nonlinear dose-response effects. The most common knots adopted (32/47, 68.1%) were 10^{th}, 50^{th}, and 90^{th} percentiles, followed by 5th, 35th, 65th and 95th percentiles (9/47, 19.2%). Almost half of the included DRMAs (45/93, 48.4%) assessed the indication of non-linearity. Dose-response plots were not presented in 14 (15.1%) of the included DRMAs.

Table 2. Statistical reporting in Dose-response meta-analysis (n/%)

Items	Frequency (n)	Proportion (%)
Was the median or mean dose of exposure for each category was assigned to the corresponding RR for every study? (yes)	44	47.31
For studies reporting the exposure by range, was the midpoint of the range used as the dose? (yes)	53	56.99
If the highest category was open-ended, how to confirm the dose?		
The dose was assigned as 20% higher than the low end of the interval.	4	4.30
The dose was assigned as 25% higher than the low end of the interval.	3	3.20
The dose was assigned as 50% higher than the low end of the interval.	5	5.34
The dose was assigned as the sum of the low end of the interval plus half of the width of the adjacent category	42	45.20
The dose was calculated as the lower bound plus 1.5 times the width of the adjacent category.	1	1.10
Not mentioned.	38	40.86
If the lowest category was open-ended, how to confirm the dose?		
The dose was assigned as half of the high end of the interval.	38	40.86
The lowest boundary was set at zero.	14	15.05
Not mentioned.	41	44.09
Dose-response assessment		
Was the linear dose-response relation assessed? (yes)	65	69.90
Was the nonlinear association assessed? (yes)	71	76.34
Were both the linear and nonlinear association assessed? (yes)	45	48.39
Neither the linear nor the nonlinear association was mentioned.	12	12.90
Was the potential nonlinear dose-response relationship assessed using restricted cubic splines with fixed knots?	47	50.54
If the potential nonlinear dose-response relationship was assessed using restricted cubic splines with fixed knots, the knots were:	47	50.54
5th, 35th, 65th and 95th percentiles	9	19.15
25th, 50th, and 75th percentiles	3	6.38
10th, 50th, and 90th percentiles	32	68.09
5th, 50th and 95th percentiles	1	2.13
First, 25th, 50th, 75th, and 99th percentiles	1	2.13
10th, 60th, and 90th percentiles	1	2.13
Was the indication of non-linearity assessed? (yes)	45	48.39

Was the Dose-response Figure presented in the article? (yes)	79	84.95

4. Discussion

4.1. Summary of findings

Generally speaking, the overall adherence rates of the PRISMA and AMSTAR were relatively suboptimal. Findings from our study demonstrated that there were deficiencies in methodological compliance and statistical analysis methods in published DRMAs. Development of reporting guidelines on DRMA is required to assist authors in writing and readers in critically appraising the reports of DRMAs.

4.2. The strengths and limitations of reporting quality

In our study, abstracts of the included DRMAs were not comprehensive. Almost half of the DRMAs lacked a structured summary, making it impossible for researchers to understand research content comprehensively and intuitively from the abstract. Due to no requirements for some magazines in structured abstracts, authors might fail to provide it. Less than one tenth of the included DRMAs provided an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS). Majority of DRMAs did not provide the information about protocol and registration. Relevant research results showed that prospective registration could effectively improve the overall methodological quality of systematic reviews, and it could slightly improve overall reporting quality [18]. Protocol registration reduced the risk of multiple reviews addressing the same research question, identified publication bias, and provided greater transparency

when updating systematic reviews [19] and avoided duplication of effort [20]. Hence, it is necessary to treat preregistration as a mandatory checkpoint for future meta-analyses to be published. It is a promising measure worth researchers' attention which might lead to a significant improvement of quality.

Meta-analyses regularly have the intrinsic limitation of heterogeneity and conclusions could be misleading because of the additional analyses. Most of the meta-analyses did report the quantified heterogeneity using I^2 value or other tests, the source of heterogeneity was not routinely explored. Subgroup analysis and meta-regression can be performed to explain the source of the significant heterogeneity [21, 22]. The interaction between the subgroups was one of the issues to be considered in the quality of meta-analysis, while the dose-response meta-analysis currently has no effective means for detection and adjustment.

About a third of DRMAs described sources of funding and other support (e.g., supply of data), as well as the roles of funders. The sources of the funding and the conflict of interests had an obvious impact on the results of the research. Giving information about funds can help users better identify them, it needs to be reported explicitly in all studies. Not reporting risk of bias assessment may be due to a lack of good quality assessment tools for dose-response studies.

4.3. The strengths and limitations of methodological quality

The overall AMSTAR adherence rate was suboptimal, some methodological flaws were emerged. It was not hard to understand that ‘‘a priori’’ design can make sure the researchers have a clear thinking and well-organized action. Having a protocol or ‘‘a priori’’ design can

partially obligate the authors from post hoc modification of inclusion criteria and analytic methods [10]. Approximately one third of the included DRMAs did not perform a comprehensive literature search. There may be good grounds for only using major database searching without grey literature in DRMAs. Avoiding research on questionable quality, which may led to the low percentage of AMSTAR results. Perfect retrieval is reflected in two aspects: first, the elements of retrieval strategy should be complete; second, the scope of retrieval should be wide. Suboptimal compliance of item 4should also be noted, since exclusion of gray literature from meta-analyses can lead to exaggerated estimates of intervention effectiveness [7]. AMSTAR item 5 (list of studies) were underreported, it gave partial search strategies such as keywords used as MESH terms. Part of the reason was that authors only considered the lists of included studies and neglected the lists of important excluded studies[23].

The majority of the included DRMAs assessed and documented the scientific quality. The scientific nature of a single study can affect the overall outcomes, and the quality grade of the original literature directly reflected the strength of evidence in systematic review. So the scientific nature of individual research needs to be further improved. It is reasonable to develop a methodological guideline of DRMA to help authors to form a clear thinking pathway.

