Association of dietary meat consumption habits with neurodegenerative cognitive impairment: an updated systematic review and dose-response meta-analysis of 24 prospective cohort studies

Wei Quan*[, a], Yang Xu[a], Jie Luo[a], Maomao Zeng[b], Zhiyong He[b], Qingwu Shen[a], Jie Chen*[, b, c]

Online Supplementary Material

CONTENTS:

Supplementary Figure 3. Funnel plots of fish intakes and neurodegenerative cognitive disorders risk in the highest *versus* lowest analysis.

Supplementary Figure 4. Funnel plots of poultry intakes and neurodegenerative cognitive disorders risk in the highest *versus* lowest analysis.

Supplementary Figure 5. Subgroup analysis (stratified by different types of adverse cognitive outcome) for total meat intakes and risk of neurodegenerative cognitive disorders.

Supplementary Figure 6. Subgroup analysis (stratified by processing method of meat, location and quality score of studies) for total meat intakes and risk of neurodegenerative cognitive disorders.

Supplementary Figure 7. Subgroup analysis (stratified by different types of adverse cognitive outcome) for read meat intakes and risk of neurodegenerative cognitive disorders.

Supplementary Figure 8. Subgroup analysis (stratified by processing method of meat, location and quality score of studies) for red meat intakes and risk of neurodegenerative cognitive disorders.

Supplementary Figure 9. Subgroup analysis (stratified by different types of adverse cognitive outcome) for fish intakes and risk of neurodegenerative cognitive disorders.

Supplementary Figure 10. Subgroup analysis (stratified by processing method of meat, location and quality score of studies) for fish intakes and risk of neurodegenerative cognitive disorders.

Supplementary Method.

[STATA commands]

(1) GLST program

```
. gen double se=(logciu-logcil)/(2*invnormal(.975))
/*calculate the standard error (se)*/
/*logciu, natural logarithm of the upper limit of confidence interval (CI); logcil, natural logarithm of the lower limit of CI*/
. glst logrr dose, se(se) cov(n cases) [cc|ir|ci]
/*generate the GLS equation and provide a correct estimate of the linear trend; cc specifies case-control data; ir specifies incidence-rate data; ci specifies cumulative incidence data*/
/*logrr, natural logarithm of dependent variable; dose, independent variable; n, number of participants; cases, number of outcome cases*/
```

(2) Establishment of cubic spline models

```
. gen se=(logciu-logcil)/(2*invnorm(0.975))
. glst logrr dose, se(se) cov(personyr case) pfirst(id type) ts(r) eform
. capture drop doses*
. _pctile dose, percentile(5 35 65 95)
. ret list
. mkspline doses=dose, knots(`=r(r1)' `=r(r2)' `=r(r3)' `=r(r4)') cubic displayknots
. glst logrr doses*, se(se) cov(personyr case) pfirst(id type)
. testparm doses2 doses3
. glst logrr dose, se(se) cov(personyr case) pfirst(id type) ts(r)
. predictnl lrr_lin=_b[dose]*dose
. gen rr_lin=exp(lrr_lin)
. glst logrr doses*, se(se) cov(personyr case) pfirst(id type)
. predictnl logrrwithref = _b[doses1]*doses1 + _b[doses2]*doses2 +
_b[doses3]*doses3, ci(lo hi)
. gen rrwithref = exp(logrrwithref)
. gen lbwithref = exp(lo)
```

. gen ubwithref = exp(hi)

. sort doses1

(3) Increment analysis

. lincom dose*dose0, eform

/*calculate the relative risk (RR) and 95% CI based on the above GLS equation when the independent variable equals dose0*/

(4) Meta-analysis

. metan rr cil ciu, label(namevar=author, yearvar=year) by(appendix) wgt(weight) nooverall

/*perform the meta-analysis after the increment analysis of each included study is completed*/

/*rr, RR; cil, lower limit of CI; ciu, upper limit of CI; author, surname of first author; year, publication year; appendix, subgroup variables; weight, weighed by random effects model (inverse variance heterogeneity)*/

Supplementary Table 1. PRISMA Checklist for this systematic review and meta-analysis

Section and Topic	Item #	Checklist item	Location where item is reported
TITLE			
Title	1	Identify the report as a systematic review.	1
ABSTRACT			
Abstract	2	See the PRISMA 2020 for Abstracts checklist.	2
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of existing knowledge.	3
Objectives	4	Provide an explicit statement of the objective(s) or question(s) the review addresses.	3
METHODS			
Eligibility criteria	5	Specify the inclusion and exclusion criteria for the review and how studies were grouped for the syntheses.	5, 6
Information sources	6	Specify all databases, registers, websites, organisations, reference lists and other sources searched or consulted to identify studies. Specify the date when each source was last searched or consulted.	5
Search strategy	7	Present the full search strategies for all databases, registers and websites, including any filters and limits used.	5
Selection process	8	Specify the methods used to decide whether a study met the inclusion criteria of the review, including how many reviewers screened each record and each report retrieved, whether they worked independently, and if applicable, details of automation tools used in the process.	5
Data collection process	9	Specify the methods used to collect data from reports, including how many reviewers collected data from each report, whether they worked independently, any processes for obtaining or confirming data from study investigators, and if applicable, details of automation tools used in the process.	5, 6
Data items	10a	List and define all outcomes for which data were sought. Specify whether all results that were compatible with each outcome domain in each study were sought (e.g. for all measures, time points, analyses), and if not, the methods used to decide which results to collect.	5, 6
	10b	List and define all other variables for which data were sought (e.g. participant and intervention characteristics, funding sources). Describe any assumptions made about any missing or unclear information.	5, 6
Study risk of bias assessment	11	Specify the methods used to assess risk of bias in the included studies, including details of the tool(s) used, how many reviewers assessed each study and whether they worked independently, and if applicable, details of automation tools used in the process.	6, 7
Effect measures	12	Specify for each outcome the effect measure(s) (e.g. risk ratio, mean difference) used in the synthesis or presentation of results.	6, 7
Synthesis methods	13a	Describe the processes used to decide which studies were eligible for each synthesis (e.g. tabulating the study intervention characteristics and comparing against the planned groups for each synthesis (item #5)).	6, 7
	13b	Describe any methods required to prepare the data for presentation or synthesis, such as handling of missing summary statistics, or data conversions.	6, 7
	13c	Describe any methods used to tabulate or visually display results of individual studies and syntheses.	6, 7

Section and Topic	Item #	Checklist item	Location where item is reported
	13d	Describe any methods used to synthesize results and provide a rationale for the choice(s). If meta-analysis was performed, describe the model(s), method(s) to identify the presence and extent of statistical heterogeneity, and software package(s) used.	6, 7
	13e	Describe any methods used to explore possible causes of heterogeneity among study results (e.g. subgroup analysis, meta-regression).	6, 7
	13f	Describe any sensitivity analyses conducted to assess robustness of the synthesized results.	6, 7
Reporting bias assessment	14	Describe any methods used to assess risk of bias due to missing results in a synthesis (arising from reporting biases).	7
Certainty assessment	15	Describe any methods used to assess certainty (or confidence) in the body of evidence for an outcome.	7
RESULTS			
Study selection	16a	Describe the results of the search and selection process, from the number of records identified in the search to the number of studies included in the review, ideally using a flow diagram.	7
	16b	Cite studies that might appear to meet the inclusion criteria, but which were excluded, and explain why they were excluded.	7
Study characteristics	17	Cite each included study and present its characteristics.	7, 8
Risk of bias in studies	18	Present assessments of risk of bias for each included study.	10
Results of individual studies	19	For all outcomes, present, for each study: (a) summary statistics for each group (where appropriate) and (b) an effect estimate and its precision (e.g. confidence/credible interval), ideally using structured tables or plots.	8
Results of syntheses	20a	For each synthesis, briefly summarise the characteristics and risk of bias among contributing studies.	8-10
	20b	Present results of all statistical syntheses conducted. If meta-analysis was done, present for each the summary estimate and its precision (e.g. confidence/credible interval) and measures of statistical heterogeneity. If comparing groups, describe the direction of the effect.	8-10
	20c	Present results of all investigations of possible causes of heterogeneity among study results.	8-10
	20d	Present results of all sensitivity analyses conducted to assess the robustness of the synthesized results.	8-10
Reporting biases	21	Present assessments of risk of bias due to missing results (arising from reporting biases) for each synthesis assessed.	10
Certainty of evidence	22	Present assessments of certainty (or confidence) in the body of evidence for each outcome assessed.	10
DISCUSSION			
Discussion	23a	Provide a general interpretation of the results in the context of other evidence.	12

