# **Preplanned Studies**

# Dose-Response Meta-Analysis on Risk of Diabetes in Relation to Red and Processed Meat Consumption — Asian Populations, 2006–2021

Hancheng Yu¹; Jijuan Zhang¹; Jinchi Xie¹; Xianli Li¹; Youjing Wang¹; Yijia Yang¹; Fengshuang Zhou¹; Meichen Liu¹; Zhe Zhang¹; Zhilei Shan¹; Gang Liu¹; An Pan¹.#

#### **Summary**

# What is already known about this topic?

Red and processed meat consumption has been positively related to an increased risk of diabetes in Western populations. However, the results remain inconclusive within Asian populations.

#### What is added by this report?

This dose-response meta-analysis of prospective cohort studies conducted in East Asian populations reveals a positive relation between the consumption of processed meat and increased risk of diabetes. Furthermore, a U-shaped association was identified between the consumption of unprocessed red meat and the risk of diabetes.

# What are the implications for public health practice?

This research presents substantive evidence advocating for the reduction of processed and unprocessed red meat consumption as a viable strategy for mitigating the risk of diabetes in East Asian populations.

The prevalence of diabetes has seen a swift escalation over the past few years. Global age-standardized prevalence for this disease was projected at 6.1% in 2021, with forecasts implying an upsurge to 10% by 2050 (1). Notably, in China, the estimated prevalence of diabetes in adults was 12.4% as of 2018 (2), leading to a substantial health and economic impact on the population.

Dietary habits play a crucial role in both the prevention and management of diabetes (3). Numerous meta-analyses consistently highlight a strong association between the consumption of unprocessed red meat or processed meat and the increased risk of diabetes among Western populations (4–5). However, the results are less conclusive in stratified analyses for Asian populations (5). Given the significant differences in types and quantities of red

and processed meats consumed (6), findings from Western demographics may not necessarily hold for Asian populations. Therefore, this meta-analysis examines the relationships between the intake of unprocessed red meat or processed meat and the incidence of diabetes, focusing specifically on prospective cohort studies within Asian populations.

We conducted a thorough search of PubMed, Web of Science, EMBASE, and the Cochrane Library, in addition to perusing the reference lists of retrieved articles up until July 8, 2023, imposing no restrictions on language. Detailed search strategies for each database can be found in Supplementary Table S1 (available in https://weekly.chinacdc.cn/). Briefly, we focused our search on prospective cohort studies examining the link between the consumption of red and/or processed meat and diabetes risk, restricting our sample population to adults located in Asian countries. Information regarding study registration, inclusion and exclusion criteria, and data extraction procedures are elucidated in the Supplementary Methods (available in https://weekly.chinacdc.cn/).

The  $\chi^2$  and  $I^2$  tests were implemented to assess the heterogeneity between studies, with a  $P_{\rm heterogeneity}$  value <0.10 and  $I^2>50\%$  denoting significant heterogeneity. If substantial heterogeneity was established, random-effects models were employed to collect hazard ratios (HRs) and 95% confidence intervals (CIs) for the highest versus the lowest consumption group. If not, fixed-effects models were utilized. The inverse-variance method was invoked to calculate study weights.

Restricted cubic spline regression models were used to configure dose-response relationships between red and/or processed meat consumption and diabetes risk. Publication bias and small-study effects were evaluated using Egger's test and by visually inspecting funnel plots. Statistical significance was noted with a two-tailed test where P<0.05. All statistical analyses were

executed using STATA (version 17.0; STATA Corp., College Station, TX, USA).

In conclusion, we identified a total of 14,125 citations, of which 14,118 were excluded after conducting a thorough examination of the titles, abstracts, or the full text. Finally, seven cohort studies were included in our meta-analysis (Supplementary Figure S1, available in https://weekly.chinacdc.cn/). The populations under study comprised East Asians from China, Japan, and the Republic of Korea, along with Chinese adults living in Singapore. Notably, no study was found from other regions in Asia. Further characteristics of the included studies are demonstrated in Supplementary Table S2 (available in https:// weekly.chinacdc.cn/). In six studies, dietary information was garnered through food frequency questionnaires, while a single study employed three consecutive 24-hour dietary recalls.

The assessment included a total of 570,296 participants for the evaluation of both red and processed meat consumption, with a further 243,296 participants for unprocessed red meat, and 251,914 for processed meat. Cases of diabetes reported were 21,316, 13,584, and 14,252 for each category, respectively (Table 1). When comparing the highest and lowest consumption groups, the combined HRs and 95% *CIs* of diabetes were 1.12 (0.98, 1.27) for overall red and processed meat consumption, 1.03 (0.89, 1.20) for unprocessed red meat, and 1.12 (1.06, 1.19) for processed meat consumption (Table 1; Figure 1).