4.4. Developing a reporting guideline specifically for DRMAs

There were no generally accepted methods to estimate doses for open-ended highest or lowest categories currently. The indicated dose should in principle use the mean provided in

the original studies, and if not provided, the median of the extracted dose interval should be used instead. For the open interval of the end, it is usually necessary to make an estimate or hypothesis. Such as taking 1.2 or 1.5 times the cut-off point as the specified dose for the interval, or assuming the same width as the adjacent interval and then taking the median. In our research, the methods used for interval selection and dose determination s were inconsistent or unclear. When the highest category was open-ended, it was often to assign the sum of the low end of the interval plus half of the width of the adjacent category as the dose. On the other hand, when the lowest category was open-ended, many DRMAs assumed the dose to be half of the high end of the interval. There were also doses specified as 20%, 25% and 50% higher than the low end of the interval, respectively. The dose-response mapping process was generally fitted by a restricted cubic spline method, defining a smooth inflection point in the curve fit as a knot. Using an insufficient number of knots is difficult to show detailed changes in the dose response, and using too many knots will result in imprecise fitting. Therefore, 3 or 4 knots were generally used in the dose response mapping[5]. There were several different methods for knots selection, including 5th, 35th, 65th and 95th percentiles, as well as 10th, 50th, and 90th percentiles. There was also a lack of criteria to determine the fixed knots that assessing restricted cubic splines when it comes to nonlinear dose-response relationship.

The complex nature of statistical analysis of DRMAs raised the necessity to develop a guideline about the reporting of statistical analysis of DRMAs. The authors may have used the appropriate method, but omitted important details in published reports, or there was no strict

research process record. The figures and tables related to the dose-response should also be presented in the article. In addition, having a reporting guideline makes the peer review process more efficient and more informed.

Overall, The adherence to the methodological items of reporting guidelines and statistical analysis of published DRMAs were suboptimal. Some methodological flaws had been identified in the published DRMAs, especially regarding to the priority design, comprehensive literature search and the status of publications. Meanwhile, some shortcomings in reporting quality had also come to light, particularly about the structured summary, objectives, protocol and registration. Further improvement could potentially be achieved by strictly adhering to PRISMA guideline and having “a priori” protocol. We propose to develop a reporting guideline specifically for DRMAs, with relevant criteria to define the dose for the open-ended intervals, and explicitly fixed knots to assess restricted cubic splines when it comes to nonlinear dose-response relationship.

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First author	Title	Q1: Was an 'a priori' design provided?	Q2: Was there duplicate study selection and data extraction?	Q3: Was a comprehensive literature search performed?	Q4: Was the status of publications (i.e. grey literature) used as an inclusion criterion?	Q5: Were a list of included studies and flow chart provided?	Q6: Were the characteristics of the included studies provided?	Q7: Was the scientific quality of the included studies assessed and documented?	Q8: Was the scientific quality of the included studies used appropriately in formulating conclusions?	Q9: Were the methods used to combine the findings of studies appropriate?	Q10: Was the likelihood of publication bias assessed?	Q11: Was the conflict of interest included?	Total score
Abar, L.	Height and body fatness and colorectal cancer risk: an update of the WCRF-AICR systematic review of published prospective studies	0	1	1	1	0	0	0	0	1	1	1	6
Akter, S.	Smoking and the risk of type 2 diabetes in Japan: A systematic review and meta-analysis	0	1	1	0	0	1	0	0	1	1	1	6
Aneni, E. C.	Estimates of Mortality Benefit From Ideal Cardiovascular Health Metrics: A Dose Response Meta-Analysis	1	1	1	0	0	1	0	0	1	1	0	6
Aune, D.	Fruit and vegetable intake and the risk of cardiovascular disease, total cancer and all-cause mortality-a systematic review and dose-response meta-analysis of prospective studies	0	1	1	0	1	1	0	0	1	1	1	7
Aune, D.	Physical activity and the risk of preterm birth: a systematic review and meta-analysis of epidemiological studies	0	1	1	0	0	0	1	1	1	1	1	7
Aune, D.	Resting heart rate and the risk of cardiovascular disease, total cancer, and all-cause mortality - A systematic review and dose-response meta-analysis of prospective studies	1	1	1	0	0	1	1	1	1	1	1	9
Aune, D.	Body mass index, abdominal fatness, fat mass and the risk of atrial fibrillation: a systematic review and dose-response meta-analysis of prospective studies	0	1	1	1	0	0	1	1	1	1	0	7
Bai, Y.	Parity and bladder cancer risk: a dose-response meta-analysis	0	1	0	0	1	1	1	1	1	1	1	8
Bechthold, A.	Food groups and risk of coronary heart disease, stroke and heart failure: A systematic review and dose-response meta-analysis of prospective studies	0	1	1	0	0	0	0	0	1	1	1	5
Chen, G. C.	Daytime napping and risk of type 2 diabetes: a meta-analysis of prospective studies	0	1	0	0	0	1	1	1	1	1	1	7
Chiavarini, M.	Dietary Intake of Meat Cooking-Related Mutagens (HCAs) and Risk of Colorectal Adenoma and Cancer: A Systematic Review and Meta-Analysis	0	1	1	0	1	1	1	1	1	1	1	9
D'Elia, L.	Coffee consumption and risk of hypertension: a dose-response meta-analysis of prospective studies	0	1	1	0	0	1	1	1	1	1	0	7
Duan, Q.	Association between water fluoride and the level of children's intelligence: a dose-response meta-analysis	0	1	1	0	0	1	1	1	1	1	1	8
Ekmekcioglu, C.	25-Hydroxyvitamin D Status and Risk for Colorectal Cancer and Type 2 Diabetes Mellitus: A Systematic Review and Meta-Analysis of Epidemiological Studies	0	1	1	0	0	1	0	0	1	1	1	6
Fan, D.	Female alcohol consumption and fecundability: a systematic review and dose-response meta-analysis	1	1	1	1	0	1	1	1	1	1	1	10
Fan, R.	Association between Homocysteine Levels and All-cause Mortality: A Dose-Response Meta-Analysis of Prospective Studies	1	1	1	1	0	1	1	1	1	1	1	10
Garland, C. F.	Dose-response of serum 25-hydroxyvitamin D in association with risk of colorectal cancer: A meta-analysis	0	0	1	1	0	0	0	1	1	0	1	5
Georgakis, M. K.	Anthropometrics at birth and risk of a primary central nervous system tumour: A systematic review and meta-analysis	0	0	1	1	0	0	1	1	1	1	1	7
Giwa, F.	Hospital esophagectomy volume and postoperative length of stay: A systematic review and meta-analysis	1	0	1	0	0	1	0	0	1	1	0	5
Guo, D.	The impact of BMI on sperm parameters and the metabolite changes of seminal plasma concomitantly	1	1	1	0	1	1	0	0	1	1	1	8

Y: Yes; N: No; CA: Cannot answer; NA: Not applicable.

