BMJ Open Association between egg consumption and metabolic syndrome in Chinese population: a cross-sectional study

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ABSTRACT

To cite: Wang H, Wang W, Shen M, et al. Association between egg consumption and metabolic syndrome in Chinese population: a crosssectional study. BMJ Open 2021;11:e050317. doi:10.1136/ bmjopen-2021-050317

 Prepublication history for this paper is available online. To view these files, please visit the journal online (http://dx.doi. org/10.1136/bmjopen-2021-050317).

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Received 19 February 2021 Accepted 06 December 2021

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Objectives Metabolic syndrome (MS) comprises a constellation of symptoms that include abdominal obesity, hypertension, hyperglycaemia and dyslipidaemia. Dietary intake is a crucial environmental risk factor for MS, but the exact association between MS and egg consumption, which accounts for more than half of the daily total cholesterol intake in Chinese population, has not been previously studied. The aim of this study was to examine the correlation between dietary egg consumption and the prevalence of MS in the context of a large population. Design A cross-sectional study.

Settings Our study was conducted in a health examination centre in China.

Participants Participants who aged ≥40 years and received routine physical examinations were included for analyses.

Main outcome measures MS was diagnosed in accordance with the clinical diagnosis criteria specified in the American Heart Association Guidelines. Egg consumption was assessed by a validated semiquantitative food frequency questionnaire.

Results A total of 11 529 participants (46.2% women) were included in the present study. On the basis of multivariable logistic regression analysis, egg consumption was negatively associated with the prevalence of MS after adjusting for dietary energy intake (OR=0.84, 95% CI 0.76 to 0.93, p value for trend=0.001). The above findings did not change with further adjustment for other potential confounders: model 2 was further adjusted for age, body mass index and sex (based on model 1) and model 3 was further adjusted for education level, physical activity level, smoking status, alcohol use status, dietary fat intake, dietary fibre intake and nutritional supplementation (based on model 2). Consistent results were obtained from the analysis in the female subgroup but not in male subjects. Conclusions A higher level of egg consumption was associated with a lower prevalence of MS in our study participants, and particularly in female subjects.

INTRODUCTION

Metabolic syndrome (MS) refers to a constellation of symptoms, which include abdominal obesity, hypertension, hyperglycaemia, as well as dyslipidaemia.¹ In past decades, the prevalence of MS has increased markedly from 13.2% to 33.1% worldwide.²⁻⁶ Owing to its

Strengths and limitations of this study

- This is the first study exploring the association between egg consumption and the prevalence of MS in Chinese population.
- The sample size of this cross-sectional study was relatively large, which may strengthen the accuracy of the results.
- Our findings were independent of several potential confounders (ie, age, sex, body mass index, smoking and drinking habits, and physical activity), suggesting that the observed associations were robust.
- The causal relationship cannot be determined explicitly, as a common shortcoming of cross-sectional studies.
- Since our study mainly enrolled urban residents, further studies are needed to confirm our findings.

associations with an increased risk of developing cardiovascular disease (CVD), type 2 diabetes mellitus and premature all-cause mortality, MS has become a critical public health issue with a high global economic burden.⁷⁸ Although the underlying aetiology of MS is unclear, many potential contributing factors have been raised, including insulin resistance, obesity, genetic factors, ageing, hormonal imbalance and dietary effects.¹⁹

Among the common daily diet intake, eggs, especially the yolks, are a major source of dietary cholesterol.¹⁰ The intake of eggs accounts for 53.8%-57.7% of the daily total cholesterol intake in middle-aged Chinese adults.^{11 12} An egg weighing around 50 g contains 6.28 g of protein, 4.75 g of total lipid, 186 mg of cholesterol and a variety of minerals and vitamins.¹³ High dietary cholesterol is frequently associated with chronic lifestyle diseases, including CVD, coronary heart disease, diabetes, as well as MS, although there is not enough evidence to indicate causation.^{14 15} Similarly, the association between the other components of eggs besides cholesterol (eg, egg white protein, lutein or zeaxanthin) and MS has not been

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fully investigated.^{16 17} To the best of our knowledge, there are two studies that examined the relationship between egg consumption and MS, which produced varying results.^{18 19} In view of this, comprehensive research on the association between dietary egg consumption and MS could provide valuable insights for the development and update of dietary guidelines.