Significant heterogeneity was observed in the associations of total red and processed meat ( $I^2$ =73.0%, P=0.011), as well as unprocessed red meat consumption and diabetes risk ( $I^2$ =71.1%, P=0.008). However, there was no significant heterogeneity in the association between processed meat consumption and diabetes risk ( $I^2$ =40.5%, P=0.135; Table 1; Figure 1). Egger's test detected no evidence of publication bias or small-study effects (all P>0.05; Table 1). Nonetheless,

the funnel plots suggested potential publication bias for the associations of both red and processed meat, as well as unprocessed red meat consumption with diabetes risk (Supplementary Figure S2, available in https://weekly.chinacdc.cn).

We observed significant non-linear relations between the consumption of total red and processed meat (P<sub>non-linearity</sub>=0.015), and unprocessed red meat (P<sub>non-linearity</sub><0.001), with diabetes (Figure 2). A Jshaped relationship was found between the consumption of total red and processed meat and the risk of diabetes. An accelerated increase in diabetes risk when noticed consumption surpassed approximately 40 grams per day. As for the consumption of unprocessed red meat, a U-shaped pattern emerged in relation to diabetes risk, with a linear increase when daily consumption exceeded roughly 40 grams (Figure 2). However, the P value for non-linearity between processed meat consumption and diabetes risk was not statistically significant (Pnonlinearity=0.065; Figure 2).

# **DISCUSSION**

Our study indicates a significant relation between high processed meat consumption and an elevated risk of diabetes in East Asian populations. Furthermore, non-linear associations were observed between total red and processed meat intake, unprocessed red meat consumption and the risk of diabetes.

A recent meta-analysis revealed no significant association between the consumption of unprocessed red meat (per 100 grams/day increment; pooled *HR*: 0.98; 95% *CI*: 0.72, 1.33) or processed red meat (per 50 grams/day increment; pooled *HR*: 0.96; 95% *CI*: 0.83, 1.10) and type 2 diabetes risk within the stratified analysis of the Asian population (5). However, these findings come under scrutiny due to the exclusion of several Asian cohorts with absent dose-

TABLE 1. Meta-analysis of red and/or processed meat consumption and risk of diabetes\*.

Characteristics	No. of studies	No. of cohorts	No. of cases/ subjects	Pooled <i>HR</i>	95% CI	P	Heterogeneity,	Pheterogeneity	P for Egger's test
Total red and processed meat <sup>†</sup>	3	3	21,316/ 570,296	1.12	0.98, 1.27	0.085	73.0	0.011	0.941
Unprocessed red meat <sup>†</sup>	4	5	13,584/ 243,296	1.03	0.89, 1.20	0.665	71.1	0.008	0.810
Processed meat§	5	6	14,252/ 251,914	1.12	1.06, 1.19	<0.001	40.5	0.135	0.876

<sup>\*</sup> Pooled hazard ratios (*HR*s) and 95% confidence intervals (*Cls*) for diabetes were comparing the highest intake groups to the lowest groups of red and/or processed meat consumption.

<sup>†</sup> Results from a random-effects model.

<sup>§</sup> Results from a fixed-effect model.

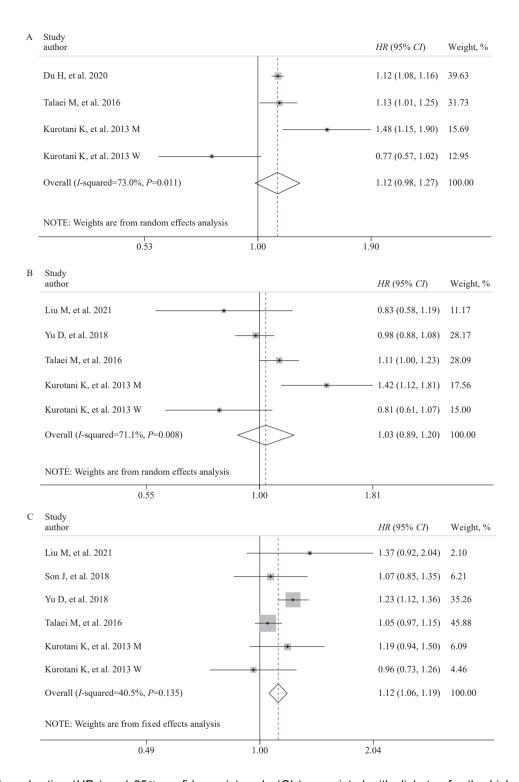


FIGURE 1. Hazard ratios (*HR*s) and 95% confidence intervals (*CI*s) associated with diabetes for the highest versus the lowest consumption categories of (A) total red and processed meat, (B) unprocessed red meat, and (C) processed meat. Note: (A) 570,296 individuals with 21,316 cases from the China Kadoorie Biobank, the Singapore Chinese Health Study (SCHS) and the Japan Public Health Center-based Prospective Study (JPHC), (B) 243,296 individuals with 13,584 cases from the China Health and Nutrition Survey (CHNS), the Shanghai Women's and Men's Health Study (SW&MHS), SCHS and JPHC, and (C) 251,914 individuals with 14,252 cases from CHNS, the Korean Genome Epidemiology Study, SW&MHS, SCHS and JPHC were included. The black squares represent the study-specific HRs, with the size of each square proportional to the study's weight in the overall meta-analysis; the horizontal lines extending from these squares indicate the respective 95% *CI*s; the open diamond in each graph symbolizes the pooled *HR*, with the diamond's width illustrating the 95% *CI*s for these pooled results.