Section and Topic	Item #	Checklist item	Location where item is reported
	23b	Discuss any limitations of the evidence included in the review.	15, 16
	23c	Discuss any limitations of the review processes used.	15, 16
	23d	Discuss implications of the results for practice, policy, and future research.	15, 16
OTHER INFORMATION			
Registration and protocol	24a	Provide registration information for the review, including register name and registration number, or state that the review was not registered.	4
	24b	Indicate where the review protocol can be accessed, or state that a protocol was not prepared.	4
	24c	Describe and explain any amendments to information provided at registration or in the protocol.	4
Support	25	Describe sources of financial or non-financial support for the review, and the role of the funders or sponsors in the review.	16
Competing interests	26	Declare any competing interests of review authors.	17
Availability of data, code and other materials	27	Report which of the following are publicly available and where they can be found: template data collection forms; data extracted from included studies; data used for all analyses; analytic code; any other materials used in the review.	17

Supplementary Table 2. MOOSE Checklist for this systematic review and meta-analysis

Criteria		Brief description of how the criteria were handled in the meta-analysis
Reporting of background should include		
√	Problem definition	Accumulating epidemiological studies suggest that meat consumption is associated with risk of neurodegenerative cognitive disorders, but results remain inconsistent.
√	Hypothesis statement	Different types of meat related to the increased risk of neurodegenerative cognitive disorders
√	Description of study outcomes	Neurodegenerative cognitive disorders
√	Type of exposure or intervention used	Different types of meat, red meat, fish, poultry
√	Type of study designs used	We included prospective cohort studies
√	Study population	People without neurodegenerative cognitive disorders
Reporting of search strategy should include		
√	Qualifications of searchers	The credentials of the two investigators WQ and YJ are indicated in the author list.
√	Search strategy, including time period included in the synthesis and keywords	PubMed from 1990 – December 2021 EMBASE from 1990 – December 2021 MEDLINE 1990 – December 2021 Web of Knowledge 1990 – December 2021 The Cochrane Library 1990 – December 2021 Keywords See search strategy section in the article
√	Databases and registries searched	PubMed, Embase, MEDLINE, Web of Knowledge, and the Cochrane Library
√	Search software used, name and version, including special features	We did not employ a search software. EndNote was used to merge retrieved citations and eliminate duplications
√	Use of hand searching	We have hand-checked the reference lists of original publications and previous meta-analyses or reviews
√	List of citations located and those excluded, including justifications	Details of the literature search process are outlined in the flow chart. The citation list is available upon request
√	Method of addressing articles published in languages other than English	We limited to studies published in the English language
√	Method of handling abstracts and unpublished studies	Unpublished data, conference papers, editorials, theses, and patents were not included
√	Description of any contact with authors	We contacted corresponding authors of studies that did not reported sufficient data in an effort to complete our data set.
Reporting of methods should include		
√	Description of relevance or appropriateness of studies assembled for assessing the hypothesis to be tested	Detailed inclusion and exclusion criteria were described in the methods section.
√	Rationale for the selection and coding of data	Data extracted from each of the studies were relevant to the first author's name; year of publication; country; duration of follow-up; age range; number of participants and incident cases; diagnostic method and criteria of outcome; dietary assessment method; food items; multivariate-adjusted risk estimate; and confounding factors of interest
√	Assessment of confounding	Restricted the analysis to meat estimates only.
√	Assessment of study quality, including blinding of quality assessors; stratification or	The Newcastle–Ottawa Scale (NOS) adapted for cohort studies was used by two investigators (Ye Jiao and Wei Quan) to assess the quality of the included articles.

	regression on possible predictors of study results	
√	Assessment of heterogeneity	Heterogeneity of the studies were explored within two types of study designs using Cochrane's Q test of heterogeneity and I^2 statistic that provides the relative amount of variance of the summary effect due to the between-study heterogeneity.
√	Description of statistical methods in sufficient detail to be replicated	Description of methods of meta-analyses, sensitivity analyses, subgroup analysis and assessment of publication bias are detailed in the methods.
√	Provision of appropriate tables and graphics	We included 1 flow chart,1 summary table, 1 table of subgroup analysis, 4 forest plot of all studies, 1 table of sensitivity analyses.
Reporting of results should include		
√	Graph summarizing individual study estimates and overall estimate	Figure 1
√	Table giving descriptive information for each study included	Table 1
√	Results of sensitivity testing	Supplementary Table 1
√	Indication of statistical uncertainty of findings	95% confidence intervals were presented with all summary estimates, I^2 values and results of sensitivity analyses
Reporting of discussion should include		
√	Quantitative assessment of bias	Sensitivity analyses indicate heterogeneity in strengths of the association due to most common biases in observational studies.
√	Justification for exclusion	We excluded studies that had not reported for the meat consumption as exposure
√	Assessment of quality of included studies	We discussed the results of the sensitivity analyses, and potential reasons for the observed heterogeneity.
Reporting of conclusions should include		
√	Consideration of alternative explanations for observed results	We discussed that potential unmeasured confounders such as Maillard reaction harmful products may related to the risk of cognitive disorders.
√	Generalization of the conclusions	A high consumption of total meat (especially for processed total meat and red meat) is associated with increased risk of neurodegenerative cognitive disorders. While higher fish and poultry intakes is associated with decreased risk of neurodegenerative cognitive disorders
√	Guidelines for future research	We recommend to exploring the potential mechanisms of processed meat products or their harmful products and the risk of cognitive impairment in the future.
√	Disclosure of funding source	This work has been supported by the National Natural Science Foundation of China (Grant No. 3217160166), The Innovation and Exploration Fund of State Key Laboratory of Food Science and Technology, Jiangnan University (No. SKLF-ZZA-202001).

Supplemental Table 3 Detailed search strategy in the three databases PubMed, Embase and MEDLINE

PubMed		
	#1	Diet [mh] OR food [mh] OR meat [mh] OR prok meats [mh] OR pig meat [mh] OR bacon [mh] OR cured ham [mh] OR ham [mh] OR meat products [tiab] OR red meat [tiab] OR meat, red [tiab] OR beef [tiab] OR lamb meat [tiab] OR lamb [tiab] OR veal [tiab] OR poultry [tiab] OR chickens [tiab] OR ducks [tiab] OR geese [tiab] OR turkeys [tiab] OR poultry meat [tiab] OR poultry products [tiab] OR animals [tiab] OR seafood [tiab] OR fish [tiab] OR shellfish [tiab] OR fish products [tiab] OR fish flour [tiab] OR shellfish protein [tiab] OR poultry protein [tiab]
	#2	"Cognitive Dysfunction" [mh] OR Dementia [mh] OR "Parkinsonian Disorders" [mh] OR cognitive [tiab] OR cognition [tiab] OR dementia [tiab] OR dementias [tiab] OR "intellectual impairment" [tiab] OR "intellectual disability" [tiab] OR "intellectual dysfunction" [tiab] OR alzheimer [tiab] OR alzheimers [tiab] OR alzheimer's [tiab] OR parkinson [tiab] OR parkinsons [tiab] OR parkinson's [tiab] OR parkinsonism [tiab] OR "lewy body disease" [tiab] OR "frontotemporal lobar degeneration" [tiab] OR neurodegenerative [tiab] OR neurodegeneration [tiab]
	#3	"Cohort Studies" [tiab] OR "Prospective Studies" [tiab] OR "Epidemiologic Studies" [tiab] OR "Studies, Prospective " [tiab]
	#4	#1 AND #2 AND #3
Embase		
	#1	Diet/exp OR food/exp OR meat/exp OR prok meats/exp OR pig meat /exp OR bacon/exp OR cured ham/exp OR ham/exp OR meat products:ti,ab OR red meat:ti,ab OR meat, red:ti,ab OR beef:ti,ab OR lamb meat:ti,ab OR lamb:ti,ab OR veal:ti,ab OR poultry:ti,ab OR chickens:ti,ab OR ducks:ti,ab OR geese:ti,ab OR turkeys:ti,ab OR poultry meat:ti,ab OR poultry products:ti,ab OR animals:ti,ab OR seafood:ti,ab OR fish:ti,ab OR shellfish:ti,ab OR fish products:ti,ab OR fish flour:ti,ab OR shellfish protein:ti,ab OR poultry protein:ti,ab
	#2	'cognitive defect'/exp OR cognition/exp OR 'intellectual impairment'/exp OR 'Alzheimer disease'/exp OR 'Parkinson disease'/exp OR cognitive:ti,ab OR cognition:ti,ab OR dementia:ti,ab OR dementias:ti,ab OR 'intellectual impairment':ti,ab OR 'intellectual disability':ti,ab OR 'intellectual dysfunction':ti,ab OR alzheimer:ti,ab OR alzheimers:ti,ab OR parkinson:ti,ab OR parkinsons:ti,ab OR parkinsonism:ti,ab OR 'lewy body disease':ti,ab OR 'frontotemporal lobar degeneration':ti,ab OR neurodegenerative:ti,ab OR neurodegeneration:ti,ab
	#3	'Cohort Studies'/exp OR 'Prospective Studies'/exp OR 'Epidemiologic Studies':ti,ab OR 'Studies, Prospective':ti,ab
	#4	#1 AND #2 AND #3
MEDLINE		
	#1	Diet [mh] OR food [mh] OR meat [mh] OR prok meats [mh] OR

