Original Article

Egg consumption and health outcomes: a global evidence mapping based on an overview of systematic reviews

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Background: Several systematic reviews and meta-analyses have assessed the association between egg consumption and human health, but the evidence is often conflicting.

Methods: We conducted a systematic literature search to find all systematic reviews and meta-analyses that assess the association between egg consumption and any type of health outcome. We used AMSTAR to evaluate the methodological quality of the reviews, and GRADE to determine the quality of evidence. We visualized the results using a human anatomy diagram and evidence mapping.

Results: Our search revealed 29 systematic reviews and meta-analyses. Eight studies were of high methodological quality, 16 studies of medium quality, and five studies of low quality. We identified 34 primary outcomes from the included 29 reviews, which were combined into a total of 22 different health outcomes. Two of the primary outcomes were based on high-quality evidence, 18 on moderate-quality evidence, and 14 on low-quality evidence. Egg consumption was associated with an increased risk of two diseases and decreased risk of six outcomes. For ten outcomes, no significant association was found, and for four outcomes, different reviews came to conflicting conclusions.

Conclusions: The association between egg consumption and the risk of cancer, diabetes, cardiovascular diseases and other related diseases has been studied in several meta-analyses. The evidence from different studies on the same topic was often conflicting, which can complicate the making of dietary recommendations.

Keywords: Egg consumption; human health; systematic review; evidence mapping; umbrella review

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Introduction

A healthy and balanced diet can bring us many benefits. Our diet should contain a variety of fresh and nutritious food to keep our body in the best condition. Therefore, the World Health Organization (WHO) recommends that our daily diet should consist of a mix of staple foods including legumes, plenty of fresh fruit and vegetables, and foods of animal origin (e.g., meat, fish, eggs and milk) (1). Eggs are considered to have a high nutritional value, and are thus widely consumed worldwide (2). Eggs are a low-energy, nutrient-dense source of food, being particularly rich of selenium and vitamin D (3). Along with certain kinds of shellfish, eggs are also the main source of dietary cholesterol: a medium-sized egg of 58 g contains 200 mg cholesterol (4). However, egg consumption may also be associated with some health problems, such as brain cancer (5) and hypertension (6).

Many systematic reviews and meta-analyses have assessed the impact of egg consumption on health outcomes. These reviews have identified several diseases that may be potentially associated with egg consumption. For example, one systematic review found a positive dose-response association between the consumption of eggs and the development of gastrointestinal (GI) neoplasms (7). Several systematic reviews addressed the association between egg consumption and cardiovascular disease (8-10). According to Xu's meta-analysis, the risk of cardiovascular disease was not higher among people consuming one egg per day than among those not consuming any eggs (8). Studies by Shin and Tran have shown that egg consumption may increase the incidence of cardiovascular disease in diabetics (9,10). Despite the large number of systematic reviews and meta-analyses, no comprehensive systematic summary or visual presentation of the overall impact of egg consumption has yet been done.

We aimed therefore to assess the existing systematic reviews and meta-analyses and summarize the results visually to fully understand the relationship between egg consumption and human health. We produced a Global Evidence Mapping (GEM) (11) to visualize the association between egg consumption and health outcomes related to different parts of the body. The study protocol was registered at the International Prospective Register of Systematic Reviews (PROSPERO): CRD42019135737 (12). We present the following article in accordance with the PRISMA reporting checklist (13,14) (available at http://dx.doi.org/10.21037/atm-20-4243).

Methods

Data sources and search strategy

We searched PubMed, Embase, Web of Science and Cochrane Library to find the systematic reviews and meta-analyses on the relationship between egg consumption and any disease published up to December 2019. We used the search term ("Egg" AND ("Systematic Review" OR "Meta-analysis")). We also searched databases of grey literature and Google Scholar. Two investigators conducted the search independently. We also checked the references of the identified articles to find additional studies.

Inclusion and exclusion criteria

We included all systematic reviews and meta-analyses related to the relationship between egg consumption and the risk of any disease published in English. We excluded conference abstracts, articles for which we could not retrieve the original data despite contacting the author, and articles for which we failed to access the full text. We also excluded systematic review proposals and umbrella reviews.

Study selection and data extraction

Two researchers screened the literature and extracted the data independently, and cross-checked the findings. In case of disagreement, a third reviewer participated in the discussion. We used Endnote X9 for document management. After deduplication, we read the titles and abstracts to exclude irrelevant articles. We then read the full texts of the remaining articles to decide about the inclusion of the study. We extracted the following data: (I) baseline data (study ID, first author, publication year, country, patients' age, study design, disease or problem, sample size, details of intervention and control, whether quantitative synthesis was conducted, and the main findings); and (II) outcome indicators and related statistical indicators (effect size, 95% CI, I^2, P). If essential information was missing, we contacted the author, or used data conversion to the largest possible extent. Data that could not be obtained were discarded.