#### China CDC Weekly

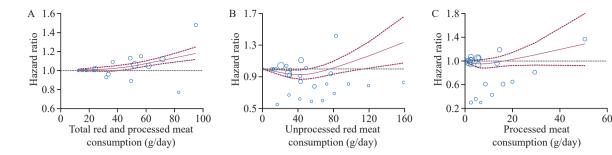


FIGURE 2. Non-linear dose-response relationship (HRs and 95% CIs) between (A) total red and processed meat ( $P_{\text{non-linearity}}$ =0.015), (B) unprocessed red meat ( $P_{\text{non-linearity}}$ <0.001) and (C) processed meat ( $P_{\text{non-linearity}}$ =0.065) daily intakes and risk of diabetes.

Note: Results from the Singapore Chinese Health Study (SCHS), the Japan Public Health Center-based Prospective Study (JPHC) and the China Kadoorie Biobank were included in (A); SCHS, the China Health and Nutrition Survey (CHNS), JPHC and the Shanghai Women's Health Study (SWHS) in (B); the Korean Genome Epidemiology Study, SCHS, CHNS, and JPHC in (C). The solid line represents the fitted dose-response curve, and the dashed line is the 95% *CI*; the position of each bubble represents the corresponding dose and effect in the included studies, and the size of the bubble represents the weight; the weight of the reference category is considered as half of the minimum weight of other categories. Abbreviation: *HR*s=hazard ratios; *CI*s=confidence intervals; g=grams.

response data from the meta-analysis. In an attempt to address these limitations, additional data was assimilated from the Shanghai Men's Health Study (SMHS) and the Japan Public Health Center-based Prospective Study (JPHC). This was exclusively for the unprocessed red meat in the extreme-category comparison analysis along with data obtained from the SMHS, JPHC, and the Singapore Chinese Health Study for processed meat (Supplementary Material, available in <a href="https://weekly.chinacdc.cn/">https://weekly.chinacdc.cn/</a>). After incorporating data from all available Asian prospective cohorts, the current study showed an increased risk of diabetes related to increased consumption of processed meat.

The dose-response investigations have unveiled a Ushaped relationship between the consumption of unprocessed red meat and the risk of diabetes, with the lowest level of risk at about 40 grams per day. This pattern may originate from the potential nutritional benefits of a moderate intake of unprocessed red meat, such as the provision of protein, iron, and various vitamins. Conversely, high consumption of red meat could potentially result in excessive intake of saturated fat, cholesterol, and heme iron, which may negatively impact insulin sensitivity and escalate diabetes risk. The non-significant impact tied to the daily increment of 100 grams of unprocessed red meat, as previously stated in an earlier meta-analysis (5), may be partially attributed to the existence of a non-linear doseresponse relation. As of 2007, the United States had an average meat consumption of 122.8 kg/year, contrasted with China, Japan, and the Republic of Korea's consumption ranging between 46.1 kg/year and

55.9 kg/year (6). Therefore, applying large daily increments, as used in the previous study (5), may not be suitable for Asian populations. Notably, certain studies did not have available dose-response data, resulting in these investigations not being included in the dose-response examination. This accounted for a lower number of included studies in this analysis as opposed to the extreme-category comparison analysis, potentially causing discrepancies between the two analyses. For instance, the Shanghai Women and Men' s Health Study findings (Supplementary Material) displayed a positive association (HR comparing highest to the lowest category: HR: 1.23; 95% CI: 1.12, 1.36) between processed meat consumption and the risk of diabetes. However, due to data limitations, this study was not incorporated into the dose-response analyses.

In Western populations, an increase in daily consumption of unprocessed red meat by 100 grams and processed red meat by 50 grams was associated with a 36% and 51% escalated risk of type 2 diabetes, respectively (5). The variation in correlations between consumption of red and processed meat and diabetes risk in Western and Asian populations could partially be due to various exposure factors such as the quantity and type of meat products (6), cooking methods (7), and dietary patterns (8). For example, the median daily intake of unprocessed red meat and processed meat in an included Chinese cohort was respectively 58.9 grams and 0 grams (9), considerably lower than that in the United States (10). Nonetheless, there has been an extraordinary surge in the levels of red meat consumption in Asian countries in recent decades due economic development (6,10). Accordingly,

findings from the cohorts incorporated in the current study, which were established nearly 20 years ago, may not accurately reflect current conditions. Given the substantial shifts in red meat consumption among Asian populations, there is a continued need for further evidence regarding the association between red and processed meat consumption and diabetes risk.

This study has several limitations. Initially, our capability to conduct sensitivity and subgroup analyses was hindered due to the paucity of prior studies on this topic. Furthermore, a number of studies did not supply the requisite data for accomplishing the dose-response analysis. Another limitation is that most surveys did not collect data concerning potential confounders, such as types of meat consumed and cooking practices. A discordance in diabetes assessment methods (Supplementary Table S2) could introduce potential bias, particularly in the form of misdiagnoses or underdiagnoses among self-reported cases. Moreover, our study population was composed of East Asians, which may limit the extent of generalizability and warrant further exploration into other Asian populations. Therefore, additional paramount in further understanding the impact of these factors on the associations between red meat consumption and diabetes risk.