		pig meat [mh] OR bacon [mh] OR cured ham [mh] OR ham [mh] OR meat products [tiab] OR red meat [tiab] OR meat, red [tiab] OR beef [tiab] OR lamb meat [tiab] OR lamb [tiab] OR veal [tiab] OR poultry [tiab] OR chickens [tiab] OR ducks [tiab] OR geese [tiab] OR turkeys [tiab] OR poultry meat [tiab] OR poultry products [tiab] OR animals [tiab] OR seafood [tiab] OR fish [tiab] OR shellfish [tiab] OR fish products [tiab] OR fish flour [tiab] OR shellfish protein [tiab] OR poultry protein [tiab]
	#2	[mh "Cognitive Dysfunction"] OR [mh Dementia] OR [mh "Parkinsonian Disorders"] OR (cognitive):ti,ab OR (cognition):ti,ab OR (dementia):ti,ab OR (dementias):ti,ab OR ("intellectual impairment"):ti,ab OR ("intellectual disability"):ti,ab OR ("intellectual dysfunction"):ti,ab OR (alzheimer):ti,ab OR (alzheimers):ti,ab OR (alzheimer's):ti,ab OR (parkinson):ti,ab OR (parkinsons):ti,ab OR (parkinson's):ti,ab OR (parkinsonism):ti,ab OR ("lewy body disease"):ti,ab OR ("frontotemporal lobar degeneration"):ti,ab OR (neurodegenerative):ti,ab OR (neurodegeneration):ti,ab
	#3	"Cohort Studies" [tiab] OR "Prospective Studies" [tiab] OR "Epidemiologic Studies" [tiab] OR "Studies, Prospective " [tiab]
	#4	#1 AND #2 AND #3

Supplementary Table 4 References and score range of diagnosis criteria of outcomes used in the included studies

Author (year)	Diagnosis criteria of outcome	Score range and reference for cognitive assessment
Anastasiou (2017)	DSM-IV; NINCDS/ADRDA	**Ref:** 1. American Psychiatric Association. Diagnostic and Statistical Manual of Mental Disorders. 4th ed ed. Washington, DC2000. 2. McKhann G, Drachman D, Folstein M, Katzman R, Price D, Stadlan EM. Clinical diagnosis of Alzheimer's disease: report of the NINCDS-ADRDA Work Group under the auspices of Department of Health and Human Services Task Force on Alzheimer's Disease. Neurology. 1984; 34(7):939–44.
Ashby-Mitchell (2014)	MMSE	**Score range:** cognitively impaired (score of 0–23) or not cognitively impaired (score of 24–30) **Ref:** Anstey, K.J.; von Sanden, C.; Luszcz, M.A. An 8-year prospective study of the relationship between cognitive performance and falling in very old adults. J. Am. Geriatr. Soc. 2006, 54, 1169–1176.
Roberts (2010)	DSM-IV	**Ref:** American Psychiatric Association: Diagnostic and Statistical Manual of Mental Disorders, ed 4. Washington, American Psychiatric Association, 1994.
Tanaka (2018)	MMSE	**Score range:** No dementia (MMSE score＞26), dementia (MMSE score≤26) **Ref:** Folstein, M.F.; Folstein, S.E.; McHugh, P.R. "Mini-mental state". A practical method for grading the cognitive state of patients for the clinician. J. Psychiatr. Res. 1975, 12, 189–198.
Barberger-Gateau (2002)	DSM-IIIR	**Ref:** American Psychiatric Association. Diagnostic and statistical manual of mental disorders, 4th ed. Washington, DC: APA Press, 1994.
Barberger-Gateau (2007)	DSM-IIIR	**Ref:** American Psychiatric Association. Diagnostic and statistical manual of mental disorders, 4th ed. Washington, DC: APA Press, 1994.
Chen (2012)	MMSE-r	**Score range:** Normal cognitive (MMSE-r score＞18), cognitive decline (MMSE-r score≤18) **Ref:** 1. Gu D DM, authors; Zeng Y, Poston DL, Vlosk Da, gu D, editors. assessment of reliability of mortality and morbidity in the 1998-2002 CLhLS waves. healthy longevity in China: Demographic, socioeconomic, and psychological dimensions. Dordrecht, The netherlands: Springer Publisher. 2008:p. 99–115. 2. Zeng Y VJ, Xiao Z, Zhang C, Liu Y,. The healthy longevity survey and the active life expectancy of the oldest old in China. Population. an english Selection 2001. p. 95–116. 3. Zhang Z. gender differentials in cognitive impairment and decline of the oldest old in China. J gerontol B Psychol Sci Soc Sci. 2006;61(2):S107-15.
Fischer (2018)	DSM- IV; NINCDS-ADRDA	**Score range:** scoring 0–55 with a higher score indicating a better performance **Ref:** 1. McKhann, G.; Drachman, D.; Folstein, M.; Katzman, R.; Price, D.; Stadlanet, E.M. Clinical diagnosis of Alzheimer's disease: Report of the NINCDS-ADRDA Work Group under the auspices of Department of Health and Human Services Task Force on Alzheimer's Disease. Neurology 1984, 34, 939–944. 2. Román, G.C.; Tatemichi, T.K.; Masdeu, J.C.; Garcia, J.H.; Amaducci, L.; Orgogozo, J.M.; Brun, A.; Hofman, A. Vascular dementia: Diagnostic criteria for research studies. Report of the NINDS-AIREN International Workshop. Neurology 1993, 43, 250–260.