Here, we designed and conducted a cross-sectional study with a large sample size to examine the association between dietary egg consumption and MS. Additionally, sex-based subgroup analyses were conducted to investigate whether there was a sex-dependent statistical difference in this association.

MATERIAL AND METHODS Study population

The outpatient electronic database of Chinese adult patients who received routine physical examination at the Department of Health Management Center of Xiangya Hospital (affiliated to Central South University) was accessed and screened for inclusion. The study period was from October 2013 to December 2015. The study design was similar to some previous publications with similar research topics.^{20–22} The research protocol had been approved by the Ethics Committee on Research of Xiangya Hospital prior to implementation (reference number: 201312459). All the participants had signed the informed consent on a voluntary basis before entering the study. Routine physical examinations included anthropometric measurements (height and body mass), vital signs (heart rate and blood pressure (BP)) and biochemical tests (routine blood tests, renal and hepatic functions).

The inclusion criteria were: (1) aged \geq 40 years; (2) availability of basic individual characteristics (eg, age, sex, body mass index (BMI), alcohol consumption, smoking history and physical activity); (3) completion of a valid semi-quantitative food frequency questionnaire (SFFQ) and (4) availability of blood test results.

A total of 32 345 subjects received routine physical examinations at the aforementioned study centre during the specified period and all of them had provided the data of basic individual characteristics. In a stepwise screening process, 703 subjects were removed due to lack of blood test results, 3349 subjects were removed due to non-conformance of age requirement and 16 571 subjects were removed due to incompletion of the SFFQ. Among 11 622 subjects who qualified for our inclusion criteria, another 93 participants were eliminated due to the following reasons: (1) missing value of egg consumption (n=88) and (2) abnormal value of egg consumption (n=5). Eventually, 11 529 participants were qualified for the final analysis.

Metabolic syndrome

Based on the American Heart Association Guidelines,¹ the clinical diagnosis criteria of MS include the presence of any three of the following risk factors: a waist circumference ≥ 90 cm for a male participant and ≥ 80 cm for a female participant; triglycerides levels ≥ 150 mg/ dL (1.7 mmol/L); the high-density lipoprotein (HDL) cholesterol level <40 mg/dL (1.03 mmol/L) for a male participant and <50 mg/dL (1.29 mmol/L) for a female participant; systolic BP (SBP) ≥ 130 mm Hg, diastolic BP (DBP) ≥ 85 mm Hg or any included patient currently on antihypertensive medications; and fasting glucose ≥ 100 mg/dL (5.6 mmol/L) or any patient currently receiving hypoglycaemic drugs.

A standard tape was used to measure the waist circumference at the level of the umbilicus, and an electronic sphygmomanometer was used to detect SBP and DBP. As a common practice, blood samples were drawn from all the participants after a 12-hour overnight fast and stored at 4°C until further testing. The hexokinase measurement method was applied to detect the serum fasting glucose, while the glucose oxidase-peroxidase method was applied to detect the total triglycerides. The HDL cholesterol was evaluated by direct assay. All blood analyses were carried out on a Beckman Coulter AU 5800 (Beckman Coulter, Brea, CA, USA).