In conclusion, our study reveals an association between higher processed meat consumption and elevated risks of diabetes among East Asian populations. Although there was no identifiable relation observed between moderate unprocessed red meat consumption and increased diabetes risk, elevated consumption levels nevertheless exhibited a heightened risk. This finding warrants further exploration. This study furnishes the most current evidence advocating for the avoidance of processed meat and the reduction of unprocessed red meat consumption, specifically for the prevention of diabetes in East Asian populations.

**Conflicts of interest**: No conflicts of interest.

**Funding:** Supported by grants 81930124, 82192902, and 82021005 from the National Natural Science Foundation of China and grant 2022YFC3600600 from the National Key Research

and Development Program of China.

doi: 10.46234/ccdcw2023.190

Submitted: August 25, 2023; Accepted: October 30, 2023

# **REFERENCES**

- GBD 2021 Diabetes Collaborators. Global, regional, and national burden of diabetes from 1990 to 2021, with projections of prevalence to 2050: a systematic analysis for the Global Burden of Disease Study 2021. Lancet 2023;402(10397):203 – 34. http://dx.doi.org/10.1016/ S0140-6736(23)01301-6.
- Wang LM, Peng W, Zhao ZP, Zhang M, Shi ZM, Song ZW, et al. Prevalence and treatment of diabetes in China, 2013-2018. JAMA 2021;326(24):2498 – 506. http://dx.doi.org/10.1001/jama.2021. 22208.
- 3. Ley SH, Hamdy O, Mohan V, Hu FB. Prevention and management of type 2 diabetes: dietary components and nutritional strategies. Lancet 2014;383(9933):1999 2007. http://dx.doi.org/10.1016/S0140-6736 (14)60613-9.
- Schwingshackl L, Hoffmann G, Lampousi AM, Knüppel S, Iqbal K, Schwedhelm C, et al. Food groups and risk of type 2 diabetes mellitus: a systematic review and meta-analysis of prospective studies. Eur J Epidemiol 2017;32(5):363 – 75. http://dx.doi.org/10.1007/s10654-017-0246-y.
- Shi WM, Huang X, Schooling CM, Zhao JV. Red meat consumption, cardiovascular diseases, and diabetes: a systematic review and metaanalysis. Eur Heart J 2023;44(28):2626 – 35. http://dx.doi.org/10. 1093/eurheartj/ehad336.
- Lee JE, McLerran DF, Rolland B, Chen Y, Grant EJ, Vedanthan R, et al. Meat intake and cause-specific mortality: a pooled analysis of Asian prospective cohort studies. Am J Clin Nutr 2013;98(4):1032 – 41. http://dx.doi.org/10.3945/ajcn.113.062638.
- Liu G, Zong G, Wu KN, Hu Y, Li YP, Willett WC, et al. Meat cooking methods and risk of type 2 diabetes: results from three prospective cohort studies. Diabetes Care 2018;41(5):1049 – 60. http:// dx.doi.org/10.2337/dc17-1992.
- 8. Hu FB. Globalization of diabetes: the role of diet, lifestyle, and genes. Diabetes Care 2011;34(6):1249 57. http://dx.doi.org/10.2337/dc11-0442.
- 9. Liu MY, Liu CZ, Zhang ZX, Zhou C, Li QQ, He PP, et al. Quantity and variety of food groups consumption and the risk of diabetes in adults: a prospective cohort study. Clin Nutr 2021;40(12):5710 17. http://dx.doi.org/10.1016/j.clnu.2021.10.003.
- Wang HH. The perspective of meat and meat-alternative consumption in China. Meat Sci 2022;194:108982. http://dx.doi.org/10.1016/j. meatsci.2022.108982.

<sup>\*</sup> Corresponding author: An Pan, panan@hust.edu.cn.

<sup>&</sup>lt;sup>1</sup> Department of Epidemiology and Biostatistics, Ministry of Education Key Laboratory of Environment and Health and State Key Laboratory of Environmental Health (incubating), School of Public Health, Tongji Medical College, Huazhong University of Science and Technology, Wuhan City, Hubei Province, China.

# **SUPPLEMENTARY MARERIAL**

# **Supplementary Methods. Registration, Study Selection, and Data Extraction**

# Registration and study selection

This study was registered in the International Prospective Register of Systematic Reviews database (identifier CRD42023423339) on May 16, 2023. In adherence to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses statement (1), study selection, data extraction, and quality assessment were independently conducted by three authors (H-CY, J-JZ, and J-CX). Any discrepancies were resolved via discussion or by consulting another author (AP). The exclusion criteria for the studies were as follows: 1) if the research did not constitute an epidemiological study; 2) if the research did not employ a prospective design; 3) if the research was unrelated to red or processed meat; 4) if the research was not conducted in the general population; 5) if the research did not originate from Asian countries; and 6) if the research was only available in the form of conference abstracts. Although the inclusion of intervention studies was initially intended, no eligible intervention studies were identified during the screening process. In this meta-analysis, "Asian populations" represent the populace residing within the geographical confines of Asia. However, two studies originating from Iran (2–3) were eliminated due to the significant variations in dietary habits concerning types of red and processed meat influenced by religious customs. Notably, in East Asian countries, pork consumption surpasses other forms of red meat (4), whereas it is almost non-existent in Iran.