Supplementary Table 4 Continued

Author (year)	Diagnosis criteria of outcome	Reference for cognitive assessment
Vercambre (2009)	OCDS	**Score range:** cognitive decline **(**DECO score＜33); cognitive troubles (non-null 4-IADL score) **Ref:** 1. Ritchie K & Fuhrer R (1996) The validation of an informant screening test for irreversible cognitive decline in the elderly: performance characteristics within a general population sample. Int J Geriatr Psychiatry 11, 149–156. 2. Barberger-Gateau P, Fabrigoule C, Helmer C, et al. (1999) Functional impairment in instrumental activities of daily living: an early clinical sign of dementia? J Am Geriatr Soc 47, 456–462.
Rahman (2007)	MSQ	**Score range:** No dementia (MSQ score＞28), dementia (MSQ score≤28) **Ref:** no reference
Katsiardanis (2013)	MMSE	**Score range:** No dementia (MMSE score＞24), cognitive impairment (MMSE score≤24) **Ref:** Fountoulakis K, Tsolaki M, Chantzi H, Kazis A: Mini-Mental State Examination (MMSE): a validation study in Greece. Am J Alzheimer's Dis Other Demen 2000;15:342–345.
Ritchie (2010)	SICT	**Ref:** Artero S, Petersen R, Touchon J, Ritchie K. Revised criteria for mild cognitive impairment: validation within a longitudinal population study. Dement Geriatr Cogn Disord 2006;22:465-70
Chuang (2019)	MMSE ICD-9	**Score range:** No dementia (MMSE score＞25), cognitive impairment (MMSE score≤25); dementia codes (ICD-9-CM: 331.0 and 290.0-290.4) **Ref:** 1. Pfeiffer E. A short portable mental status questionnaire for the assessment of organic brain deficit in elderly patients. J Am Geriatr Soc 1975;23: 433e441. 2. Folstein MF, Folstein SE, McHugh PR. "Mini-mental state". A practical method for grading the cognitive state of patients for the clinician. J Psychiatr Res 1975; 12:189e198. 3. Katzman R, Zhang MY, Ouang YQ, et al. A Chinese version of the Mini-Mental State Examination: Impact of illiteracy in a Shanghai dementia survey. J Clin Epidemiol 1988;41:971e978
Trichopoulou (2015)	MMSE	**Score range:** mild performance decline (change in MMSE −4 to −1), substantial performance decline (change in MMSE≤−5) **Ref:** 1. Folstein MF, Folstein SE, McHugh PR (1975) "Mini-mental state". A practical method for grading the cognitive state of patients for the clinician. J Psychiatr Res 12(3):189–198. 2. Fountoulakis KN, Tsolaki M, Chantzi H, Kazis A (2000) Mini mental state examination (MMSE): a validation study in Greece. Am J Alzheimers Dis Other Dement 15(6):342–345.
Albanese (2009)	ICD-10	**Ref:** 1. Copeland JR, Dewey ME, Griffiths-Jones HM. A computerized psychiatric diagnostic system and case nomenclature for elderly subjects: GMS and AGECAT. Psychol Med 1986;16:89–99. 2. WHO. Clinical descriptions and diagnostic guidelines, MNH/MEP/87.1. In: WHO, ed. Tenth revision of the International Classification of Diseases. Geneva, Switzerland: WHO, 1987.

Supplementary Table 4 Continued

Author (year)	Diagnosis criteria of outcome	Reference for cognitive assessment
Wang (2010)	MMSE	**Score range:** MCI (MMSE score 19-24), normal (MMSE score 25-30) **Ref:** 1. Huang CQ, Dong BR, Wu HM, Zhang YL, Wu JH, Lu ZC, Flaherty JH: Association of cognitive impairment with serum lipid/lipoprotein among Chinese nonagenarians and centenarians. Dementia and geriatric cognitive disorders 2009, 27:111-116. 2. Dufouil C, Clayton D, Brayne C, Chi LY, Dening TR, Paykel ES, O'Connor DW, Ahmed A, McGee MA, Huppert FA: Population norms for the MMSE in the very old: estimates based on longitudinal data. Mini-Mental State Examination. Neurology 2000, 55:1609-1613.
Ylilauri (2022)	MMSE ICD-10	**Score range:** AD (ICD-10 codes F00 and G30) **Ref:** 1. Ylilauri MPT, Voutilainen S, Lönnroos E, Mursu J, Virtanen HEK, Koskinen TT, Salonen JT, Tuomainen T, Virtanen JK (2017) Association of dietary cholesterol and egg intakes with the risk of incident dementia or Alzheimer disease: the Kuopio Ischaemic Heart Disease Risk Factor Study. Am J Clin Nutr 105:476–484. 2. Koivisto K (1995) Population-based dementia screening program in the city of Kuopio, Eastern Finland: evaluation of screening methods, prevalence of dementia and dementia subtypes. Dissertation, University of Kuopio
Franca (2018)	MMSE	**Ref:** Bertolucci PHF, Brucki SMD, Campacci SR, Juliano Y. O Mini Exame do Estado Mental em uma população geral: impacto da escolaridade. Arq. Neuropsiquiatr. 1994; 52(1): 1–7.
Tsurumaki (2019)	LTCI	**Score range:** The Dementia Scale is classified into six ranks (0, I–IV and M), dementia-related behavioural disturbance (rank M), dementia (rank≥II) **Ref:** 1. Ikeda A, Yamagishi K, Tanigawa T, et al. (2008) Cigarette smoking and risk of disabling dementia in a Japanese rural community: a nested case-control study. Cerebrovas Dis 25, 324–331. 2. Imahashi K, Kawagoe M, Eto F, et al. (2007) Clinical status and dependency of the elderly requiring long-term care in Japan. Tohoku J Exp Med 212, 229–238.
Jiang (2018)	MMSE	**Score range:** No dementia (MMSE score＞24), cognitive impairment (MMSE score≤24) **Ref:** Feng L, Chong MS, Lim WS, Ng TP (2012) The Modified MiniMental State Examination test: normative data for Singapore Chinese older adults and its performance in detecting early cognitive impairment. Singap Med J 53(7):458–46.
Zhang (2021)	ICD-9 ICD-10	**Score range:** AD (ICD-9 code 331.0 and ICD-10 codes F00 and G30); dementia (ICD-9 codes 290, 291.2, 294.1, 331.0–331.2, and 331.5, and ICD-10 codes A81.0, F02, F05.1, F10.6, G31.0, G31.1, and G31.8) **Ref:** Power MC, Weuve J, Sharrett AR, Blacker D, Gottesman RF. Statins, cognition, and dementia—systematic review and methodological commentary. Nat Rev Neurol 2015;11:220–9.
Ngabirano (2019)	DSM-IV; NINCDS/ADRDA	**Ref:** 1. American Psychiatrique Association (1994) Diagnostic and statistical manual of mental disorders, 4th ed., APA Press, Washington, DC. 2. McKhann G, Drachman D, Folstein M, Katzman R, Price D, Stadlan EM (1984) Clinical diagnosis of Alzheimer's disease: report of the NINCDS-ADRDA Work Group under the auspices of Department of Health and Human Services Task Force on Alzheimer's Disease. Neurology 34, 939-944.

Supplementary Table 5 References for FFQs used in the included studies

Author (year)	Food frequency assessment	Reference for food frequency assessment
Anastasiou (2017)	Semi-quantitative food frequency questionnaire	Bountziouka V, Bathrellou E, Giotopoulou A, Katsagoni C, Bonou M, Vallianou N, et al. Development, repeatability and validity regarding energy and macronutrient intake of a semi-quantitative food frequency questionnaire: methodological considerations. Nutr Metab Cardiovasc Dis. 2012; 22(8):659–67.
Ashby-Mitchell (2014)	121 items Semi-quantitative food frequency questionnaire	Grantham, N.M.; Magliano, D.J.; Hodge, A.; Jowett, J.; Meikle, P.; Shaw, J.E. The association between dairy food intake and the incidence of diabetes in Australia: The Australian diabetes obesity and lifestyle study (AusDiab). Public Health Nutr. 2013, 16, 339–345.
Roberts (2010)	128 items Health Habits and History Questionnaire	Block G, Coyle LM, Hartman AM, Scoppa SM: Revision of dietary analysis software for the Health Habits and History Questionnaire. Am J Epidemiol 1994;139:1190–1196.
Tanaka (2018)	food frequency questionnaire	Bartali, B.; Turrini, A.; Salvini, S.; Lauretani, F.; Russo, C.R.; Corsi, A.M.; Bandinelli, S.; D'Amicis, A.; Palli, D.; Guralnik, J.M.; et al. Dietary intake estimated using different methods in two Italian older populations. Arch. Gerontol. Geriatr. 2004, 38, 51–60.
Barberger-Gateau (2002)	food frequency questionnaire	Barberger Gateau P, Fabrigoule C, Helmer C, Rouch I, Dartigues JF. Functional impairment in instrumental activities of daily living: an early clinical sign of dementia? J Am Geriatr Soc 1999;47:456›62.
Barberger-Gateau (2007)	food frequency questionnaire	Barberger Gateau P, Fabrigoule C, Helmer C, Rouch I, Dartigues JF. Functional impairment in instrumental activities of daily living: an early clinical sign of dementia? J Am Geriatr Soc 1999;47:456›62.
Chen (2012)	8 items interviewer-administrated questionnaire	Wang Z, Dong B, Zeng g, Li J, Wang W, Wang B, et al. Is there an association between Mild Cognitive Impairment and Dietary Pattern in Chinese elderly? Results from a Crosssectional Population Study. BMC Public health. 2010;10(1):595.
Fischer (2018)	8-item "cognitive health" food intake screener	Cooper, B.; Bickel, H.; Schaufele, M. The ability of general-practitioners to detect dementia and cognitive impairment in their elderly patients—A study in Mannheim. Int. J. Geriatr. Psychiatry 1992, 7, 591–598.
Vercambre (2009)	dietary questionnaire	van Liere MJ, Lucas F, Clavel F, et al. (1997) Relative validity and reproducibility of a French dietary history questionnaire. Int J Epidemiol 26, Suppl. 1, S128–S136.
Rahman (2007)	food frequency questionnaire	No references
Katsiardanis (2013)	157 items Semi-quantitative food frequency questionnaire	Gnardellis C, Trichopoulou A, Katsouyanni K, Polychronopoulos E, Rimm EB, Trichopoulos D: Reproducibility and validity of an extensive semiquantitative food frequency questionnaire among Greek school teachers. Epidemiology 1995;6:74–77.