Dietary assessment

A validated SFFQ that was described in previous publications was used to assess the dietary intake.^{23 24} SFFQ is a dietary assessment tool widely used in epidemiological studies investigating the relationship between dietary intake and disease or risk factors. There are three main components of this questionnaire, including the list of foods, frequency of consumption and the portion size consumed. This SFFQ consists of 63 food items that are commonly consumed in Hunan province. All the participants were provided with colour pictures illustrating the weight of each food item in order to facilitate the completion of this SFFQ with accurate results. The participants were also requested to elaborate the frequency (never, once per month, 2-3 times per month, 1-3 times per week, 4-5 times per week, once per day, two times per day or ≥ 3 times per day) in which they consumed each food item in the last 1 year. The average weight of food consumption each time was classified into 6 levels: <100 g, 100–200 g, 201–300 g, 301–400 g, 401–500 g and >500 g. Based on the data collected, the Chinese Food Composition Table was referred to for calculating the total energy intake, dietary fibre intake and dietary fat intake, respectively.²⁵ Furthermore, the study participants were asked whether or not they were currently taking any oral supplements (eg, calcium, vitamins, minerals, and others).

Assessment of non-dietary covariates

The BMI was calculated based on the measurements of weight and height. The demographic characteristics (eg, age, sex and education level) and the information of health-related habits (eg, smoking status, alcohol consumption and frequency of physical activity) were inquired using a standard questionnaire during the faceto-face interview. The smoking status was assessed by two specific sets of questions: 'Are you a current smoker, a former smoker, or never smoker?' and 'How many cigarettes do vou smoke per day (<10/day, 11-20/day, 21-30/day, 21-3day or >30/day?'. For alcohol consumption, the participants were requested to record both the frequency (never, once per month, 2-3 times per month, 1-3 times per week, 4-5 times per week, once per day, two times per day or ≥ 3 times per day) and the amount of consumption on each occasion (<100 g, 100-200 g, 201-300 g, 301-400 g, 401–500 g or >500 g). Frequency of physical activity (never, 1–2 times per week, 3–4 times per week and ≥ 5 times per week) and the average duration of each activity session (<30 min, 0.5-1 hour, 1-2 hours and >2 hours) were recorded. Then the overall activity level was calculated by multiplying the two values (hours per week). The data of physical activity was presented as continuous data (hours per week) in the regression model.

Statistical analysis

Data were presented either as mean±SD (for continuous data) or in percentage (for categorical data). The Kruskal-Wallis H test was performed to evaluate the difference in continuous data since the normality assumption was not met, while the Pearson χ^2 test was performed to evaluate the difference in categorical data. Egg consumption was categorised into three levels based on tertile distribution: ≤ 3 eggs per week, 4–7 eggs per week and >7 eggs per week.

The association between egg consumption and the prevalence of MS was examined using logistic regression. The ORs and the related 95% CI were computed for each level of egg consumption by considering the lowest tertile as the benchmark. Covariates were chosen by referencing similar studies that were previously published.^{18 19} Thereafter, three models were established for multivariable

analysis. The first model was adjusted for dietary energy intake (tertiles); the second model adjusted for age (continuous), sex (male and female), BMI ($\geq 30 \text{ kg/m}^2$ and $\langle 30 \text{ kg/m}^2 \rangle$ and dietary energy intake (tertiles); while the third model further adjusted for education level (whether the participant has at least a high school education or not), activity level (tertiles), smoking status (yes or no), alcohol consumption (yes or no), dietary fat intake (tertiles), dietary fibre intake (tertiles) and nutritional supplementation (yes or no) on the basis of the second model. Tests for linear trends were performed by logistic regression with the median value of egg consumption in each category since the ordinal covariate is non-uniformly distributed. Lastly, subgroup analyses were conducted by repeating the multivariable analysis for male and female populations, respectively.

SPSS V.21.0 was used for all data analyses and p <0.05 was taken as statistically significant.

Patient and public involvement

Patients and the public were not involved in setting the research question or the outcome measures, nor were they involved in the design or implementation of the study. There were no plans to disseminate the results of the research to study participants.