#### Data extraction

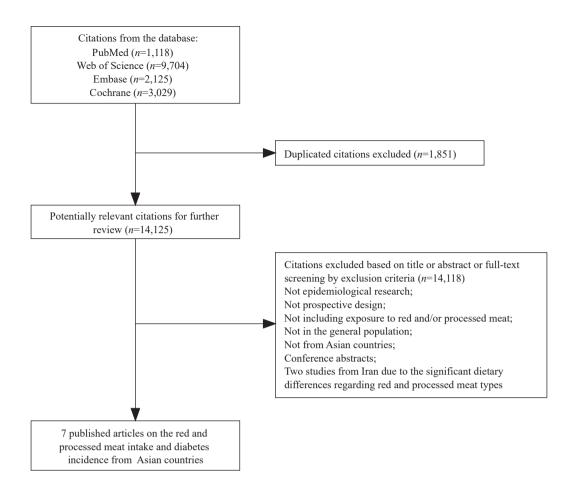
This research paper includes details such as the authors' information, publication year, cohort names, participants' native countries and count, age, assessment of exposures and outcomes, follow-up period (or person-year), acquisition of red and processed meats, covariates incorporated in fully adjusted models, hazard ratios (*HR*s) with corresponding confidence intervals (*CIs*), and specific diabetes cases per group, all of which were extracted (Supplementary Table S2). In instances wherein intake categories were left undefined, we estimated the median by assuming that the distance from the lower boundary to the median reflects the adjacent category with a defined range.

The study encompasses red and processed meat, namely all mammalian meat such as beef, pork, and lamb, and meat products treated through methods like salting, curing, fermentation, smoking, or with added preservatives. The term 'unprocessed red meat' specifically refers to raw, unaltered mammalian meats including beef, pork, and lamb. On the other hand, 'processed meat' includes all meat products that have been modified using salting, curing, fermentation, smoking, or the application of chemical preservatives to boost flavor or enhance preservation.

We made use of the Newcastle-Ottawa Scale to gauge the quality of the study (Supplementary Table S2), with a score of >6 denoting high quality (5). Eventually, there were three studies of total red and processed meat (6-8), four studies of unprocessed red meat (6-7,9-10), and five studies of processed meat (6-7,9-11) that furnished the data required to compute the pooled relative ratios and confidence intervals.

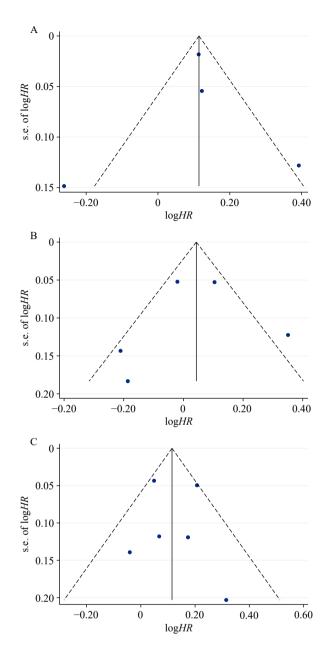
Three studies of total red and processed meat (6-8), four studies of unprocessed red meat (6-7,9,12), and four studies of processed meat (6-7,9,11) furnished the information necessary for dose-response analyses. Considering the relatively low diabetes incidence (about 2%) in the included study with odds ratios (7), we assumed that odds ratios closely resemble the HR estimates. Hence, no transformations were performed.

# China CDC Weekly



SUPPLEMENTARY FIGURE S1. Flow chart of study selection.

# China CDC Weekly



SUPPLEMENTARY FIGURE S2. Funnel plots of risks of diabetes associated with the highest versus lowest consumption categories of (A) total red and processed meat, (B) unprocessed red meat, and (C) processed meat. Abbreviation: s.e.=standard error; *HR*=hazard ratio.