Supplementary Table 5 Continued

Author (year)	Food frequency assessment	Reference for food frequency assessment
Ritchie (2010)	food frequency questionnaire	Akbaraly TN, Portet F, Fustinoni S, Dartigues JF, Artero S, Rouaud O, et al. Leisure activities and the risk of dementia in the elderly: results from the Three-City Study. Neurology 2009;73:854-61.
Chuang (2019)	79-item food-frequency questionnaire	Pan WH, Lee MM, Yu SL, Huang PC. Foods predictive of nutrient intake in Chinese diet in Taiwan: II. Vitamin A, vitamin B1, vitamin B2, vitamin C and calcium. Int J Epidemiol 1992;21:929e934. Lee MM, Pan WH, Yu SL, Huang PC. Foods predictive of nutrient intake in Chinese diet in Taiwan: I. Total calories, protein, fat and fatty acids. Int J Epidemiol 1992;21:922e928.
Trichopoulou (2015)	150 items Semi-quantitative food frequency questionnaire	Katsouyanni K, Rimm EB, Gnardellis C, Trichopoulos D, Polychronopoulos E, Trichopoulou A (1997) Reproducibility and relative validity of an extensive semi-quantitative food frequency questionnaire using dietary records and biochemical markers among Greek schoolteachers. Int J Epidemiol 26(Suppl 1):S118–S127.
Albanese (2009)	food frequency questionnaire	Prince M, Ferri CP, Acosta D, et al. The protocols for the 10/66 dementia research group population-based research programme. BMC Public Health 2007;7:165
Wang (2010)	food frequency questionnaire	Huang CQ, Dong BR, Wu HM, Zhang YL, Wu JH, Lu ZC, Flaherty JH: Association of cognitive impairment with serum lipid/lipoprotein among Chinese nonagenarians and centenarians. Dementia and geriatric cognitive disorders 2009, 27:111-116
Ylilauri (2022)	food recording of 4 days	Willet W (2013) Implications of total energy intake for epidemiologic analyses. In: Willet W (ed) Nutritional epidemiology. Monographs in epidemiology and biostatistics, 3rd edn. Oxford University Press, Oxford, pp 260–286
Franca (2018)	food frequency questionnaire	World Health Organization. Diet, nutrition and the prevention of chronic diseases. Report of a Joint WHO/FAO Expert Consultation. WHO Technical Report Series 916. Geneva. 2003
Tsurumaki (2019)	39 items Semi-quantitative food frequency questionnaire	Ogawa K, Tsubono Y, Nishino Y, et al. (2003) Validation of a food-frequency questionnaire for cohort studies in rural Japan. Public Health Nutr 6, 147–157.
Jiang (2018)	150 items Semi-quantitative food frequency questionnaire	Talaei M, Wang YL, Yuan JM, Pan A, Koh WP (2017) Meat, dietary heme iron, and risk of type 2 diabetes mellitus: the Singapore Chinese Health Study. Am J Epidemiol 186(7):824–833.
Zhang (2021)	47 items Semi-quantitative food frequency questionnaire	Bradbury KE, Young HJ, Guo W, Key TJ. Dietary assessment in UK Biobank: an evaluation of the performance of the touchscreen dietary questionnaire. J Nutr Sci 2018;7:e6.
Ngabirano (2019)	food frequency questionnaire	Larrieu S, Letenneur L, Berr C, Dartigues JF, Ritchie K, Alperovitch A, Tavernier B, BarbergerGateau P (2004) Sociodemographic differences in dietary habits in a population-based sample of elderly subjects: the 3C study. J Nutr Health Aging 8, 497-502.

Supplementary Table 6 Quality assessment of the publications included in the meta-analysis

Author, (year)	Selection (0-4)			Comparability (0-2)		Outcome (0-3)			Overall quality
	Representative of cases	Selection of controls	Exposure ascertainment	No history of outcome	Comparable on confounders	Outcome assessment	Adequate follow-up	Follow-up rate	
Anastasiou (2017)	0	1	1	1	1	1	0	0	5
Ashby-Mitchell (2014)	0	1	1	1	1	1	1	0	4
Roberts (2010)	0	1	1	0	1	1	1	0	5
Tanaka (2018)	1	1	1	1	2	1	1	0	8
Barberger-Gateau (2002)	1	0	1	1	0	1	0	0	4
Barberger-Gateau (2007)	1	1	1	1	1	1	1	0	7
Chen (2012)	1	1	1	1	2	1	1	0	8
Fischer (2018)	1	1	1	0	2	1	1	1	8
Vercambre (2009)	1	1	1	0	2	0	1	1	7
Rahman (2007)	1	1	1	0	1	1	0	0	5
Katsiardanis (2013)	0	1	1	1	1	1	0	0	5
Ritchie (2010)	0	1	0	1	0	0	0	1	3
Chuang (2019)	0	1	1	1	1	1	0	0	5
Trichopoulou (2015)	0	1	1	0	1	1	1	0	5
Albanese (2009)	1	1	1	1	2	1	0	0	7
Wang (2010)	0	1	0	1	1	1	1	0	5
Ylilauri (2022)	0	1	1	1	0	1	1	0	5

Franca (2018)	0	1	1	0	1	1	1	0	5
Tsurumaki (2019)	1	1	1	1	1	1	1	1	8
Jiang (2018)	1	1	1	1	2	1	1	1	9
Zhang (2021)	1	1	1	1	2	1	1	1	9
Ngabirano (2019)	0	1	1	1	2	1	1	1	8

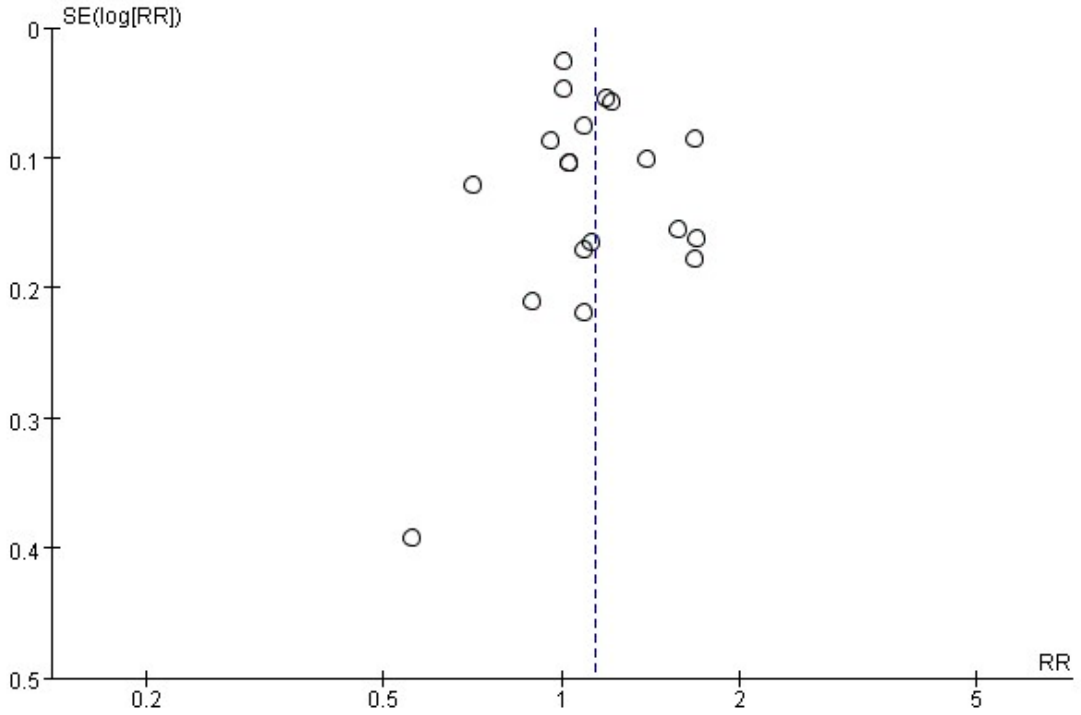
Supplementary Table 7. Data extracted for dose-response analysis.