Guo, L.	Association between ideal cardiovascular health metrics and risk of cardiovascular events or mortality: A meta-analysis of prospective studies	0	0	0	0	1	1	1	1	1	1	1	7
Han, H.	Dose-response relationship between dietary magnesium intake, serum magnesium concentration and risk of hypertension: a systematic review and meta-analysis of prospective cohort studies	1	0	1	1	1	1	1	1	1	1	1	10
Han, X.	Alcohol consumption and gastric cancer risk: a meta-analysis of prospective cohort studies	1	0	1	1	0	0	1	1	1	1	1	8
He, Q.	Sleep duration and risk of stroke: a dose-response meta-analysis of prospective cohort studies	1	0	1	1	1	1	1	1	1	1	1	10
Heslehurst, N.	Maternal body mass index and post-term birth: a systematic review and meta-analysis	1	0	1	1	1	1	1	1	1	1	1	10
Huang, X. Z.	Aspirin and non-steroidal anti-inflammatory drugs use reduce gastric cancer risk: A dose-response meta-analysis	0	1	0	0	0	1	1	1	1	1	1	7
Jayedi, A.	Vitamin D status and all-cause mortality in patients with chronic kidney disease: A systematic review and dose-response meta-analysis	1	0	0	0	1	1	0	0	1	1	1	6
Kim, H. B.	Use of benzodiazepine and risk of cancer: A meta-analysis of observational studies	0	0	0	0	1	1	1	1	1	1	1	7
Kwon, Y.	Body Mass Index-Related Mortality in Patients with Type 2 Diabetes and Heterogeneity in Obesity Paradox Studies: A Dose-Response Meta-Analysis	1	0	1	1	0	1	1	1	1	1	0	8
Li, X.	Abdominal obesity and risk of hip fracture: a meta-analysis of prospective studies	1	0	0	1	1	1	1	1	1	1	1	9
Li, Y.	Association of urinary cadmium with risk of diabetes: a meta-analysis	0	1	1	1	0	1	0	0	1	1	1	7
Liu, H.	Association between duration of oral contraceptive use and risk of hypertension: A meta-analysis	0	1	1	1	0	1	0	0	1	1	1	7
Liu, T. Z.	Sleep duration and risk of all-cause mortality: A flexible, non-linear, meta-regression of 40 prospective cohort studies	1	0	1	1	1	1	1	1	1	1	1	10
Liu, W.	Associations between dietary folate intake and risks of esophageal, gastric and pancreatic cancers: an overall and dose-response meta-analysis	0	1	1	0	1	1	0	0	1	1	1	7
Liu, X.	Association between tea consumption and risk of cognitive disorders: A dose-response meta-analysis of observational studies	1	0	1	0	1	1	1	1	1	1	1	9
Loeb, S.	Meta-Analysis of the Association Between Phosphodiesterase Inhibitors (PDE5Is) and Risk of Melanoma	1	1	1	1	1	1	1	1	1	1	1	11
Lu, L.	Aspirin as a potential modality for the chemoprevention of breast cancer: A dose-response meta-analysis of cohort studies from 857,831 participants	0	0	1	0	1	1	1	1	1	1	1	8
Ma, P.	Daily sedentary time and its association with risk for colorectal cancer in adults: A dose-response meta-analysis of prospective cohort studies	0	1	0	0	1	1	0	0	1	1	1	6
Ng, W. L.	Does intentional weight loss improve daytime sleepiness? A systematic review and meta-analysis	0	1	1	1	0	1	1	1	1	1	1	9
Peng, Y.	Potassium measurements and risk of type 2 diabetes: a dose-response meta-analysis of prospective cohort studies	1	1	0	0	1	1	1	1	1	1	1	9
Qin, W.	A U-shaped association of body mass index and all-cause mortality in heart failure patients: A dose-response meta-analysis of prospective cohort studies	0	1	1	0	0	1	1	1	1	1	1	8
Qiu, S. H.	Attenuated heart rate recovery predicts risk of incident diabetes: insights from a meta-analysis	1	0	1	1	1	1	1	1	1	0	1	9
Rahimlu, M.	Body Mass Index and All-cause Mortality in Chronic Kidney Disease: A Dose-response Meta-analysis of Observational Studies	1	1	1	1	1	1	1	1	1	1	1	11