Quality assessment

Two researchers independently evaluated the quality of the included studies and cross-checked the results. If necessary, a third reviewer participated in the discussion. Methodological quality assessment of included literature

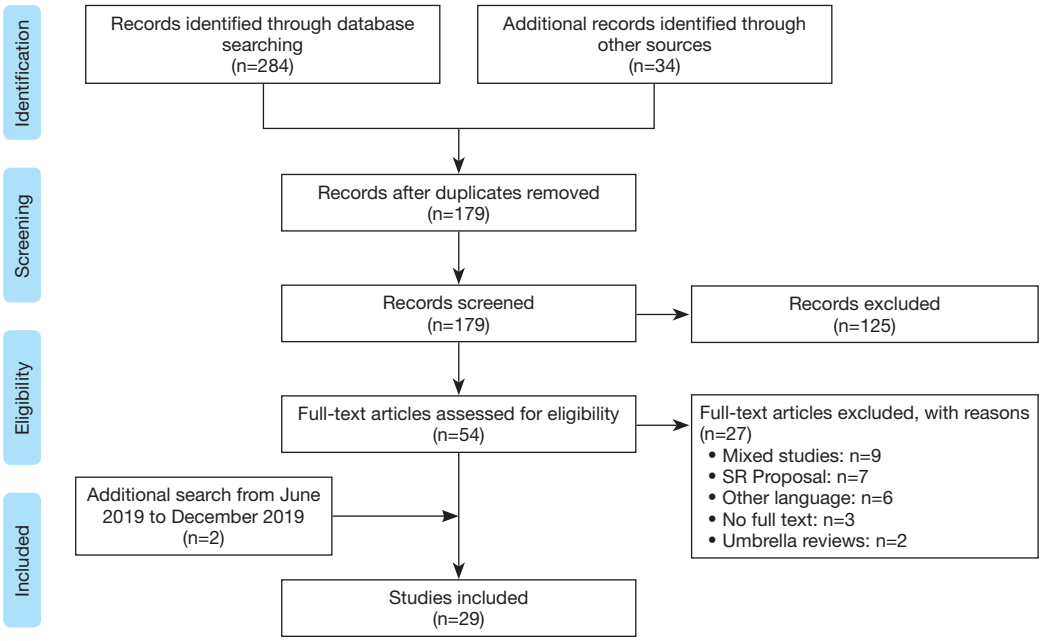

Figure 1 Flow chart of the literature search and screening process.

was performed using the AMSTAR tool (15). The AMSTAR score has a maximum of 11 points, with studies scoring between 9 and 11 being considered to be of high quality, studies scoring between 6 and 8 of medium quality, and studies scoring between 0 and 5 of low quality. We evaluated the quality of evidence for the primary outcome of each included systematic review using the GRADE system method (16).

Statistical analysis

We performed descriptive analyses of the general characteristics, quality and findings of the included systematic reviews. We present the outcomes visually using a human anatomy diagram and a bubble chart.

Results

Search results

A total of 318 articles were identified. After removing duplicates and screening the titles and abstracts, we finally included 29 systematic reviews (*Figure 1*).

Characteristics of the included studies

Thirteen (44.8%) of the 29 included reviews were conducted in China (5,6,8,17-26), 6 in the USA (10,27-31), three in Iran (32-34), and 1 each in France (35), the Netherlands (36), Japan (9), Australia (7), Sweden (37), Canada (38) and Singapore (39). Twenty-six reviews were quantitative analyses and the remaining three (10,35,38) were qualitative studies.

Fourteen reviews (48.3%) (7,10,17-21,23-25,27,35-37) did not report the participants' age (*Table 1*). Only four reviews (32,34,38,39) included randomized controlled trials; other reviews were limited to cohort and case-control studies. Nine reviews (5,6,8,21,24,31,34,35,39) included less than ten original studies. Most (n=21) reviews (6-10,17,19-31,33,37) had a total sample of more than 10,000 participants.

We identified 34 primary outcomes from the 29 included systematic reviews. After we combined the same health outcomes from different studies, we ended up with a total of 22 different outcomes. Among the outcomes, eating eggs was found protective against two diseases and harmful for six types of health outcomes. For ten outcomes, no significant association with egg consumption was found, and on four outcomes the results were controversial.

Quality of included studies

According to the AMSTAR scores, eight studies (6,9,24-26,32-34) were of high quality, 16 studies (6-8,19-