Study	Author	logRR	Variance	Cat	Cases	Per years	Dose	Se
				Fish				
1	Roberts	0	0	0	58	353	8.7	0
1	Roberts	0.0086	0.007529	1	58	354	15	0.086767
1	Roberts	-0.00436	0.008273	2	47	363	21.3	0.090956
2	Ylilauri	0	0	0	78	623	0	0
2	Ylilauri	0.049218	0.004493	1	94	625	18	0.067032
2	Ylilauri	-0.08619	0.005184	2	72	624	48	0.071997
2	Ylilauri	0.033424	0.004733	3	93	625	102	0.068799
3	Tsurumaki	0	0	0	336	15536	17.05	0
3	Tsurumaki	-0.04576	0.002018	1	132	7913	43.75	0.044921
3	Tsurumaki	-0.07058	0.001139	2	344	21452	74.9	0.033753
3	Tsurumaki	-0.07572	0.001415	3	306	20029	96.4	0.037611
4	Jiang	0	0	0	652	4237	28.46	0
4	Jiang	-0.04096	0.000845	1	605	4237	45.77	0.029067
4	Jiang	-0.06048	0.000775	2	593	4237	61.11	0.027843
4	Jiang	-0.05061	0.000883	3	593	4237	83.95	0.029721
				Total meat				
1	Roberts	0	0	0	54	357	41.6	0
1	Roberts	0.064458	0.007676	1	59	353	107.75	0.087611
1	Roberts	-0.05061	0.00856	2	50	360	132.3	0.092522
2	Ylilauri	0	0	0	89	624	77	0
2	Ylilauri	0.0086	0.004564	1	88	625	128	0.067556
2	Ylilauri	0.012837	0.004688	2	86	623	174	0.068471
2	Ylilauri	0.004321	0.006386	3	74	624	261	0.079914
3	Zhang	0	0	0	146	77261	63	0
3	Zhang	0.053078	0.002278	1	188	90065	86	0.047726
3	Zhang	0.068186	0.001881	2	322	162570	96	0.043372
3	Zhang	0.143015	0.00196	3	316	143519	113	0.044271
4	Zhang	0	0	0	459	77261	63	0
4	Zhang	-0.02228	0.000775	1	509	90065	86	0.027843
4	Zhang	-0.01773	0.000637	2	875	162570	96	0.025236
4	Zhang	0.082785	0.000652	3	959	143519	113	0.02554
				Red meat				
1	Jiang	0	0	0	610	4237	11.81	0
1	Jiang	-0.01323	0.000893	1	585	4237	23.75	0.029876
1	Jiang	0.049218	0.000927	2	636	4237	33.06	0.03045

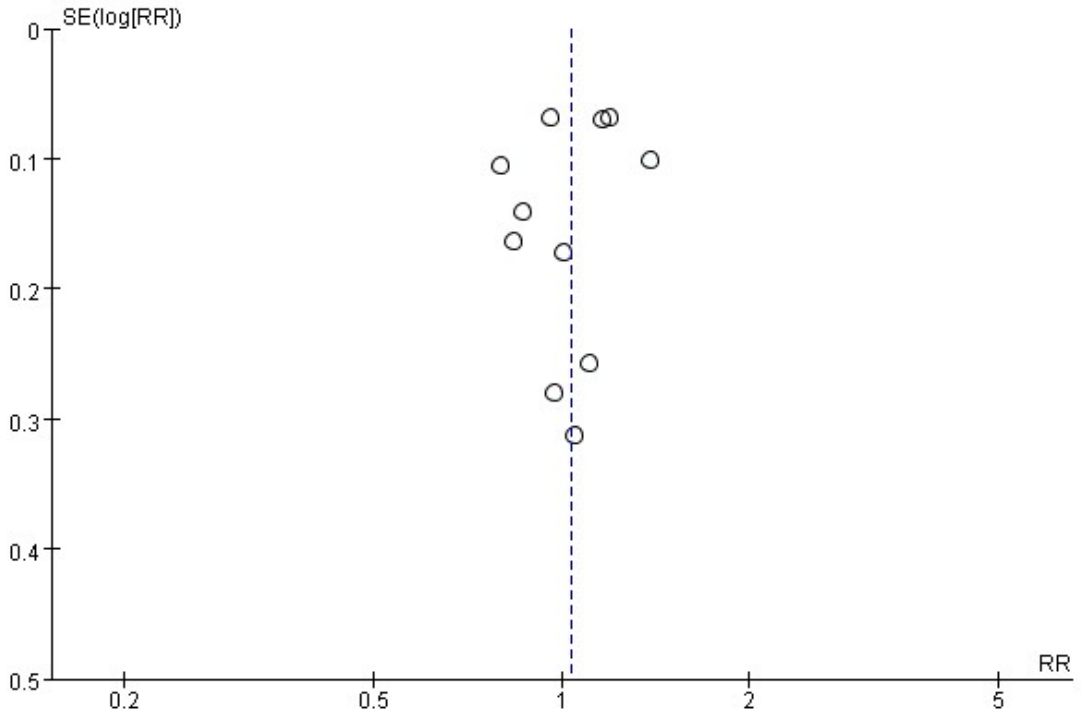
1	Jiang	0.064458	0.000879	3	612	4237	48.61	0.029656
2	Ylilauri	0	0	0	91	624	65	0
2	Ylilauri	-0.00877	0.004307	1	88	625	113	0.065625
2	Ylilauri	-0.01323	0.004605	2	85	624	156	0.06786
2	Ylilauri	-0.03152	0.006028	3	73	624	230	0.077642
3	Zhang	0	0	0	369	57433	24	0
3	Zhang	-0.06048	0.000775	1	812	153797	35	0.027843
3	Zhang	-0.10237	0.000775	2	722	138648	44	0.027843
3	Zhang	-0.01773	0.000833	3	791	110441	54	0.028864
4	Zhang	0	0	0	146	57433	24	0
4	Zhang	-0.10237	0.002122	1	284	153797	35	0.046069
4	Zhang	-0.14267	0.003509	2	253	138648	44	0.059237
4	Zhang	-0.09691	0.002173	3	255	110441	54	0.046613
				Poultry				
1	Jiang	0	0	0	645	4237	6	0
1	Jiang	-0.02687	0.000792	1	642	4237	15.22	0.028139
1	Jiang	-0.04096	0.000928	2	602	4237	22.68	0.030461
1	Jiang	-0.05061	0.000883	3	554	4237	37.18	0.029721
2	Zhang	0	0	0	425	53001	19	0
2	Zhang	-0.06048	0.000714	1	1063	177074	28	0.026718
2	Zhang	-0.05552	0.000625	2	1190	227200	39	0.025002
2	Zhang	0.017033	0.003456	3	65	11142	61	0.058788
3	Zhang	0	0	0	46	53001	19	0
3	Zhang	-0.08619	0.001969	1	143	177074	28	0.044369
3	Zhang	-0.03621	0.001761	2	364	227200	39	0.041967
3	Zhang	0.041393	0.010762	3	433	11142	61	0.103741
				Processed meat				
1	Jiang	0	0	0	95	637	10	0
1	Jiang	0.025306	0.004424	1	91	608	40	0.066514
1	Jiang	0.045323	0.004761	2	83	626	76	0.069003
1	Jiang	0.049218	0.00579	3	78	626	139	0.07609
2	Zhang	0	0	0	724	150758	16	0
2	Zhang	0.053078	0.000508	1	796	144076	22	0.022528
2	Zhang	0.136721	0.000509	2	914	133365	28	0.022557
2	Zhang	0.222716	0.001415	3	170	19331	32	0.037614
3	Zhang	0	0	0	263	150758	16	0
3	Zhang	0.029384	0.001456	1	256	144076	22	0.038153
3	Zhang	0.193125	0.001462	2	325	133365	28	0.03824