Ralston, G. W.	The Effect of Weekly Set Volume on Strength Gain: A Meta-Analysis	0	1	1	1	1	1	0	0	1	1	1	8
Ren, L.	Number of parity and the risk of rheumatoid arthritis in women: A dose-response meta-analysis of observational studies	1	1	0	0	0	1	1	1	1	1	1	8
Schiattarella, G. G.	Gut microbe-generated metabolite trimethylamine-N-oxide as cardiovascular risk biomarker: a systematic review and dose-response meta-analysis	1	1	1	1	1	1	1	1	1	1	1	11
Schlesinger, S.	Carbohydrates, glycemic index, glycemic load, and breast cancer risk: a systematic review and dose-response meta-analysis of prospective studies	1	1	1	1	1	1	0	0	1	1	1	9
Schwingshackl, L.	Food groups and risk of type 2 diabetes mellitus: a systematic review and meta-analysis of prospective studies	1	1	1	1	1	1	1	1	1	1	1	11
Schwingshackl, L.	Food Groups and Risk of Hypertension: A Systematic Review and Dose-Response Meta-Analysis of Prospective Studies	1	1	1	1	0	1	0	0	1	1	1	8
Schwingshackl, L.	Food groups and risk of colorectal cancer	1	1	1	0	0	1	0	0	1	1	1	7
Schwingshackl, L.	Food groups and risk of all-cause mortality: a systematic review and meta-analysis of prospective studies	1	1	1	0	1	1	0	0	1	1	1	8
Shao, X.	Antibiotic Exposure in Early Life Increases Risk of Childhood Obesity: A Systematic Review and Meta-Analysis	0	1	1	0	0	1	1	1	1	1	0	7
Godos, Justyna	Coffee Consumption and Risk of Biliary Tract Cancers and Liver Cancer: A Dose–Response Meta-Analysis of Prospective Cohort Studies	1	1	0	0	1	1	1	1	1	1	1	9
Shen, N.	Associations between body mass index and the risk of mortality from lung cancer: A dose-response PRISMA-compliant meta-analysis of prospective cohort studies	1	1	0	1	1	1	1	1	1	1	0	9
Shi, J.	Nonsteroidal anti-inflammatory drugs using and risk of head and neck cancer: a dose-response meta analysis of prospective cohort studies	1	1	0	0	1	1	1	1	1	1	1	9
Torquati, L.	Shift work and the risk of cardiovascular disease. A systematic review and meta-analysis including dose-response relationship	1	1	1	0	1	1	0	0	1	1	1	8
Wan, Y.	Fish, long chain omega-3 polyunsaturated fatty acids consumption, and risk of all-cause mortality: a systematic review and dose-response meta-analysis from 23 independent prospective cohort studies	0	1	1	0	1	1	0	0	1	1	1	7
Wang, F.	Carbohydrate and protein intake and risk of ulcerative colitis: Systematic review and dose-response meta-analysis of epidemiological studies	0	1	1	0	1	1	1	1	1	1	1	9
Wang, J.	Gamma-glutamyltransferase and risk of cardiovascular mortality: A dose-response meta-analysis of prospective cohort studies	1	1	1	1	1	1	1	1	1	1	1	11
Weng, K. G.	Soy food intake and risk of gastric cancer: A dose-response meta-analysis of prospective studies	0	1	0	0	1	1	1	1	1	1	1	8
Wu, L.	Sleep duration and falls: a systemic review and meta-analysis of observational studies	1	1	0	0	0	1	1	1	1	1	1	8
Wu, L.	Adherence to Mediterranean diet and risk of developing cognitive disorders: An updated systematic review and meta-analysis of prospective cohort studies	0	1	0	0	1	1	1	1	1	1	1	8
Wu, S.	Advanced parental age and autism risk in children: a systematic review and meta-analysis	1	1	1	1	1	1	1	1	1	1	1	11
Xiong, J.	Tea consumption and the risk of biliary tract cancer: a systematic review and dose-response meta-analysis of observational studies	0	1	1	0	0	1	1	1	1	1	1	8

Xiong, S.	Time spent in outdoor activities in relation to myopia prevention and control: a meta-analysis and systematic review	0	0	1	1	0	1	1	1	1	1	1	8
Xu, T.	Adherence to Antihypertensive Medications and Stroke Risk: A Dose-Response Meta-Analysis	1	0	0	0	1	1	1	1	1	1	0	7
Xu, W.	Alcohol consumption and dementia risk: a dose-response meta-analysis of prospective studies	1	1	1	0	1	1	1	1	1	1	1	10
Yan, J. J.	Predictive value of plasma copeptin level for the risk and mortality of heart failure: a meta-analysis	0	1	0	0	1	1	1	1	1	1	1	8
Yao, K. F.	Meta-analysis reveals gender difference in the association of liver cancer incidence and excess BMI	0	1	1	0	1	1	1	1	1	1	1	9
Ye, Y.	Association between dietary carbohydrate intake, glycemic index and glycemic load, and risk of gastric cancer	1	1	0	0	1	1	1	1	1	1	1	9
Yen, H.	Alcohol intake and risk of nonmelanoma skin cancer: a systematic review and dose-response meta-analysis	1	1	0	0	1	1	1	1	1	1	1	9
Yoon, B. H.	Alcohol intake and the risk of osteonecrosis of the femoral head in Japanese populations: a dose-response meta-analysis of case-control studies	0	1	1	1	1	1	1	1	1	1	1	10
Yuan, S.	Chocolate Consumption and Risk of Coronary Heart Disease, Stroke, and Diabetes: A Meta-Analysis of Prospective Studies	0	1	0	0	1	1	1	1	1	1	0	7
Yin, J.	Relationship of Sleep Duration With All-Cause Mortality and Cardiovascular Events: A Systematic Review and Dose-Response Meta-Analysis of Prospective Cohort Studies	1	1	1	1	1	1	1	1	1	1	1	11
Zeng, L.	Macronutrient Intake and Risk of Crohn's Disease: Systematic Review and Dose-Response Meta-Analysis of Epidemiological Studies	0	1	0	0	1	1	1	1	1	1	1	8
Zhang, D.	Total bilirubin level may be a biomarker of nephropathy in type 2 diabetes mellitus: A meta-analysis of observational studies based on MOOSE compliant	1	1	1	1	1	1	1	1	1	1	1	11
Zhao, R.	Steroid therapy and the risk of osteonecrosis in SARS patients: a dose-response meta-analysis	1	1	1	1	1	1	0	0	1	1	1	9
Xu, T.	Statin Adherence and the Risk of Stroke: A Dose-Response Meta-Analysis	0	1	0	0	1	1	1	1	1	1	1	8
Zhong, C.	Sex-Specific Relationship Between Serum Uric Acid and Risk of Stroke: A Dose-Response Meta-Analysis of Prospective Studies	1	1	1	1	1	1	1	1	1	1	0	10
Zhang, R.	Serum 25-hydroxyvitamin D and the risk of cardiovascular disease: dose-response meta-analysis of prospective studies	1	1	1	0	0	1	1	1	1	1	0	8
Chen, H. L.	Length of surgery and pressure ulcers risk in cardiovascular surgical patients: a dose-response meta-analysis	0	1	0	0	1	1	1	1	1	1	1	8
Lafranconi, A.	Coffee Decreases the Risk of Endometrial Cancer: A Dose-Response Meta-Analysis of Prospective Cohort Studies	1	1	0	0	1	1	1	1	1	1	1	9
Lee, S. W. H.	The impact of sleep amount and sleep quality on glycemic control in type 2 diabetes: A systematic review and meta-analysis	1	1	1	1	1	1	1	1	1	1	1	11
Qiu, S.	Association between physical activity and risk of nonalcoholic fatty liver disease: a meta-analysis	1	1	1	1	1	1	1	1	1	1	1	11
Zhang, S.	Consumption of fruits and vegetables and risk of renal cell carcinoma: a meta-analysis of observational studies	0	1	1	0	1	1	1	1	1	1	1	9
Zhang, S.	Intake of red and processed meat and risk of renal cell carcinoma: a meta-analysis of observational studies	0	1	0	0	1	1	1	1	1	1	1	8
Zhang, T.	Association between nonsteroidal anti-inflammatory drugs use and risk of central nervous system tumors: a dose-response meta analysis	1	1	0	0	1	1	1	1	1	1	1	9