Table 1 Baseline characteristics of the included studies

First author, publication year, country	Disease/problem	Design of primary studies	Number of primary studies	No. of participants	Age of participants	Exposure	Reference category	Quantitative synthesis	Main findings	AMSTAR score
Yoon 2000, France (35)	colorectal adenomas	Case-control studies	5	NA	NA	Egg consumption	NA	No	No consistent association with egg consumption was found in the five available studies	Low
Weggemans 2001, Netherlands (36)	ratio of total cholesterol to high-density lipoprotein cholesterol in humans	Studies were included if they had a crossover or parallel design with a control group	17	556	NA	Egg consumption	NA	Yes	Dietary cholesterol raises the ratio of total to HDL cholesterol and, therefore, adversely affects the cholesterol profile	Low
Fang 2012, China (17)	bladder cancer	4 cohort and 9 case-control studies	13	133,690	NA	Highest egg intake	Lowest egg intake	Yes	No strong evidence of a significant association of egg consumption with bladder cancer incidence, but a protective effect shown in Japanese population	Low
Xie 2012, China (18)	prostate cancer	9 cohort studies and 11 case-control studies	20	5,791	NA	High intake of eggs	NA	Yes	No evidence of a significant influence of egg consumption on prostate cancer incidence or mortality	Low
Li 2013, China (19)	bladder cancer	4 cohort studies and 9 case-control studies	13	184,727	NA	Highest egg intake	Lowest egg intake	Yes	No significant association between bladder cancer risk and egg consumption, except a possible positive relationship with the intake of fried eggs based on the limited number of studies	Medium
Li 2013, China (20)	cardiovascular diseases and diabetes	11 cohort, 1 case-control or 2 cross-sectional design	14	320,778	NA	Highest egg intake; each 4/week increment in egg intake	Lowest egg intake	Yes	Dose response positive association found between egg consumption and the risk of CVD and diabetes	Medium
Rong 2013, China (21)	coronary heart disease and stroke	Prospective cohort studies	8	474,342	NA	1 egg/day; Highest	NA; lowest	Yes	Higher consumption of eggs (up to one egg per day) is not associated with an increased risk of coronary heart disease or stroke	Medium
Shin 2013, Japan (9)	cardiovascular disease and diabetes	Prospective cohort studies	16	579,970	>17	The highest category (>1 egg/d) of egg consumption	The lowest egg consumption (1 egg/week or less)	Yes	Egg consumption is not associated with the risk of CVD and cardiac mortality in the general population. Egg consumption may be associated with an increased incidence of type 2 diabetes among the general population and CVD comorbidity among diabetic patients	High
Tse 2014, Australia (7)	gastrointestinal (GI) neoplasms	37 case-control studies; 7 cohort studies	44	424,867	NA	The number of eggs consumed or the frequency of consumption	NA	Yes	Egg consumption is associated with a positive dose-response association with the development of GI neoplasms	Medium
Si 2014, China (22)	breast cancer	8 case control studies and 5 cohort studies	13	825,504	>20	1–2, 2–5, >5 eggs/week	NA	Yes	Egg consumption was associated with increased breast cancer risk among the European, Asian and postmenopausal populations and those who consumed 2 to 5 eggs per week	Medium
Tran 2014, USA (10)	cardiovascular disease among diabetic individuals	6 prospective cohort studies; 4 case-control studies	10	83,099	NA	NA	NA	No	Four of the six studies that examined CVD and mortality and egg consumption among diabetics found a statistically significant association	Low
Zeng 2015, China (23)	ovarian cancer	6 case-control studies and 6 cohort studies	12	629,453	NA	Highest egg intake	Lowest egg intake	Yes	Egg consumption may increase the risk of ovarian cancer	Medium
Keum 2015, USA (27)	cancers of the breast, ovary and prostate	NA	18	16,023	NA	2, 5, 9 eggs/week	NA	Yes	No evidence was found for an association with the risk of total prostate cancer	Medium
Wu 2016, China (24)	breast cancer	Cohort studies	9	639,720	NA	Highest egg intake	Lowest egg intake	Yes	No association between egg and breast cancer risk was found	High
Tamez 2016, USA (28)	type 2 diabetes	Prospective cohort studies	10	251,213	>30	Highest egg intake	lowest egg intake	Yes	The association of egg intake with increased risk of incident type 2 diabetes found only in US cohort studies	Medium
Djoussé 2016, USA (29)	type 2 diabetes	12 prospective cohorts from 8 unique cohorts after full-text review	12	219,979	20–98	Highest egg intake	Lowest egg intake	Yes	No relation between infrequent egg consumption and DM risk but suggests a modest elevated risk of DM with ≥3 eggs/week that is restricted to US studies	Medium
Wallin 2016, Sweden (37)	type 2 diabetes	Cohort studies and case-control studies	11	39,610	NA	1–2, 3, 3–4, ≥5 times/week	<1 time/week	Yes	No support found for an association between egg consumption and risk of type 2 diabetes	Medium
Alexander 2016, USA (30)	coronary heart disease and stroke	Cohort studies	14	548,000	≥15	0–1, 1–3.5, 3.5–7, >7 eggs/week	NA	Yes	Consumption of up to one egg daily may contribute to a decreased risk of stroke, and daily egg intake does not appear to be associated with risk of CHD	Medium