3	Zhang	0.227887	0.004942	3	49	19331	32	0.070302

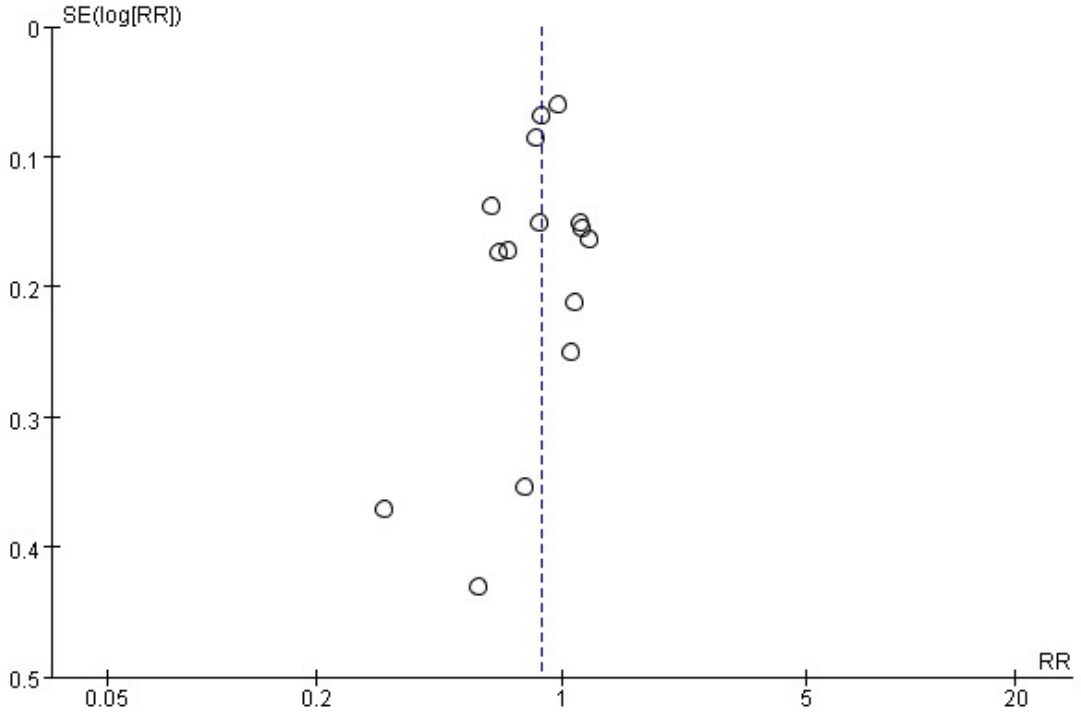
NOTE: Cat: categories; Person year: no. of participants multiplied by follow-up years; Cases: no. of cases multiplied by follow-up years; the unit of dose: g/day.



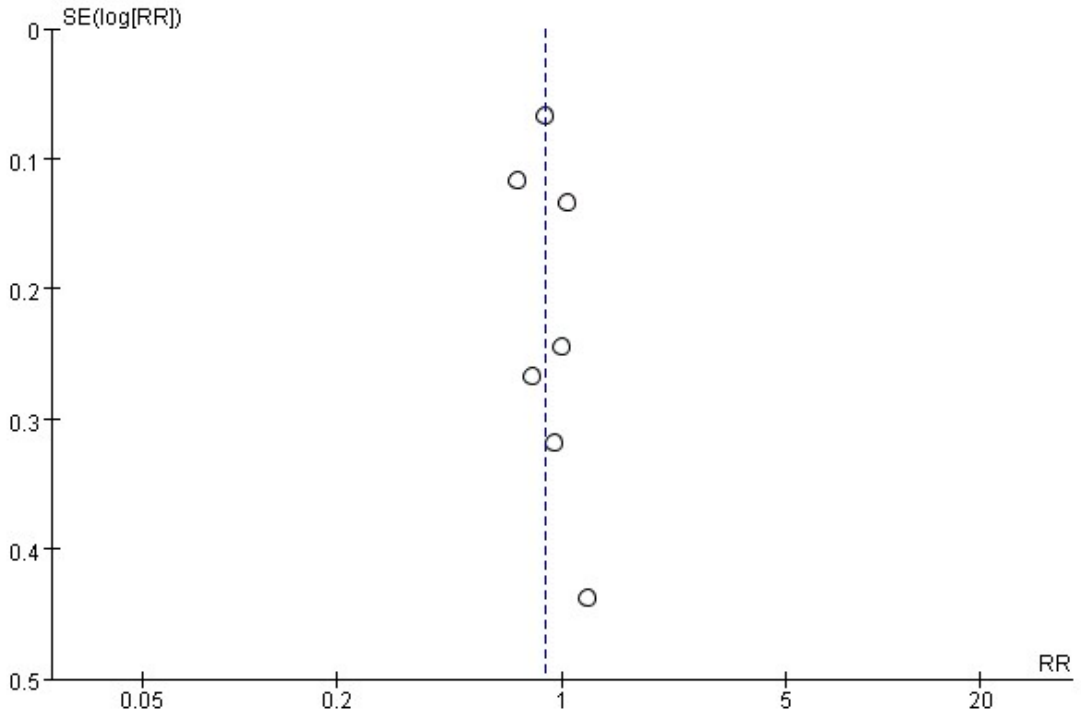
Supplementary Figure 1. Funnel plots of total meat intakes and neurodegenerative cognitive disorders risk in the highest *versus* lowest analysis.



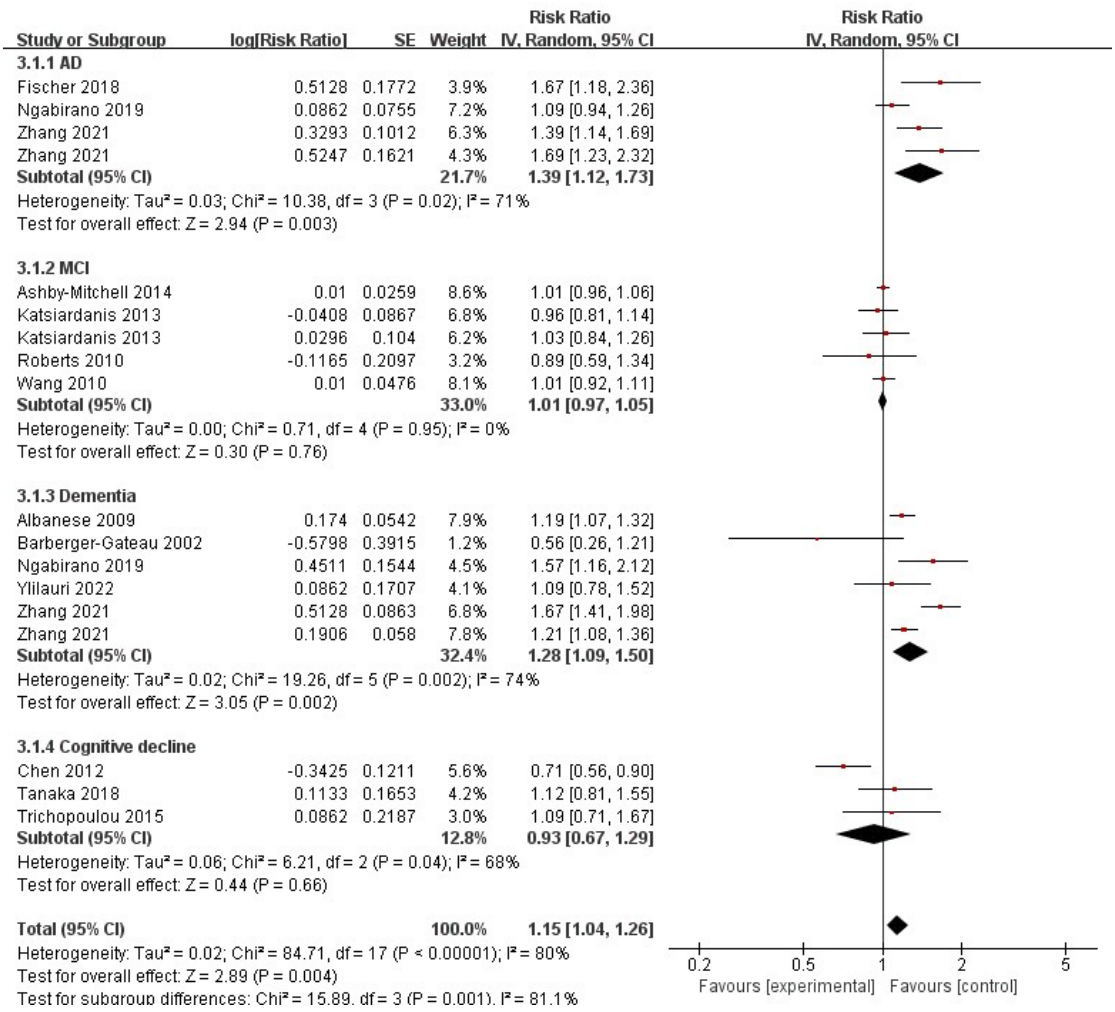
Supplementary Figure 2. Funnel plots of read meat intakes and neurodegenerative cognitive disorders risk in the highest *versus* lowest analysis.