#### SUPPLEMENTARY TABLE S1. Search strategies used for each database.

#### **Database** Search strategies #1(red meat[MeSH Terms] OR meat products[MeSH Terms] OR red meat\*[Title/Abstract] OR meat product\*[Title/Abstract] OR processed meat\*[Title/Abstract] OR beef[Title/Abstract] OR pork[Title/Abstract] OR hot dog\*[Title/Abstract] OR salami\*[Title/Abstract] OR veal[Title/Abstract] OR sausage\*[Title/Abstract] OR lamb\*[Title/Abstract] OR goat\*[Title/Abstract] OR bacon[Title/Abstract] OR mutton[Title/Abstract] OR ham[Title/Abstract] OR luncheon meat\*[Title/Abstract] OR pastrami\*[Title/Abstract] OR diet pattern[Title/Abstract] OR diet quality[Title/Abstract]) AND (intake\*[Title/Abstract] OR consumption\*[Title/Abstract] OR diet\*[Title/Abstract]) AND (diabetes mellitus[MeSH Terms] OR T2DM[Title/Abstract] OR Type 2 Diabetes[Title/Abstract] OR blood glucose[MeSH Terms] OR fasting glucose[Title/Abstract] OR glycated PubMed hemoglobin[Title/Abstract] OR glycemic control[Title/Abstract] OR insulin resistance[MeSH Terms] OR impaired glucose regulation[Title/Abstract] OR impaired fasting glucose[Title/Abstract] OR impaired glucose tolerance[Title/Abstract] OR hyperglycemia[Title/Abstract]) #2systematic review[Publication Type] OR systematic review[Title/Abstract] OR meta-analysis[Publication Type] OR metaanalysis[Title/Abstract] OR review [Publication Type] OR review [Title/Abstract] OR meta analysis[Title/Abstract] #1 NOT #2 Filters: Humans #1(TS=(red meat\*) OR TS=(meat product\*) OR TS=(processed meat\*) OR TS=(beef) OR TS=(pork) OR TS=(hot dog\*) OR TS=(salami\*) OR TS=(veal) OR TS=(sausage\*) OR TS=(lamb\*) OR TS=(goat\*) OR TS=(bacon) OR TS=(mutton) OR TS=(ham) OR TS=(luncheon meat\*) OR TS=(pastrami\*) OR TS=(diet pattern) OR TS=(diet quality)) AND (TS=(intake\*) OR TS=(consumption\*) OR TS=(diet\*)) AND (TS=(diabetes mellitus) OR TS=(T2DM) OR TS=(Type 2 Diabetes) OR TS=(blood Web of glucose) OR TS=(fasting glucose) OR TS=(glycated hemoglobin) OR TS=(glycemic control) OR TS=(insulin resistance) OR TS=(impaired glucose regulation) OR TS=(impaired fasting glucose) OR TS=(impaired glucose tolerance) OR Science TS=(hyperglycemia)) #2TS=(systematic review) OR TS=(meta-analysis) OR TS=(review) OR TS=(meta analysis) #1 NOT #2 #1('red meat'/exp OR 'processed meat'/exp OR 'smoked meat'/exp OR 'red meat\*':ti.ab.kw OR 'meat product\*':ti.ab.kw OR 'processed meat\*':ti,ab,kw OR beef:ti,ab,kw OR pork:ti,ab,kw OR 'hot dog\*':ti,ab,kw OR salami\*:ti,ab,kw OR veal:ti,ab,kw OR sausage\*:ti,ab,kw OR lamb\*:ti,ab,kw OR goat\*:ti,ab,kw OR bacon:ti,ab,kw OR mutton:ti,ab,kw OR ham:ti,ab,kw OR 'luncheon meat\*:ti,ab,kw OR pastrami\*:ti,ab,kw OR 'diet pattern':ti,ab,kw OR 'diet quality':ti,ab,kw) AND (intake\*:ti,ab,kw OR consumption\*:ti.ab.kw OR diet\*:ti.ab.kw) AND ('diabetes mellitus'/exp OR T2DM: ti.ab.kw OR 'Type 2 Diabetes':ti.ab.kw OR 'glucose blood level'/exp OR 'fasting glucose':ti,ab,kw OR 'glycated hemoglobin':ti,ab,kw OR 'glycemic control':ti,ab,kw OR **Embase** 'insulin resistance'/exp OR 'impaired glucose regulation':ti,ab,kw OR 'impaired fasting glucose':ti,ab,kw OR 'impaired glucose tolerance':ti,ab,kw OR hyperglycemia:ti,ab,kw) #2'systematic review'/exp OR systematic review':ti,ab,kw OR 'meta analysis'/exp OR meta-analysis:ti,ab,kw OR 'review'/exp OR review:ti,ab,kw OR 'meta analysis':ti,ab,kw #1 NOT #2 #1 (red meat\* or meat product\* or processed meat\* or beef or pork or hot dog\* or salami\* or veal or sausage\* or lamb\* or goat\* or bacon or mutton or ham or luncheon meat\* or pastrami\* or diet pattern or diet quality):ti,ab,kw #2 MeSH descriptor: [Red Meat] explode all trees #3 MeSH descriptor: [Meat Products] explode all trees #4 (intake\* or consumption\* or diet\*):ti,ab,kw #5 (#1 or #2 or #3) and #4 #6 MeSH descriptor: [Diabetes Mellitus] explode all trees #7 MeSH descriptor: [Insulin Resistance] explode all trees Cochrane #8 (T2DM or Type 2 Diabetes or blood glucose or fasting glucose or glycated hemoglobin or glycemic control or impaired glucose regulation or impaired fasting glucose or impaired glucose tolerance or hyperglycemia):ti,ab,kw #9 #5 and (#6 or #7 or #8) #10 MeSH descriptor: [Systematic Review] explode all trees #11 MeSH descriptor: [Meta-Analysis] explode all trees #12 MeSH descriptor: [Review] explode all trees #13 (systematic review or meta-analysis or meta analysis or review):ti,ab,kw