Table 1 *(continued)*

Table 1 *(continued)*

First author, publication year, country	Disease/problem	Design of primary studies	Number of primary studies	No. of participants	Age of participants	Exposure	Reference category	Quantitative synthesis	Main findings	AMSTAR score
Khawaja 2017, USA (31)	heart failure	Prospective Cohort Studies	4	105,999	53–63	The highest category (≥1/day) of egg consumption	The lowest egg consumption (<1 egg/week)	Yes	An elevated risk of incident heart failure with frequent egg consumption was found	Medium
Richard 2017, Canada (38)	individuals with type 2 diabetes and at risk for developing diabetes	Original RCTs	10	768	≥18	NA	NA	No	Egg consumption is not associated with adverse effect on major CVD risk factors in individuals at risk for developing diabetes or with type 2 diabetes	Medium
Dong 2017, China (25)	non-Hodgkin lymphoma	9 case control studies or 3 cohort studies	12	11,271	NA	Highest egg intake	Lowest egg intake	Yes	Consumption of poultry and eggs is unlikely related to the risk of NHL	High
Rouhani 2018, Iran (32)	blood lipids	RCTs (cross-over & parallel)	27	1,734	10–75	NA	NA	Yes	Consumption of eggs increases total cholesterol, LDL-C and HDL-C, but not the LDL-C:HDL-C ratio, TC: HDL-C ratio and TG compared with low egg control diets	High
Zhang 2018, China (6)	hypertension	Prospective cohort studies	8	291,687	≥18	Highest egg intake	Lowest egg intake	Yes	Egg consumption was associated with a lower risk of HTN	High
Aminianfar 2019, Iran (33)	upper aero-digestive tract cancers	4 cohort, 2 nested case-control studies, 32 case control and 2 others	40	165,197	All ages	Highest egg consumption (ranging from ≥1 meal/d to ≥3 times/month)	Lowest egg consumption (ranging from 0–20 g/d to never)	Yes	High egg consumption was associated with increased risk of UADT cancers only in HCC studies but not in PCC or prospective cohort studies	High
Xu 2019, China (8)	cardiovascular disease and all-cause mortality	Cohort	13	28,024	≥50	Highest egg intake (<1, 1–2, 3–4, 5–6, >7 egg/day)	Lowest egg consumption (≤1 egg /week or less)	Yes	Eating one egg daily is not associated with increase in CVD or all-cause mortality	Medium
Wang 2019, Singapore (39)	blood pressure, lipids and lipoproteins in middle-aged and older population	RCTs	8	412	≥51.9	At least 3–4 whole eggs/week	<3 whole eggs/week	Yes	Quantity of whole eggs consumed per week does not affect CVD risk factors, and consuming egg substitutes may also be beneficial compared to eggs on lowering CVD risk in the middle-aged and older population	Medium
Luo 2019, China (5)	brain cancer	Population-based case-control studies; hospital-based case-control studies; cohort	5	5425	≥18	Highest egg intake	Lowest egg intake	Yes	Consumption of poultry and eggs are unlikely associated with the risk of brain cancer	Medium
Sajadi Hezaveh 2019, Iran (34)	inflammatory markers	RCTs (cross-over & parallel)	9	481	≥18	Egg consumption	No egg consumption	Yes	Egg consumption had no significant effect on serum biomarkers of inflammation in adults	High
Mazidi 2019, China (26)	coronary heart disease and stroke	Prospective cohort studies	10	110,400	>17	Egg consumption	NA	Yes	No association between CHD or total mortality and egg consumption, but a negative association between egg intake and stroke mortality was found	High

NA, not available; DM, diabetes mellitus; CHD, coronary heart disease; CVD, cardiovascular disease; RCTs, randomized controlled trials; UADT, upper aero-digestive tract; HCC, hospital-based case-control studies; PCC, population-based case-control studies.

23,27-31,37-39) of medium quality, and five studies (10,17,18,35,36) of low quality (*Table 1*). According to our assessment using the GRADE approach, two of the 34 primary outcomes were based on high-quality evidence, 18 on moderate-quality evidence, and 14 on low-quality evidence (*Table 2*).

Risk of cancer

Twelve studies (5,7,17-19,22-25,27,33,35) examined the association between the risk of different types of cancer and egg consumption. Three of these studies assessed the risk of breast cancer (22,24,27), two the risk of bladder cancer (17,19), two the risk of ovarian cancer (23,27), two the risk of prostate cancer (18,27), and one each the risk of colorectal adenomas (35), GI neoplasms (7), non-Hodgkin's lymphoma (25), upper aero-digestive tract cancers (33), and brain cancer (5).

A meta-analysis (22) of 13 observational studies showed that egg consumption was associated with a slightly increased risk of breast cancer among postmenopausal women of European and Asian origin [relative risk (RR) =1.04, 95% CI: 1.01–1.08 for those consuming 2 to 5 eggs/week, compared with <1 eggs/week]. Another meta-analysis (24) published in 2016 found similar results between egg consumption and the risk of breast cancer, although the results were not significant (RR of highest versus lowest category of egg consumption: 1.04, 95% CI: 0.98–1.11).

The meta-analysis assessing the risk of cancers of the upper aero-digestive tract (33) found no significant association between egg consumption and the risk of cancer in population-based case-control [odds ratio (OR) =1.25; 95% CI: 0.59–2.67] or prospective cohort studies (OR =0.86; 95% CI: 0.71–1.04). However, a positive significant association was observed in hospital-based case-control studies (OR =1.50; 95% CI: 1.34–1.68). A meta-analysis (7) of 44 observational studies found a positive dose-response association between egg consumption and the development of GI neoplasms. Two systematic reviews (23,27) showed that the risk of ovarian cancer may be elevated among people who consume eggs. No significant association was found between egg consumption and colorectal adenomas, bladder cancer, prostate cancer, non-Hodgkin's lymphoma, or brain cancer (*Figure 2*).