Zhang, T.	Benzodiazepine drug use and cancer risk: a dose-response meta analysis of prospective cohort studies	1	1	1	0	1	1	1	1	1	1	1	10
Zhao, L.	Association of body mass index with bladder cancer risk: a dose-response meta-analysis of prospective cohort studies	1	1	1	1	1	1	1	1	1	1	1	11
Zhou, Q.	Does alcohol consumption modify the risk of endometrial cancer? A dose-response meta-analysis of prospective studies	1	1	1	0	1	1	1	1	1	1	1	10
Zhu, B.	Effect of bilirubin concentration on the risk of diabetic complications: A meta-analysis of epidemiologic studies	0	1	1	0	1	1	1	1	1	1	1	9
Zhu, Y. J.	Association of dietary vitamin E intake with risk of lung cancer: a dose-response meta-analysis	0	1	0	0	0	1	0	0	1	1	1	5
Zuo, J. J.	Characteristics of cigarette smoking without alcohol consumption and laryngeal cancer: overall and time-risk relation. A meta-analysis of observational studies	1	1	1	1	1	1	1	1	1	1	1	11

First author	Title	Q1：Title	Q2：Structured summary	Q3：Rationale	Q4：Objectives	Q5：Protocol and registration	Q6：Eligibility criteria	Q7：Information sources	Q8：Search	Q9：Study selection	Q10：Data collection process	Q11：Data items	Q12：Risk of bias in individual studies	Q13：Summary measures	Q14：Synthesis of results	Q15：Risk of bias across studies	Q16：Additional analyses	Q17：Study selection	Q18：Study characteristics	Q19：Risk of bias within studies	Q20：Results of individual studies	Q21：Synthesis of results	Q22：Risk of bias across studies	Q23：Additional analysis	Q24：Summary of evidence	Q25：Limitations	Q26：Conclusions	Q27：Funding	Total score
Abar, L.	Height and body fatness and colorectal cancer risk: an update of the WCRF-AICR systematic review of published prospective studies	1	1	1	0	0	1	1	1	1	1	1	0	1	1	1	0	1	1	0	1	1	1	0	1	1	1	1	21
Akter, S.	Smoking and the risk of type 2 diabetes in Japan: A systematic review and meta-analysis	1	0	1	0	0	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	0	23
Aneni, E. C.	Estimates of Mortality Benefit From Ideal Cardiovascular Health Metrics: A Dose Response Meta-Analysis	1	1	1	0	1	1	1	1	1	0	1	0	1	1	0	0	1	1	0	1	1	0	0	1	1	1	0	18
Aune, D.	Fruit and vegetable intake and the risk of cardiovascular disease, total cancer and all-cause mortality-a systematic review and dose-response meta-analysis of prospective studies	1	1	1	0	0	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	25
Aune, D.	Physical activity and the risk of preterm birth: a systematic review and meta-analysis of epidemiological studies	1	1	1	0	0	1	1	1	1	1	1	0	1	1	1	1	1	1	0	1	1	1	1	1	1	1	1	23
Aune, D.	Resting heart rate and the risk of cardiovascular disease, total cancer, and all-cause mortality - A systematic review and dose-response meta-analysis of prospective studies	1	1	1	0	0	1	1	1	1	1	1	0	1	1	1	1	1	1	0	1	1	1	1	1	1	1	1	23
Aune, D.	Body mass index, abdominal fatness, fat mass and the risk of atrial fibrillation: a systematic review and dose-response meta-analysis of prospective studies	1	0	1	0	0	1	1	1	1	1	1	0	1	1	1	1	1	1	0	1	1	1	1	1	1	1	0	21
Bai, Y.	Parity and bladder cancer risk: a dose-response meta-analysis	1	1	1	0	0	1	1	1	1	1	1	0	1	1	1	0	1	1	0	1	1	1	0	1	1	1	1	21
Bechthold, A.	Food groups and risk of coronary heart disease, stroke and heart failure: A systematic review and dose-response meta-analysis of prospective studies	1	1	1	0	0	1	1	1	1	1	1	0	1	1	1	1	1	1	0	1	1	1	1	1	1	1	0	22
Chen, G. C.	Daytime napping and risk of type 2 diabetes: a meta-analysis of prospective studies	1	1	1	0	0	1	1	1	1	1	1	0	1	1	0	1	1	1	0	1	1	1	1	1	1	1	0	21
Chiavarini, M.	Dietary Intake of Meat Cooking-Related Mutagens (HCAs) and Risk of Colorectal Adenoma and Cancer: A Systematic Review and Meta-Analysis	1	0	1	0	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	25
D'Elia, L.	Coffee consumption and risk of hypertension: a dose-response meta-analysis of prospective studies	1	1	1	0	1	1	1	1	1	1	1	1	1	1	1	1	1	1	0	1	1	1	1	1	1	1	0	24
Duan, Q.	Association between water fluoride and the level of children's intelligence: a dose-response meta-analysis	1	1	1	0	0	1	1	1	1	1	1	1	1	1	1	1	1	1	0	1	1	1	1	1	1	1	0	23
Ekmekcioglu, C.	25-Hydroxyvitamin D Status and Risk for Colorectal Cancer and Type 2 Diabetes Mellitus: A Systematic Review and Meta-Analysis of Epidemiological Studies	1	1	1	0	0	1	1	1	1	1	1	0	1	1	0	0	1	1	0	1	1	1	0	1	1	1	0	19
Fan, D.	Female alcohol consumption and fecundability: a systematic review and dose-response meta-analysis	1	0	1	0	1	1	1	1	1	1	1	0	1	1	1	1	1	1	1	1	1	1	1	1	1	1	0	23
Fan, R.	Association between Homocysteine Levels and All-cause Mortality: A Dose-Response Meta-Analysis of Prospective Studies	1	0	1	0	1	1	1	1	1	1	1	0	1	1	0	1	1	1	0	1	1	1	1	1	1	1	0	21
Garland, C. F.	Dose-response of serum 25-hydroxyvitamin D in association with risk of colorectal cancer: A meta-analysis	1	0	1	0	0	1	1	1	1	1	1	0	1	1	0	0	0	1	0	1	1	0	1	1	0	1	1	17
Georgakis, M. K.	Anthropometrics at birth and risk of a primary central nervous system tumour: A systematic review and meta-analysis	1	1	1	0	1	1	1	1	1	1	1	1	1	1	0	1	1	1	0	1	1	1	1	1	1	1	0	23
Giwa, F.	Hospital esophagectomy volume and postoperative length of stay: A systematic review and meta-analysis	1	1	1	0	1	1	1	1	1	0	1	0	1	1	1	1	0	1	1	1	1	1	1	1	1	1	0	22
Guo, D.	The impact of BMI on sperm parameters and the metabolite changes of seminal plasma concomitantly	1	0	1	0	0	1	1	1	1	1	1	0	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	23
Guo, L.	Association between ideal cardiovascular health metrics and risk of cardiovascular events or mortality: A meta-analysis of prospective studies	1	1	1	0	0	1	1	1	1	1	1	0	1	1	1	1	1	1	0	1	1	0		1	1	1	0	20
Han, H.	Dose-response relationship between dietary magnesium intake, serum magnesium concentration and risk of hypertension: a systematic review and meta-analysis of prospective cohort studies	1	1	1	0	1	1	1	1	1	1	1	1	1	1	0	1	0	1	0	1	1	1	1	1	1	1	1	23
Han, X.	Alcohol consumption and gastric cancer risk: a meta-analysis of prospective cohort studies	1	0	1	0	1	1	1	1	1	1	1	1	1	1	0	1	0	1	1	1	1	1	1	1	1	1	0	22
He, Q.	Sleep duration and risk of stroke: a dose-response meta-analysis of prospective cohort studies	1	1	1	0	1	1	1	1	1	1	1	0	1	1	1	1	1	1	0	1	1	1	1	1	1	1	0	23
Heslehurst, N.	Maternal body mass index and post-term birth: a systematic review and meta-analysis	1	0	1	0	1	1	1	1	1	0	1	1	1	1	1	1	0	1	1	1	1	1	1	1	1	1	1	23
Huang, X. Z.	Aspirin and non-steroidal anti-inflammatory drugs use reduce gastric cancer risk: A dose-response meta-analysis	1	1	1	0	0	1	1	1	1	1	1	1	1	1	0	0	0	1	1	1	1	1	1	1	1	1	0	21
Jayedi, A.	Vitamin D status and all-cause mortality in patients with chronic kidney disease: A systematic review and dose-response meta-analysis	1	1	1	0	1	1	1	1	1	1	1	0	1	1	1	1	1	1	0	1	1	0	0	1	1	1	0	21
Kim, H. B.	Use of benzodiazepine and risk of cancer: A meta-analysis of observational studies	1	0	1	0	0	1	1	1	1	0	1	0	1	1	1	1	1	1	0	1	1	0	0	1	1	1	0	18
Kwon, Y.	Body Mass Index-Related Mortality in Patients with Type 2 Diabetes and Heterogeneity in Obesity Paradox Studies: A Dose-Response Meta-Analysis	1	1	1	0	1	1	1	1	1	1	1	1	1	1	0	1	1	1	1	1	1	1	1	1	1	1	0	24
Li, X.	Abdominal obesity and risk of hip fracture: a meta-analysis of prospective studies	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	0	1	1	1	1	1	1	1	0	25
Li, Y.	Association of urinary cadmium with risk of diabetes: a meta-analysis	1	0	1	0	0	1	1	1	1	0	1	0	1	1	1	0	1	1	1	1	1	1	1	1	1	1	1	21
Liu, H.	Association between duration of oral contraceptive use and risk of hypertension: A meta-analysis	1	1	1	0	0	1	1	1	1	1	1	1	1	1	1	1	1	1	0	1	1	1	1	1	1	1	0	23
Liu, T. Z.	Sleep duration and risk of all-cause mortality: A flexible, non-linear, meta-regression of 40 prospective cohort studies	1	0	1	0	1	1	1	1	1	0	1	0	1	1	0	1	1	1	0	1	1	0	1	1	1	1	0	19
Liu, W.	Associations between dietary folate intake and risks of esophageal, gastric and pancreatic cancers: an overall and dose-response meta-analysis	1	0	1	0	0	1	1	1	1	1	1	1	1	1	0	1	1	1	1	1	1	1	1	1	1	1	0	22