#14 #9 not (#10 or #11 or #12 or #13)

SUPPLEMENTARY TABLE S2. Characteristics of the studies included in the meta-analysis

Quality score	ø	თ	φ	~	ω
Covariates in fully adjusted model	Age, sex, BMI, waist circumference, smoking and drinking status, systolic blood pressure, diastolic blood pressure, education, region, occupation, physical activity, urban residence, as well as total energy, and 12 food groups were mutually adjusted.	Age, sex, region, education, income, smoking, alcohol consumption, physical activity, family history of diabetes, and fresh fruit consumption, two main dietary exposure variables, and BMI.	Total energy intake, education, income, smoking, alcohol drinking, leisure-time exercise, family history of diabetes, history of hypertension, history of dyslipidemia, and, in women, menopausal status, BMI, and all eight food groups were mutually adjusted.	Age, sex, educational level, monthly household income, and residential area, smoking, physical activity, BMI, alcohol meat)  2005–2006 levels of dietary fat, crude fiber, sodium, fruit and vegetable, current use of antihypertensive and antihyperlipidemic medications.	Age, sex, dialect, year of interview, and educational level, BMI, physical activity level, smoking status, alcohol use, baseline history of self-reported hypertension, adherence to the vegetable-, fruit-, and soy-rich dietary pattern, and total energy intake, heme iron intake
Year of recruitment	7661	2004–2008	1996–2000 (women); 2002–2006 (men)	2001–2002 an 2005–2006	1993–1998
Daily consumption (exposure)	Median: 58.9 g (unprocessed red meat); median: 0 g (processed meat)	Mean: 55.1 g (total red and processed meat)	<b>∀</b> Z	Median: 0 g (processed meat)	Median of Q1–Q4 (total red and processed meat): 12.3 g, 24.2 g, 33.4 g, 48.8 g; median of Q1–Q4 (unprocessed red meat): 10.5 g, 20.7 g, 29.0 g, 43.5 g; median of Q1–Q4 (processed meat): 0 g, 14.9, 2.57 g, 5.39 g
Outcome assessment	Self-reported	Linkages with chronic disease registries and national health insurance claim databases	Self-reported diagnosis	Self-reported interviews	Self-reported interviews
Exposure and assessment method (exposure)	Three consecutive 24-hour dietary recalls (unprocessed red meat, processed meat)	Laptop-based FFQ (total red and processed meat)	Mean: 11.5 years (13.6Semiquantitative years for FFQ (unprocessed Self-reported women; red meat, diagnosis 8.8 years processed meat) for men).	Semiquantitative FFQ (processed meat)	Mean: 10.9 Semiquantitative years; ProC (total red and 494,741 unprocessed red person- meat, processed years meat)
Follow-up period	Median: 9.0 years; 158,018 person- years	Mean: 9 years; 4.5 million person- years	Mean: 11.5 years (13.6 years for women; 8.8 years for men).	62,130 person- years	Mean: 10.5 years; 494,741 person- years
Endpoints (no. of cases)	Меап: 43.0 DM (1,088) (SD: 15.2)	Mean: 51.2 (SD: 10.5); DM (14,931) 35–74 years	Mean: 11 years (13 years for T2DM (6,111) women; 8.8 years for men).	T2DM (668)	Mean: 1 years; T2DM (5,207) 494,741 person- years
Age s (years)	Mean: 43.( (SD: 15.2)	Mean: 51.2 (SD: 10.5); 35–74 years	40–74   years	40–69 years	Mean: 55.2 (SD: 7.6); 45–74 years
No. of participants	16,117	461,036	64,802 Women and 40–74 53,117 men years )	8,618 of	45,411
Study	Liu et al. (2021) CHNS, China (9)	Du et al. (2020) CKB, China (8)	Yu et al. (2018) SWHS & SMHS, China (10)	Son et al. (2018) KoGES, Republic of Korea (11)	Talaei et al. (2017) SCHS, Singapore (6)

Continued	Ф									
Study	No. of participants	Age (years)	No. of Age Endpoints Follow-up participants (years) (no. of cases) period	Follow-up period	Exposure and assessment method (exposure)	Outcome assessment	Daily consumption (exposure)	Year of recruitment	Covariates in fully adjusted model	Quality
Kurotani et al. (2013) JPHC, Japan (7)	63,849	45–75 years	T2DM (1,178) Max: 5 years		Self-administered FFQ (total red and processed meat, unprocessed red meat, processed meat)		Men: median of Q1–Q4 (total red and processed meat): 17.9 g, 36.5 g, 56.4 g, 94.9 g; median of Q1–Q4 (unprocessed red meat): 15.1 g, 31.4 g, 49.0 g, 82.7 g; median of Q1–Q4 (processed meat): 0 g, 2.4 g, 5.6 g, 14.6 g; women: median of Q1–Q4 (total red and processed meat): 15.2 g, 32.0 g, 49.5 g, 82.9 g; median of Q1–Q4 (unprocessed red meat): 12.3 g, 26.9 g, 42.4 g, 72.2 g; median of Q1–Q4 (processed meat): 0 g, 2.4 g, 5.6 g, 13.5 g	1990 and 1993	Age, public health center area, BMI, smoking status, alcohol consumption, total physical activity, the history of hypertension, coffee consumption, the family history of diabetes, Mg intake, Ca intake, rice intake, fish intake, vegetable intake, soft drink consumption and energy intake	ω
Villegas et al. (2006) SWHS, China (12)		Mean: 51.7 (SD: 8.97); 40–70 years	T2DM (1,972)	9	Self-repoint type 2 discription of the control of t	Self-reported type 2 diabetes 1 identified through the baseline and follow-up	Median: 42.6 g 1997–20 (unprocessed red meat) (women)	1997–2000 (women)	Age, energy intake, BMI, WHR, smoking, alcohol consumption, physical activity, vegetable intake, income level, education level, occupation status, hypertension, and chronic disease	9