RESULTS

A total of 11 529 participants (53.8% men and 46.2% women) aged ≥ 40 years (mean= 52.6 ± 17.66 years) were included in the present cross-sectioned study. Table 1 presents the participants' basic characteristics. The prevalence of MS was 28.3% in the entire sample (29.7% in male and 26.8% in female). Significant differences were

	MS status		P value for
	MS	Non-MS	trend
Number	3267	8262	_
Age (years)	53.79±7.65	52.14±7.61	<0.001
Female, n (%)	1424 (43.6)	3897 (47.2)	0.001
BMI (kg/m²)	26.58±2.95	23.52±2.84	<0.001
<30 kg/m², n (%)	2885 (88.3)	8142 (98.5)	
≥30 kg/m², n (%)	382 (11.7)	120 (1.5)	
Education level (n (%) with or above high school background)	1508 (46.2)	3830 (46.4)	0.847
Smoking, n (%)	777 (23.8)	1876 (22.7)	0.216
Alcohol use status, n (%)	1355 (41.5)	3236 (39.2)	0.023
Activity level (hours/week)	2.15±3.37	2.42±3.56	<0.001
Dietary energy intake (kcal/day)	1675.94±808.49	1619.00±770.04	<0.001
Dietary fat intake (g/day)	75.00±35.78	73.39±35.38	0.016
Dietary fibre intake (g/day)	18.17±15.07	17.76±15.13	0.019
Nutritional supplementation, n (%)	1167 (35.7)	3070 (37.2)	0.149

Data are presented as mean±SD, unless otherwise indicated. BMI, body mass index; MS, metabolic syndrome. observed between the participants with and without MS in terms of age, sex, BMI, alcohol consumption condition, activity level, dietary energy intake, dietary fat intake and dietary fibre intake.

Table 2 presents the characteristics among MS and non-MS subjects according to tertiles of egg consumption. Significant differences were also observed across different tertiles in terms of age, BMI, education level, alcohol consumption condition, activity level, dietary energy intake, dietary fat intake, dietary fibre intake and nutritional supplementation.

Table 3 illustrates the correlation between egg consumption and the prevalence of MS using all the three models. In the first model (with adjustment for dietary intake), the ORs and 95% CIs for MS from the second to the highest egg consumption tertiles were 0.93 (95% CI 0.82 to 1.06) and 0.84 (95% CI 0.76 to 0.93) respectively, relative to the lowest tertile (p value for trend=0.001). In the second model (with further adjustment for age, BMI and sex in addition to dietary intake), the association between egg consumption and MS remained significant. The multivariable-adjusted ORs and 95% CIs for MS from the second to the highest tertiles were 0.95 (95% CI 0.83 to 1.08) and 0.82 (95% CI 0.74 to 0.91), respectively, relative to the lowest tertile (p value for trend: <0.001). In the third model (when further adjustments for education level, activity level, smoking status, alcohol consumption, dietary fat intake, dietary fibre intake and nutritional supplementation), the multivariable-adjusted ORs and 95% CIs for MS in the second (OR=0.94; 95% CI 0.83 to 1.08) and third (OR=0.82; 95% CI 0.74 to 0.91) tertiles (p value for trend <0.001) did not change significantly.

Table 3 also presents the results of subgroup analysis, which confirmed the significant inverse association between egg consumption and MS in the female subgroup (model 1: OR=0.82, 95% CI 0.70 to 0.95 in the highest tertile, p value for trend=0.003; model 2: OR=0.77, 95% CI 0.66 to 0.90 in the highest tertile, p value for trend=0.001; model 3: OR=0.78, 95% CI 0.66 to 0.92 in the highest tertile, p value for trend=0.002). However, the inverse association between egg consumption and MS in the male subgroup was not significant (model 1: OR=0.88, 95% CI 0.77 to 1.00 in the highest tertile, p value for trend=0.089; model 2: OR=0.87, 95% CI 0.76 to 1.00 in the highest tertile, p value for trend=0.082; model 3: OR=0.86, 95% CI 0.75 to 0.99 in the highest tertile, p value for trend=0.077). Additionally, egg consumption was as a continuous variable in the regression model, and the multivariable-adjusted β coefficients were -0.012 (95% CI -0.022 to -0.002), -0.006 (95% CI -0.018 to 0.006) and -0.021 (95% CI -0.037 to -0.005) among the total population, male population and female population, respectively.