Liu, X.	Association between tea consumption and risk of cognitive disorders: A dose-response meta-analysis of observational studies	1	1	1	0	1	1	1	1	1	1	1	1	1	1	1	1	1	1	0	1	1	1	1	1	1	1	0	23
Loeb, S.	Meta-Analysis of the Association Between Phosphodiesterase Inhibitors (PDE5Is) and Risk of Melanoma	1	1	1	0	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	26
Lu, L.	Aspirin as a potential modality for the chemoprevention of breast cancer: A dose-response meta-analysis of cohort studies from 857,831 participants	1	1	1	0	0	1	1	1	1	1	1	1	1	1	0	1	1	1	0	1	1	1	1	1	1	1	1	23
Ma, P.	Daily sedentary time and its association with risk for colorectal cancer in adults: A dose-response meta-analysis of prospective cohort studies	1	0	1	0	0	1	1	1	1	1	1	0	1	1	0	1	1	1	1	1	1	1	1	1	1	1	0	21
Ng, W. L.	Does intentional weight loss improve daytime sleepiness? A systematic review and meta-analysis	1	0	1	0	0	1	1	1	1	1	1	0	1	1	0	0	1	1	1	1	1	1	1	1	1	1	1	21
Peng, Y.	Potassium measurements and risk of type 2 diabetes: a dose-response meta-analysis of prospective cohort studies	1	1	1	0	1	1	1	1	1	1	1	0	1	1	0	1	1	1	1	1	1	1	1	1	1	1	1	24
Qin, W.	A U-shaped association of body mass index and all-cause mortality in heart failure patients: A dose-response meta-analysis of prospective cohort studies	1	1	1	0	0	1	1	1	1	1	1	0	1	1	1	1	1	1	1	1	1	1	1	1	1	1	0	23
Qiu, S. H.	Attenuated heart rate recovery predicts risk of incident diabetes: insights from a meta-analysis	1	1	1	0	0	1	1	1	1	1	1	0	1	1	0	1	1	1	0	1	1	0	1	1	1	1	0	20
Rahimlu, M.	Body Mass Index and All-cause Mortality in Chronic Kidney Disease: A Dose-response Meta-analysis of Observational Studies	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	0	26
Ralston, G. W.	The Effect of Weekly Set Volume on Strength Gain: A Meta-Analysis	1	1	1	0	0	1	1	1	1	1	1	0	1	1	1	1	1	1	1	1	1	1	1	1	1	1	0	23
Ren, L.	Number of parity and the risk of rheumatoid arthritis in women: A dose-response meta-analysis of observational studies	1	1	1	0	1	1	1	1	1	1	1	0	1	1	1	1	1	1	1	1	1	1	1	1	1	1	0	24
Schiattarella, G. G.	Gut microbe-generated metabolite trimethylamine-N-oxide as cardiovascular risk biomarker: a systematic review and dose-response meta-analysis	1	1	1	0	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	26
Schlesinger, S.	Carbohydrates, glycemic index, glycemic load, and breast cancer risk: a systematic review and dose-response meta-analysis of prospective studies	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	0	1	1	1	26
Schwingshackl, L.	Food groups and risk of type 2 diabetes mellitus: a systematic review and meta-analysis of prospective studies	1	0	1	0	0	1	1	1	1	1	1	1	1	1	1	1	1	1	0	1	1	1	1	1	1	1	1	23
Schwingshackl, L.	Food Groups and Risk of Hypertension: A Systematic Review and Dose-Response Meta-Analysis of Prospective Studies	1	0	1	0	0	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	0	23
Schwingshackl, L.	Food groups and risk of colorectal cancer	1	0	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	0	25
Schwingshackl, L.	Food groups and risk of all-cause mortality: a systematic review and meta-analysis of prospective studies	1	0	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	26
Shao, X.	Antibiotic Exposure in Early Life Increases Risk of Childhood Obesity: A Systematic Review and Meta-Analysis	1	0	1	0	0	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	24
Godos, Justyna	Coffee Consumption and Risk of Biliary Tract Cancers and Liver Cancer: A Dose–Response Meta-Analysis of Prospective Cohort Studies	1	0	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	0	1	1	1	1	1	1	0	24
Shen, N.	Associations between body mass index and the risk of mortality from lung cancer: A dose-response PRISMA-compliant meta-analysis of prospective cohort studies	1	1	1	0	1	1	1	1	1	1	1	0	1	1	1	1	1	1	1	1	1	1	1	1	1	1	0	24
Shi, J.	Nonsteroidal anti-inflammatory drugs using and risk of head and neck cancer: a dose-response meta analysis of prospective cohort studies	1	0	1	0	1	1	1	1	1	1	1	1	1	1	0	1	1	1	1	1	1	1	1	1	1	1	1	24
Torquati, L.	Shift work and the risk of cardiovascular disease. A systematic review and meta-analysis including dose-response relationship	1	1	1	0	1	1	1	1	1	1	1	0	1	1	0	1	1	1	0	1	1	0	1	1	1	1	0	21
Wan, Y.	Fish, long chain omega-3 polyunsaturated fatty acids consumption, and risk of all-cause mortality: a systematic review and dose-response meta-analysis from 23 independent prospective cohort studies	1	1	1	0	0	1	1	1	1	1	1	0	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	24
Wang, F.	Carbohydrate and protein intake and risk of ulcerative colitis: Systematic review and dose-response meta-analysis of epidemiological studies	1	1	1	0	0	1	1	1	1	1	1	0	1	1	1	1	1	1	0	1	1	1	1	0	1	1	1	21
Wang, J.	Gamma-glutamyltransferase and risk of cardiovascular mortality: A dose-response meta-analysis of prospective cohort studies	1	1	1	0	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	0	25
Weng, K. G.	Soy food intake and risk of gastric cancer: A dose-response meta-analysis of prospective studies	1	0	1	0	0	1	1	1	1	1	1	1	1	1	1	1	1	1	0	1	1	1	1	1	1	1	0	22
Wu, L.	Sleep duration and falls: a systemic review and meta-analysis of observational studies	1	0	1	0	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	0	24
Wu, L.	Adherence to Mediterranean diet and risk of developing cognitive disorders: An updated systematic review and meta-analysis of prospective cohort studies	1	0	1	0	0	1	1	1	1	1	1	0	1	1	1	1	1	1	1	1	1	1	1	1	1	1	0	22
Wu, S.	Advanced parental age and autism risk in children: a systematic review and meta-analysis	1	1	1	0	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	0	25
Xiong, J.	Tea consumption and the risk of biliary tract cancer: a systematic review and dose-response meta-analysis of observational studies	1	0	1	0	0	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	24
Xiong, S.	Time spent in outdoor activities in relation to myopia prevention and control: a meta-analysis and systematic review	1	0	1	0	0	1	1	1	1	1	1	0	1	1	0	1	1	1	0	1	1	0	1	1	1	1	0	19
Xu, T.	Adherence to Antihypertensive Medications and Stroke Risk: A Dose-Response Meta-Analysis	1	1	1	0	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	26
Xu, W.	Alcohol consumption and dementia risk: a dose-response meta-analysis of prospective studies	1	0	1	0	1	1	1	1	1	1	1	0	1	1	1	1	1	1	1	1	1	1	1	0	1	1	0	22
Yan, J. J.	Predictive value of plasma copeptin level for the risk and mortality of heart failure: a meta-analysis	1	0	1	0	0	1	1	1	1	0	1	0	1	1	1	1	1	1	1	1	1	1	1	1	1	1	0	21
Yao, K. F.	Meta-analysis reveals gender difference in the association of liver cancer incidence and excess BMI	1	0	1	0	0	1	1	1	1	1	1	0	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	23