Abbreviation: CHNS=China Health and Nutrition Survey (China); CKB=China Kadoorie Biobank (China); SW(M)HS=Shanghai Women's (Men's) Health Study (China); KoGES=Korean Genome Epidemiology Study (Republic of Korea); SCHS=Singapore Chinese Health Study (Singapore); JPHC=Japan Public Health Center-based Prospective Study (Japan). DM=diabetes mellitus; FRQ=food frequency questionnaire; g=grams; Q=quartile; SD=standard deviation; NA=not applicable.

# **REFERENCES**

- 1. Moher D, Liberati A, Tetzlaff J, Altman DG. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. J Clin Epidemiol 2009;62(10):1006 12. http://dx.doi.org/10.1016/j.jclinepi.2009.06.005.
- 2. Esfandiar Z, Hosseini-Esfahani F, Mirmiran P, Azizi F. Diet quality indices and the risk of type 2 diabetes in the Tehran Lipid and Glucose Study. BMJ Open Diabetes Res Care 2022;10(5):e002818. http://dx.doi.org/10.1136/BMJDRC-2022-002818.
- 3. Hosseini-Esfahani F, Beheshti N, Koochakpoor G, Mirmiran P, Azizi F. Meat food group intakes and the risk of type 2 diabetes incidence. Front Nutr 2022;9:891111. http://dx.doi.org/10.3389/FNUT.2022.891111.
- 4. Lee JE, McLerran DF, Rolland B, Chen Y, Grant EJ, Vedanthan R, et al. Meat intake and cause-specific mortality: a pooled analysis of Asian prospective cohort studies. Am J Clin Nutr 2013;98(4):1032 41. http://dx.doi.org/10.3945/ajcn.113.062638.
- 5. Cook DA, Reed DA. Appraising the quality of medical education research methods: the medical education research study quality instrument and the Newcastle-Ottawa Scale-Education. Acad Med 2015;90(8):1067 76. http://dx.doi.org/10.1097/ACM.0000000000000786.
- 6. Talaei M, Wang YL, Yuan JM, Pan A, Koh WP. Meat, dietary heme iron, and risk of type 2 diabetes mellitus: the Singapore Chinese health study. Am J Epidemiol 2017;186(7):824 33. http://dx.doi.org/10.1093/aje/kwx156.
- 7. Kurotani K, Nanri A, Goto A, Mizoue T, Noda M, Oba S, et al. Red meat consumption is associated with the risk of type 2 diabetes in men but not in women: a Japan Public Health Center-based Prospective Study. Br J Nutr 2013;110(10):1910 8. http://dx.doi.org/10.1017/S0007114513001128.
- 8. Du HD, Guo Y, Bennett DA, Bragg F, Bian Z, Chadni M, et al. Red meat, poultry and fish consumption and risk of diabetes: a 9 year prospective cohort study of the China Kadoorie Biobank. Diabetologia 2020;63(4):767 79. http://dx.doi.org/10.1007/s00125-020-05091-x.
- 9. Liu MY, Liu CZ, Zhang ZX, Zhou C, Li QQ, He PP, et al. Quantity and variety of food groups consumption and the risk of diabetes in adults: a prospective cohort study. Clin Nutr 2021;40(12):5710 17. http://dx.doi.org/10.1016/j.clnu.2021.10.003.
- 10. Yu DX, Zheng W, Cai H, Xiang YB, Li HL, Gao YT, et al. Long-term diet quality and risk of type 2 diabetes among urban Chinese adults. Diabetes Care 2018;41(4):723 30. http://dx.doi.org/10.2337/dc17-1626.
- 11. Son J, Lee Y, Park K. Effects of processed red meat consumption on the risk of type 2 diabetes and cardiovascular diseases among Korean adults: the Korean Genome and Epidemiology Study. Eur J Nutr 2019;58(6):2477 84. http://dx.doi.org/10.1007/s00394-018-1799-6.
- 12. Villegas R, Shu XO, Gao YT, Yang G, Cai H, Li HL, et al. The association of meat intake and the risk of type 2 diabetes may be modified by body weight. Int J Med Sci 2006;3(4):152 9. http://dx.doi.org/10.7150/ijms.3.152.