Diseases of circulatory system

Ten studies (6,8-10,20,21,26,30,31,39) examined the

Table 2 Summary of findings for the primary outcomes

Studies	No. of studies	Factors that can reduce the quality of the evidence						Relative effect (95% CI)	Quality of evidence
		Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations		
Weggemans 2001: the effect of dietary cholesterol on the ratio of total to HDL cholesterol (36)	17	OS	Serious[a]	Not serious	Not serious	Not serious	None	0.02 (0.01–0.03)	Moderate
Fang 2012: Risk of bladder cancer (17)	13	OS	Serious[a]	Serious[b]	Not serious	Not serious	None	0.94 (0.69–1.18)	Low
Xie 2012: Risk of prostate cancer (cohort studies) (18)	6	OS	Serious[a]	Not serious	Not serious	Not serious	None	0.97 (0.87–1.07)	Moderate
Xie 2012: Risk of prostate cancer (case-control studies) (18)	11	OS	Serious[a]	Serious[b]	Not serious	Not serious	None	1.07 (0.86–1.31)	Low
Li 2013: Risk of bladder cancer (19)	13	OS	Serious[a]	Serious[b]	Not serious	Not serious	None	1.11 (0.90–1.35)	Low
Li 2013: Risk of cardiovascular diseases (20)	12	OS	Serious[a]	Serious[b]	Not serious	Not serious	None	1.19 (1.02–1.38)	Low
Li 2013: Risk of diabetes (20)	6	OS	Serious[a]	Not serious	Not serious	Not serious	None	1.83 (1.42–2.37)	Moderate
Rong 2013: Risk of coronary heart disease (21)	9	OS	Serious[a]	Not serious	Not serious	Not serious	None	0.99 (0.85–1.16)	Moderate
Rong 2013: Risk of stroke (21)	8	OS	Serious[a]	Not serious	Not serious	Not serious	None	0.91 (0.81–1.02)	Moderate

Table 2 *(continued)*

Table 2 *(continued)*

Studies	Factors that can reduce the quality of the evidence							Relative effect (95% CI)	Quality of evidence
	No. of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations		
Shin 2013: Risk of cardiovascular diseases (9)	12	OS	Serious[a]	Not serious	Not serious	Not serious	None	0.96 (0.88–1.05)	Moderate
Shin 2013: Risk of diabetes (9)	5	OS	Serious[a]	Not serious	Not serious	Not serious	None	1.42 (1.09–1.86)	Moderate
Tse 2014: Risk of gastrointestinal (GI) neoplasms (7)	44	OS	Serious[a]	Serious[b]	Not serious	Not serious	None	1.15 (1.09–1.22)	Low
Si 2014: Risk of breast cancer (22)	13	OS	Serious[a]	Serious[b]	Not serious	Not serious	None	1.04 (1.01–1.08)	Low
Zeng 2015: Risk of ovarian cancer (23)	12	OS	Serious[a]	Not serious	Not serious	Not serious	None	1.21 (1.06–1.38)	Moderate
Keum 2015: Risk of breast cancer (27)	10	OS	Serious[a]	Not serious	Not serious	Not serious	None	1.05 (0.99–1.11)	Moderate
Keum 2015: Risk of ovarian cancer (27)	12	OS	Serious[a]	Not serious	Not serious	Not serious	None	1.09 (0.96–1.24)	Moderate
Keum 2015: Risk of prostate cancer (27)	10	OS	Serious[a]	Not serious	Not serious	Not serious	None	1.00 (0.88–1.14)	Moderate
Wu 2016: Risk of breast cancer (24)	9	OS	Serious[a]	Not serious	Not serious	Not serious	None	1.04 (0.98–1.11)	Moderate
Tamez 2016: Risk of type 2 diabetes (28)	10	OS	Serious[a]	Serious[b]	Not serious	Not serious	None	1.13 (1.04–1.22)	Low
Djoussé 2016: Risk of type 2 diabetes (29)	12	OS	Serious[a]	Serious[b]	Not serious	Not serious	None	1.09 (0.99–1.20)	Low
Wallin 2016: Risk of type 2 diabetes (37)	11	OS	Serio[u]sa	Serious[b]	Not serious	Not serious	None	1.03 (0.96–1.10)	Low
Alexander 2016: Risk of coronary heart disease (30)	7	OS	Serious[a]	Not serious	Not serious	Not serious	None	0.97 (0.88–1.07)	Moderate
Alexander 2016: Risk of stroke (30)	7	OS	Serious[a]	Not serious	Not serious	Not serious	None	0.88 (0.81–0.97)	Moderate
Khawaja 2017: Risk of heart failure (31)	4	OS	Not serious	Not serious	Not serious	Not serious	None	1.25 (1.12–1.39)	High
Dong 2017: Risk of non-Hodgkin lymphoma (25)	7	OS	Serious[a]	Serious[b]	Not serious	Not serious	None	1.15 (0.87–1.51)	Low
Rouhani 2018: Risk of blood lipids (32)	27	RCT	Serious[a]	Serious[b]	Not serious	Not serious	None	7.17 (4.34–10.01)	Low
Zhang 2018: Risk of hypertension (6)	3	OS	Not serious	Not serious	Not serious	Not serious	None	0.79 (0.68–0.91)	High
Aminianfar 2019: Risk of upper aero-digestive tract cancers (33)	40	OS	Serio[u]sa	Serious[b]	Not serious	Not serious	None	1.42 (1.19–1.68)	Low
Xu 2019: Risk of cardiovascular disease (8)	13	OS	Serious[a]	Not serious	Not serious	Not serious	None	0.97 (0.90–1.05)	Moderate
Wang 2019: Risk of blood pressure (39)	8	RCT	Serious[a]	Not serious	Not serious	Not serious	None	0.20 (0.06–0.34)	Moderate
Luo 2019: Risk of brain cancer (5)	5	OS	Serious[a]	Serious[b]	Not serious	Not serious	None	1.00 (0.55–1.81)	Low
Sajadi Hezaveh 2019: Risk of inflammatory markers (34)	8	RCT	Serious[a]	Serious[b]	Not serious	Not serious	None	0.24 (–0.43 to 0.90)	Low
Mazidi 2019: Risk of coronary heart disease (26)	6	OS	Serious[a]	Not serious	Not serious	Not serious	None	1.23 (0.88–1.71)	Moderate
Mazidi 2019: Risk of stroke (26)	8	OS	Serious[a]	Not serious	Not serious	Not serious	None	0.72 (0.54–0.96)	Moderate