Ye, Y.	Association between dietary carbohydrate intake, glycemic index and glycemic load, and risk of gastric cancer	1	0	1	0	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	25
Yen, H.	Alcohol intake and risk of nonmelanoma skin cancer: a systematic review and dose-response meta-analysis	1	0	1	0	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	24
Yoon, B. H.	Alcohol intake and the risk of osteonecrosis of the femoral head in Japanese populations: a dose-response meta-analysis of case-control studies	1	0	1	0	0	1	1	1	1	1	1	1	1	1	1	1	1	1	1	0	1	1	1	1	1	1	1	1	1	22
Yuan, S.	Chocolate Consumption and Risk of Coronary Heart Disease, Stroke, and Diabetes: A Meta-Analysis of Prospective Studies	1	0	1	0	0	1	1	1	1	0	1	0	1	0	0	1	1	1	1	1	1	1	1	1	1	1	1	1	1	19
Yin, J.	Relationship of Sleep Duration With All-Cause Mortality and Cardiovascular Events: A Systematic Review and Dose-Response Meta-Analysis of Prospective Cohort Studies	1	1	1	0	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	26
Zeng, L.	Macronutrient Intake and Risk of Crohn's Disease: Systematic Review and Dose-Response Meta-Analysis of Epidemiological Studies	1	0	1	0	0	1	1	1	1	1	1	1	1	1	0	1	1	1	1	1	1	1	1	1	1	1	1	1	1	22
Zhang, D.	Total bilirubin level may be a biomarker of nephropathy in type 2 diabetes mellitus: A meta-analysis of observational studies based on MOOSE compliant	1	0	1	0	0	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	23
Zhao, R.	Steroid therapy and the risk of osteonecrosis in SARS patients: a dose-response meta-analysis	1	1	1	0	0	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	25
Zhong, C.	Sex-Specific Relationship Between Serum Uric Acid and Risk of Stroke: A Dose-Response Meta-Analysis of Prospective Studies	1	1	1	0	0	1	1	1	1	1	1	0	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	24
Zhang, R.	Serum 25-hydroxyvitamin D and the risk of cardiovascular disease: dose-response meta-analysis of prospective studies	1	1	1	0	1	1	1	1	1	1	1	1	1	1	0	1	1	1	1	1	1	1	1	1	1	1	1	1	1	25
Chen, H. L.	Length of surgery and pressure ulcers risk in cardiovascular surgical patients: a dose-response meta-analysis	1	0	1	0	0	1	1	1	1	1	1	0	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	22
Lafranconi, A.	Coffee Decreases the Risk of Endometrial Cancer: A Dose-Response Meta-Analysis of Prospective Cohort Studies	1	0	1	0	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	25
Lee, S. W. H.	The impact of sleep amount and sleep quality on glycemic control in type 2 diabetes: A systematic review and meta-analysis	1	0	1	0	1	1	1	1	1	1	1	0	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	23
Qiu, S.	Association between physical activity and risk of nonalcoholic fatty liver disease: a meta-analysis	1	1	1	0	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	25
Zhang, S.	Consumption of fruits and vegetables and risk of renal cell carcinoma: a meta-analysis of observational studies	1	0	1	0	0	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	23
Zhang, S.	Intake of red and processed meat and risk of renal cell carcinoma: a meta-analysis of observational studies	1	0	1	0	0	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	23
Zhang, T.	Association between nonsteroidal anti-inflammatory drugs use and risk of central nervous system tumors: a dose-response meta analysis	1	0	1	0	1	1	1	1	1	0	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	23
Zhang, T.	Benzodiazepine drug use and cancer risk: a dose-response meta analysis of prospective cohort studies	1	0	1	0	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	24
Zhao, L.	Association of body mass index with bladder cancer risk: a dose-response meta-analysis of prospective cohort studies	1	0	1	0	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	0	1	1	1	1	1	1	1	1	1	23
Zhao, Y.	Folate intake, serum folate levels and esophageal cancer risk: an overall and dose-response meta-analysis	1	0	1	0	0	1	1	1	1	1	1	0	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	22
Zhou, Q.	Does alcohol consumption modify the risk of endometrial cancer? A dose-response meta-analysis of prospective studies	1	0	1	0	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	25
Zhu, B.	Effect of bilirubin concentration on the risk of diabetic complications: A meta-analysis of epidemiologic studies	1	0	1	0	0	1	1	1	1	1	1	0	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	22
Zhu, Y. J.	Association of dietary vitamin E intake with risk of lung cancer: a dose-response meta-analysis	1	1	1	0	0	1	1	1	1	1	1	0	1	1	1	1	1	1	1	0	1	1	1	1	1	1	1	1	1	22
Zuo, J. J.	Characteristics of cigarette smoking without alcohol consumption and laryngeal cancer: overall and time-risk relation. A meta-analysis of observational studies	1	0	1	0	1	1	1	1	1	1	1	0	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	24