DISCUSSION

In this study, we observed that a higher level of egg consumption was associated with lower odds for MS prevalence in the Chinese population. The observed results are robust because major confounding factors, including dietary intake, age, BMI, sex, education level, activity level, smoking condition, alcohol consumption, dietary fat intake, dietary fibre intake and nutritional supplementation, were adjusted for in the study models. However, sex-based subgroup analysis showed a valid association in the female population but not in the male population.

Several studies have examined the association between egg consumption and MS; however, the conclusions were inconsistent. Shin et al¹⁸ conducted a cross-sectional study of the Korean population and showed that a higher level of egg consumption was associated with a lower odds for MS. Notably, this association was only confirmed in female subjects in the sex-based subgroup analysis, but not in male subjects, which was consistent with our findings. Woo et al¹⁹ also studied 1663 Korean subjects and found that a higher level of egg consumption was correlated with a reduced risk of MS in both men and women. Recently, Park *et al*²⁶ conducted a review to examine the association between egg consumption and MS in Korean adults. The authors analysed data from 23 993 Korean adults aged 19 years and older and found that a moderate level of egg consumption (4-6 times per week or once per day) was significantly associated with a reduced risk of MS compared with a low level of egg consumption (less than once per month), whereas a high level of egg consumption (two times or more per day) was not significantly associated with MS. Although studies have been undertaken to determine the cause of these inconsistent findings, plausible reasons for varying results may include the following. There may exist difference between different populations and that populations may also have different dietary habits. Additionally, several covariates that we adjusted for in our study were different from previous studies, which may have influenced the study outcomes. However, in our study, the magnitude of the ORs changed minimally in model 3 after the adjustment for several confounders. This is likely because the potential confounding factors had relatively small effects on the relationship between egg consumption and MS in our study.

Eggs are a major source of dietary cholesterol in addition to many other nutrients such as high-quality proteins, vitamins, minerals and saturated and unsaturated fatty acids.²⁷ The inverse association between egg consumption and MS may be attributed to other components of egg rather than cholesterol, which might have favourable effects on inhibiting the development of MS. Shirouchi and Matsuoka¹⁶ suggested that dietary egg white protein and lactic-fermented egg white (an easily consumable form of egg white) could both prevent or alleviate the development of MS. A randomised control study comparing the whole-egg group with the yolkfree substitute group in terms of MS reported that the whole egg had positive effects on the plasma carotenoid status and enrichment of HDL and LDL with lutein and