[a], downgraded because of the risk of bias of included studies; [b], downgraded because of I^2 ≥50%. Quality of evidence: high: we are very confident that the true effect lies close to that of the estimate of the effect; moderate: we are moderately confident in the effect estimate: the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different; low: our confidence in the effect estimate is limited: the true effect may be substantially different from the estimate of the effect; very low: we have very little confidence in the effect estimate: the true effect is likely to be substantially different from the estimate of effect. OS, observational study; RCT, randomized controlled trial.

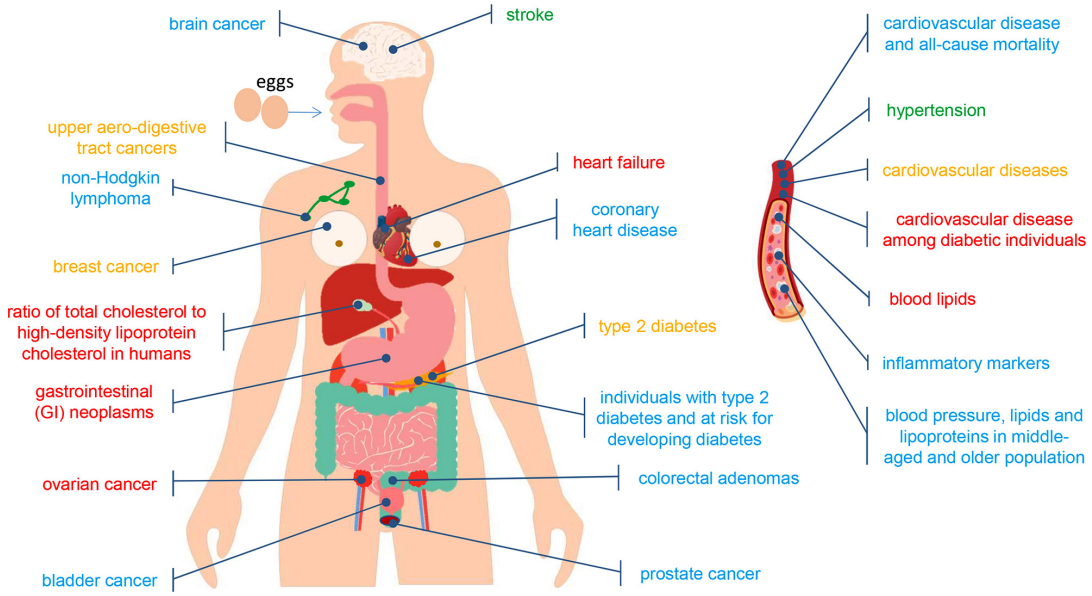

Figure 2 Human anatomy diagram of diseases or problems (localization). Color: green indicates that egg consumption is a beneficial factor for health outcomes; red indicates that egg consumption is a harmful factor for health outcomes; blue indicates that there is no significant association between egg consumption and health outcomes; yellow indicates that the stake in egg consumption and health outcomes is controversial.

association between circulatory system diseases and egg consumption. Among these, four meta-analyses focused on cardiovascular diseases (8-10,20), three on coronary heart disease and stroke (21,26,30), two on blood pressure (6,39), and one on heart failure (31).

The results of the four meta-analyses on cardiovascular diseases (8-10,20) were controversial. Two meta-analyses (9,11) showed that egg consumption was not associated with the risk of cardiovascular diseases in the general population. However, another meta-analysis found that egg consumption may be associated with an increased incidence of cardiovascular diseases among diabetic patients (10). One meta-analysis (11) concluded that eating one egg daily is not associated with a higher risk of cardiovascular disease or all-cause mortality, but another (10) found a positive dose-response association between egg consumption and the risk of cardiovascular diseases among diabetic patients.