What is new?

Key findings

- The methodological quality and statistical analysis of published DRMAs were suboptimal. The compliance rates of several PRISMA or AMSTAR checklist items, such as structured summary, objectives, funding, protocol and registration, and status of publication, were less than 50%.
- In these included DRMAs, there were no consistent criteria to estimate the doses for the open-ended intervals of exposure or intervention doses. When the restricted cubic splines were used to fit nonlinear dose-response relationships, there were also no accordant criteria to determine the fixed knots.

What this adds to what was known?

- A comprehensive appraisal evaluating the reporting characteristics, methodological quality, and statistical analysis of published DRMAs is imperative but reporting guidelines for DRMAs is lacking. Our study has summarized the reported key statistical analysis process, which is the important difference between DRMAs and traditional meta-analyses. We proposed a brief recommendation to help further re-view authors to better conduct DRMAs.

What is the implication and what should change now?

- Our study clearly proposes to develop reporting guidelines

specifically for DRMAs. Then there needs to have consistent criteria for defining the dose for the open-ended intervals, simultaneously needs explicitly fixed knots for assessing restricted cubic splines when it comes to nonlinear dose-response relationship.

Authors' contributions:

S-Y.C., Z-X.L., Q-Q.J. and Q-Y.L. conceived and designed the study; F-J.S. and Z-X.L. contributed to the quality assessment; Q-Q.J. and Q-Y.L. conducted the data collection; F.C. and X-T.Z. conducted the literature search, analyzed the data, plotted the figures and tables. Q-Q.J. drafted the article; S-Y.C. and F-J.S. provided statistical guidance; Q-Q.J., Q-Y.L., F.C., X-T.Z., F-J.S., Z-X.L. and S-Y.C. provided careful comments and revised the article. All authors approved the final version. The primary data can be obtained from the first author (Q-Q.J. and Q-Y.L.).

Conflict of interest: None

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