Table 2 Basic characteristics among non-MS and MS participants according to tertiles of egg consumption	iong non-MS and I	MS participants acc	cording to tertiles o	f egg consi	umption			
	Non-MS partici	Non-MS participants (egg/week)		P value	MS participants (egg/week)	s (egg/week)		
	T1 (≤3)	Т2 (4–7)	T3 (>7)	for trend T1 (≤3)	T1 (≤3)	T2 (4–7)	T3 (>7)	P for trend
Number	5070	1003	2189	I	2081	395	791	1
Age (years)	52.19±7.63	52.01±7.59	52.23±7.62	<0.001	54.54±7.75	53.90±7.85	53.03±7.30	<0.001
Female, n (%)	2401 (47.4)	470 (46.9)	1026 (46.9)	0.910	938 (45.1)	150 (38.0)	336 (42.5)	0.026
BMI (kg/m ²)	23.07±2.79	23.59±2.82	23.91±2.85	0.508	26.20±2.90	26.50±2.93	27.00±2.96	0.022
<30 kg/m ² , n (%)	4998 (98.6)	993 (99.0)	2151 (98.3)		1835 (88.2)	343 (86.8)	707 (89.4)	
≥30 kg/m², n (%)	72 (1.4)	10 (1.0)	38 (1.7)		246 (11.8)	52 (13.2)	84 (10.6)	
Education level (n (%) with or above high school background)	2118 (41.8)	505 (50.3)	1207 (55.1)	<0.001	908 (43.6)	193 (48.9)	407 (51.5)	<0.001
Smoking, n (%)	1197 (23.6)	227 (22.6)	452 (20.6)	0.022	482 (23.2)	104 (26.3)	191 (24.1)	0.384
Alcohol use status, n (%)	1889 (37.3)	437 (43.6)	910 (41.6)	<0.001	818 (39.3)	182 (46.1)	355 (44.9)	0.004
Activity level (hours/week)	2.09±3.36	2.40±3.52	2.77±3.76	<0.001	1.81±3.17	2.22±3.36	2.38±3.54	<0.001
Dietary energy intake (kcal/day)	996.23±202.99	1501.88±141.22	2394.94±871.97	<0.001	998.97±191.94	1508.54 ± 139.89	2440.58±884.35	<0.001
Dietary fat intake (g/day)	51.49±13.77	69.33±15.21	100.61±46.84	<0.001	51.87±13.59	69.48±15.08	100.93 ± 45.53	<0.001
Dietary fibre intake (g/day)	9.01 ± 5.53	16.39±8.15	28.36±20.39	<0.001	9.21±5.35	16.35±8.22	27.90±19.65	<0.001
Nutritional supplementation, n (%) 1677 (33.1)	1677 (33.1)	414 (41.3)	979 (44.7)	<0.001	691 (33.2)	155 (39.2)	321 (40.6)	<0.001
Data are presented as mean±SD, unless otherwise indicated. BMI, body mass index; MS, metabolic syndrome.	ss otherwise indicate syndrome.	ġ.						

	Tertiles of egg consumption (egg/week)			P value for
	T1 (≤3)	T2 (4–7)	T3 (>7)	trend
Total				
Model 1 (95% CI)	1.00 (reference)	0.93 (0.82 to 1.06)	0.84 (0.76 to 0.93)	0.001
Model 2 (95% CI)	1.00 (reference)	0.95 (0.83 to 1.08)	0.82 (0.74 to 0.91)	<0.001
Model 3 (95% CI)	1.00 (reference)	0.94 (0.83 to 1.08)	0.82 (0.74 to 0.91)	<0.001
Male				
Model 1 (95% CI)	1.00 (reference)	1.05 (0.88 to 1.24)	0.88 (0.77 to 1.00)	0.089
Model 2 (95% CI)	1.00 (reference)	1.04 (0.88 to 1.24)	0.87 (0.76 to 1.00)	0.082
Model 3 (95% CI)	1.00 (reference)	1.04 (0.88 to 1.24)	0.86 (0.75 to 0.99)	0.077
Female				
Model 1 (95% CI)	1.00 (reference)	0.81 (0.66 to 0.98)	0.82 (0.70 to 0.95)	0.003
Model 2 (95% CI)	1.00 (reference)	0.85 (0.69 to 1.04)	0.77 (0.66 to 0.90)	0.001
Model 3 (95% CI)	1.00 (reference)	0.86 (0.70 to 1.06)	0.78 (0.66 to 0.92)	0.002

Data are presented as ORs (95% CI), unless otherwise indicated.

Model 1: adjusted for dietary energy intake (tertiles).

Model 2: further adjusted for age (continuous), BMI (<30 kg/m² and ≥30 kg/m²), sex (male and female) on the basis of model 1 (age, BMI and dietary energy intake for the sex subgroup).