Three meta-analyses (21,26,30) suggested that a consumption of up to one egg per day is not associated with increased risk of coronary heart disease, and consumption of up to one egg daily may contribute to a decreased risk of total stroke compared to consuming no eggs.

One meta-analysis (6) showed that people with the highest consumption of eggs had a lower risk of hypertension than those with the lowest consumption (RR =0.79, 95% CI: 0.68–0.91). Another systematic review (39) found no difference in blood pressure between the consumption of more than four whole eggs/week compared to up to four whole eggs/week.

One meta-analysis (31) suggested that the risk of incident heart failure is associated with frequent egg consumption (RR of consuming at least one egg/day *vs.* the lowest egg consumption category: 1.25, 95% CI: 1.12–1.39) (*Figure 2*).

Metabolic diseases

We identified ten meta-analyses (9,20,28,29,32,35-39) of randomized controlled trials and observational studies assessing the relationship between metabolic diseases and egg consumption. Among these, six meta-analyses presented the association of egg consumption with type 2 diabetes (9,20,28,29,37,38), three with blood lipids (32,36,39) and one with cholesterol (35).

Three of the six meta-analyses on diabetes (9,20,28) indicated that egg consumption may be associated with an increased incidence of type 2 diabetes. The remaining three systematic reviews (29,37,38) did not support an association between egg consumption and the risk of type 2 diabetes.

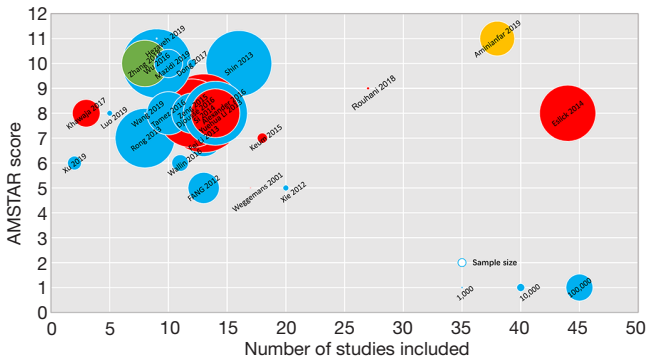

Figure 3 Evidence mapping of egg consumption and health outcomes. Bubbles: the studies included in this article (first author, publication year). Bubble size: sample size. X-axis: number of studies included. Y-axis: AMSTAR score. Color: green bubbles indicate that egg consumption is a beneficial factor for health outcomes; red bubbles indicate that egg consumption is a harmful factor for health outcomes; blue bubbles indicate that there is no significant association between egg consumption and yellow bubbles indicate that the stake in egg consumption and health outcomes is controversial.

A meta-analysis (36) including 17 studies involving 556 subjects found that dietary cholesterol raises the ratio of total to high-density lipoprotein cholesterol and, therefore, adversely affects the cholesterol profile. Another meta-analysis (32) showed that consumption of eggs increases total cholesterol (TC), low density lipoprotein-cholesterol (LDL-C) and high-density lipoprotein-cholesterol (HDL-C), but not the LDL-C to HDL-C ratio, TC to HDL-C ratio or triglyceride (TG).

Finally, a meta-analysis (34) published in 2019 studied the relationship between egg consumption and inflammatory markers, and found that egg consumption had no significant effect on serum biomarkers of inflammation in adults (*Figure 2*).

Evidence mapping

Figure 3 visualizes the association between egg consumption and health outcomes. The bubble plot includes 26 meta-analyses; the reviews by Yoon *et al.* (35), Tran *et al.* (10) and Richard *et al.* (38) were excluded because they did not include quantitative analyses. The X-axis, Y-axis, size and color of the bubbles represent the number of studies included, AMSTAR score, sample size (participants), and main findings, respectively. Every included systematic review corresponds to one single bubble in the bubble chart.

We used four colors to distinguish the main findings of the 26 studies. Green bubbles indicate that egg consumption is a beneficial factor for health outcomes; red bubbles indicate that egg consumption is a harmful factor for health outcomes; blue bubbles indicate that there is no significant association between egg consumption and health outcomes; and yellow bubbles indicate that the stake in egg consumption and health outcomes is controversial, meaning that studies have found both positive and negative associations.

The X-axis shows the number of studies included in each systematic review or meta-analysis, and the Y-axis the AMSTAR score.

Discussion

Our study identified 29 systematic reviews of randomized controlled trials and observational studies on egg consumption. We found no evidence for neither beneficial nor harmful association between egg consumption and range of health outcomes, including colorectal adenomas, bladder cancer, prostate cancer, non-Hodgkin's lymphoma and brain cancer. For some health outcomes, such as heart failure, GI neoplasms, and ovarian cancer, egg consumption was found to be harmful, and for some health outcomes, including hypertension and stroke, protective. For diabetes, breast cancer, cardiovascular diseases and upper aero-digestive tract cancers, different systematic reviews came to controversial conclusions. The quality of evidence was high only for 2 of the 34 included primary outcomes. For 14 outcomes the quality of evidence was low, and for 18 outcomes moderate.