Model 3: further adjusted for education level (with or above high school background or not), activity level (continuous), smoking status (yes or no), alcohol use status (yes or no), dietary fat intake (tertiles), dietary fibre intake (tertiles) and nutritional supplementation (yes or no) on the basis of model

BMI, body mass index; MS, metabolic syndrome.

zeaxanthin; these factors may influence the development of MS-related degenerative conditions.¹⁷ Similar results were reported by other randomised control studies.²⁸ ²⁹ The severity of MS is likely correlated with the degree of metabolic imbalance, an influential factor that affects lipoprotein metabolism, including low-grade systemic inflammation and insulin resistance, to a certain extent.³⁰ Blesso *et al*³¹ administered a 12-week dietary intervention and weight loss programme in patients with MS and reported that egg yolk did not exacerbate the inflammatory status, but rather improved inflammation when combined with carbohydrate restriction and weight loss. Thus, components in whole egg may be beneficial for inflammation associated with MS.

Our study indicates that the evidence for the association between egg consumption and MS is weaker in the males, potentially because of sex variations in the risk factors for MS.³² For instance, a sex difference in glucose metabolism has been described by many studies, which found women tend to have a greater insulin sensitivity than men;³³ moreover, the occurrence of insulin resistance seems to be higher in men, even when adjusted for age and BMI.^{34–37} Egg consumption has been reported to improve factors associated with insulin sensitivity,^{28 38} which could explain, in part, the negative association between egg consumption and risk of MS. In addition, sex differences in terms of gene expression and hormonal regulation, and their effects on organ systems, may also play a role in the development of MS.³⁹

The strength of evidence of our study is twofold. First, this study was conducted in a relatively large sample size, which may strengthen the accuracy of the results. Second, this was the first study that revealed an inverse association between egg consumption and the prevalence of MS in Chinese population, and the results were independent and adjusted for common confounding factors.

The limitations of our study include the inability to explicitly determine the causal relationship between egg consumption and MS, a common shortcoming of cross-sectional studies. This could be a result of reverse causation, as the patients diagnosed with MS might take the initiative to change their lifestyle and dietary habits such as reducing egg consumption. Therefore, further prospective studies are needed to comprehensively investigate the true cause of the observed associations. Moreover, since our study mainly enrolled urban residents who had received routine physical examinations at Xiangya Hospital, it cannot be extrapolated to all populations, such as rural populations, and, therefore, the findings should be interpreted with caution. In addition, misclassification bias might exist since eggs are a common ingredient in many mixed dishes in China, which might affect the accuracy of the calculation of total egg consumption. Therefore, further studies are needed to confirm our findings.

CONCLUSION

A higher level of egg consumption was associated with a lower prevalence of MS in our study participants, particularly in female subjects. Well-designed randomised control trials or longitudinal studies are needed to verify the cause–effect relationship between egg consumption and MS. Acknowledgements The authors would like to thank all participants for volunteering for this study. And we would like to thank Dr Omar Abdihamid for proofreading and editing our paper. We thank Georgia Lenihan-Geels from Liwen Bianji (Edanz) (www.liwenbianji.cn) for editing the English text of a draft of this manuscript.

Contributors HW and DX participated in designing of the study. HW drafted the manuscript. ZY analysed and interpreted the data. WW, MS, NW and ZZ advised data analysis and critically reviewed the manuscript. DX and ZW revised the manuscript for important intellectual content and final approval of the version to be published. DX is responsible for the overall content as a guarantor. All authors have read and approved the manuscript.

Funding This work was funded by the National Natural Science Foundation of China (grant numbers: 81772413, 81702207 and 81702206) and the Key Research and Development Program of Hunan Province (grant numbers: 2018SK2070, 2018SK2072, 2018SK2073, 2018SK2074, 2018SK2075 and 2018SK2076).

Competing interests None declared.

Patient and public involvement Patients and/or the public were not involved in the design, or conduct, or reporting, or dissemination plans of this research.

Patient consent for publication Consent obtained directly from patient(s)

Ethics approval This study was approved by the Ethics Committee on Research of Xiangya Hospital (reference number: 201312459).

Provenance and peer review Not commissioned; externally peer reviewed.

Data availability statement No data are available.

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