Three meta-analyses (22,24,27) assessed the relationship between breast cancer and egg consumption. Two out of the three found a non-significantly increased risk of breast cancer among people consuming eggs moderately. Consuming more than five eggs per week was however associated with a significantly higher risk of breast cancer than no egg consumption (27). One potential reason for the increased risk of breast cancer is that the nutritional ingredients of eggs may promote the accumulation of cholesterol and may alter the signaling pathways such as steroid hormone receptors to promote cancer progression (40). Another possible reason is that some cooking methods may affect the composition of the eggs in a way that increases the risk of cancer (41).

Our study found controversies regarding egg consumption and the risk of cardiovascular diseases. A meta-analysis (20) involving 320,000 participants found a positive dose-response association between egg consumption and the risk of cardiovascular diseases. However, three other systematic reviews on the same topic found no association. A recent review (42) of egg consumption and heart disease showed that the risk of cardiovascular diseases differs across risk groups. A cohort study (43) involving 29,615 US adults suggested that high consumption of dietary cholesterol or eggs has a significant positive dose-response association both with the risk of incident cardiovascular diseases and with all-cause mortality.

Eggs are a major source of dietary cholesterol (44). However, the consumption of eggs should be kept within reasonable limits to prevent cardiovascular or other diseases. Most national dietary recommendations have removed the restrictions on dietary cholesterol and egg consumption (45). High quality and indigenized practice guidelines on dietary cholesterol are needed.

We found inconsistent results on the association between high egg consumption and the incidence of diabetes. Results from Shin *et al.*, Li *et al.* and Tamez *et al.* (9,20,28) indicated that egg intake was associated with an increased incidence of type 2 diabetes. However, evidence from the Djoussé *et al.*, Wallin *et al.* and Richard *et al.* (29,37,38) did not support an association between egg consumption and the risk of type 2 diabetes. There may be several reasons for these inconsistent findings. First, meta-analyses may have been affected by the inherent limitations of primary studies. Second, different systematic reviews had different inclusion and exclusion criteria. Third, the variety in the methods of preparation (boiled, fried, or raw) and ways of consumption (separately, or as a part of dishes such as pasta, cake, omelets, or mixed dishes) may also contribute to heterogeneity in the results (29).

Eggs are one of the major sources of protein (46). Diets high in cholesterol, saturated fat, and trans-fatty acid can raise blood cholesterol levels, which may induce abnormal blood lipids and blood glucose metabolism. A recent review (47) showed that the effect of increased consumption of eggs on risk markers for type 2 diabetes in healthy subjects was not significant. Another review (48) indicated that consuming more eggs than recommended (by some countries) as part of an otherwise healthy diet is safe, also for people with high risk of type 2 diabetes. A meta-analysis published in 2017 suggested that egg intake was not associated with a risk of type 2 diabetes (49). Some dietary clinical practice guidelines on diabetes have not suggested to limit egg intake (50), whereas some recommend to restrict egg consumption to a low level (51,52). These conflicting findings may be caused by differences in dietary patterns and socioeconomic factors. Another explanation could be that eggs may also offer some protective effect against diabetes: egg white hydrolysate, lutein, zeaxanthin, and angiotensin I-converting enzyme inhibitory tripeptides from eggs have been shown to protect against glucose and insulin resistance, oxidative stress, and inflammation in the context of type 2 diabetes (53).

Two previous articles have addressed a topic similar with this study (54,55). One studied the association of egg consumption and human health, covering 21 systematic reviews on different types of cancer, type 2 diabetes and cardiovascular disease. The results showed no strong evidence of detrimental effects of egg consumption on human health. This finding is consistent with our study. Another study examined the effect of egg consumption on cardiometabolic health outcomes using the results of 23 systematic reviews, and found no associated between egg consumption and the risk of cardiovascular disease in the general population. However, these two studies did not appraise the quality of the evidence. The quality of the evidence, preferably using established methods such as the GRADE approach, is an essential factor when interpreting the findings of systematic reviews (56).

Strengths and limitations of this study

To our knowledge, this is the first study using evidence mapping and visual diagrams to present the association between egg consumption and health outcomes. Moreover, this overview, unlike the previous ones, systematically summarizes the current evidence for all types of health outcomes without restrictions. We also evaluated the methodological quality and certainty of the evidence by the AMSTAR tool and GRADE approach. However, this umbrella review also has several limitations. First, most of the included reviews were based on observational studies, which may cause confounding and bias. Second, we did not conduct any sensitivity analyses excluding the studies at high risk of bias. Finally, we did not estimate the effect size of primary outcomes because of the heterogeneity between the studies.

Conclusions

The associations between egg consumption and the

incidence of cancer, diabetes, cardiovascular diseases and other possibly related diseases have been assessed in numerous meta-analyses. However, in many cases several systematic reviews on the same subject, often only of low or moderate quality, have produced controversial results that can confuse people when making choices related to their daily diet. To achieve high quality and unambiguous evidence for these associations, future studies should focus on solving the inconsistencies between studies. Large sample, multicentre, and multinational randomized controlled trials are needed.

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Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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