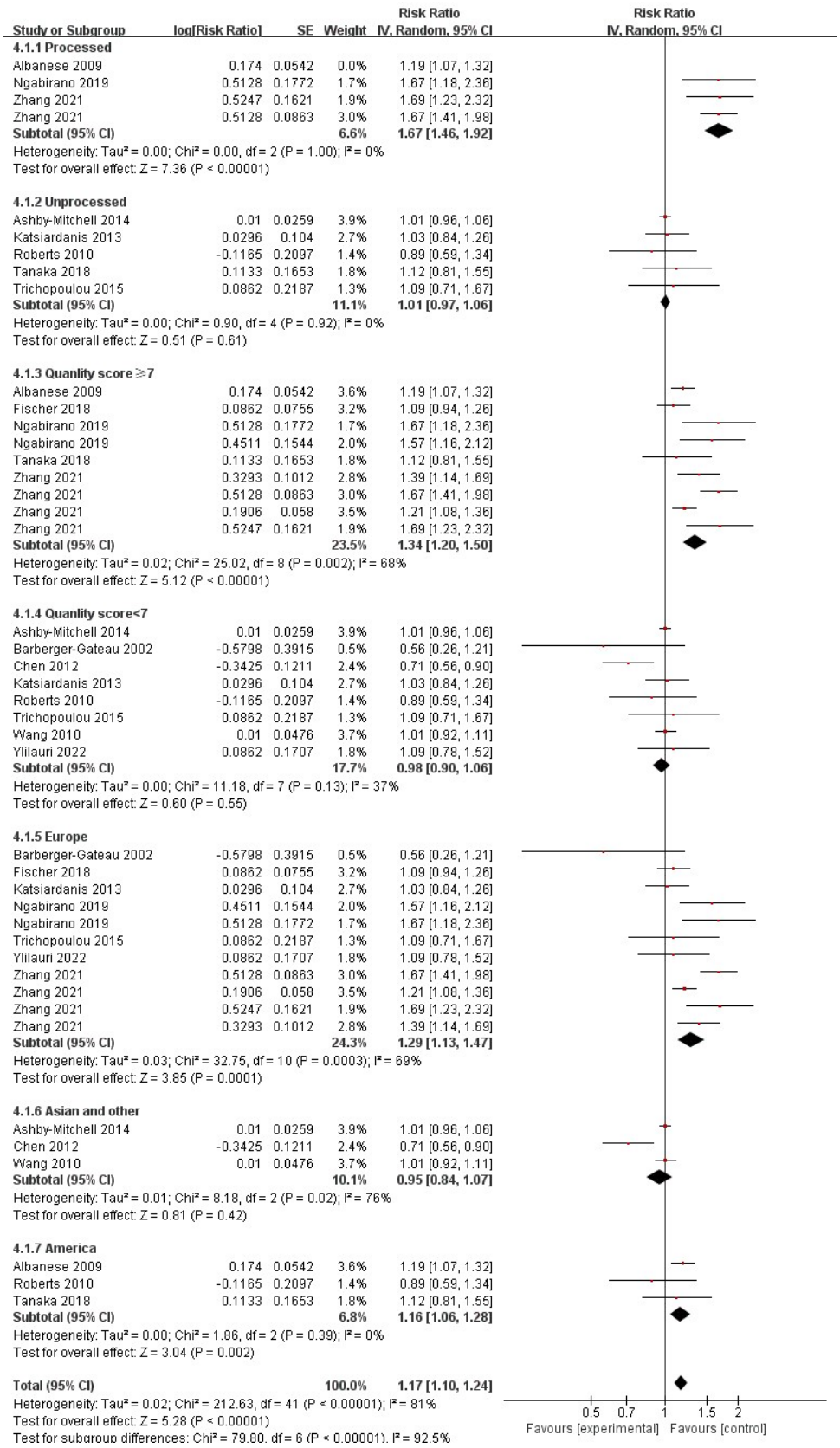
Supplementary Figure 3. Funnel plots of fish intakes and neurodegenerative cognitive disorders risk in the highest *versus* lowest analysis.



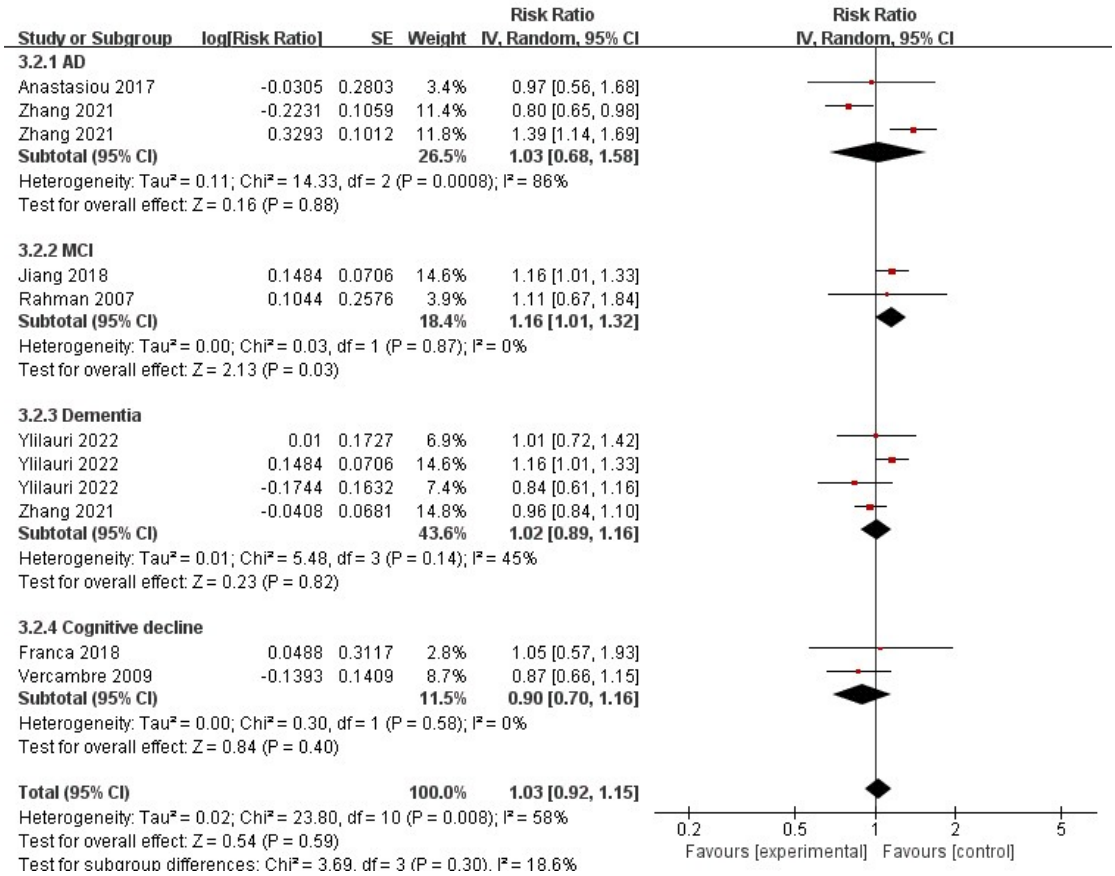
Supplementary Figure 4. Funnel plots of poultry intakes and neurodegenerative cognitive disorders risk in the highest *versus* lowest analysis.



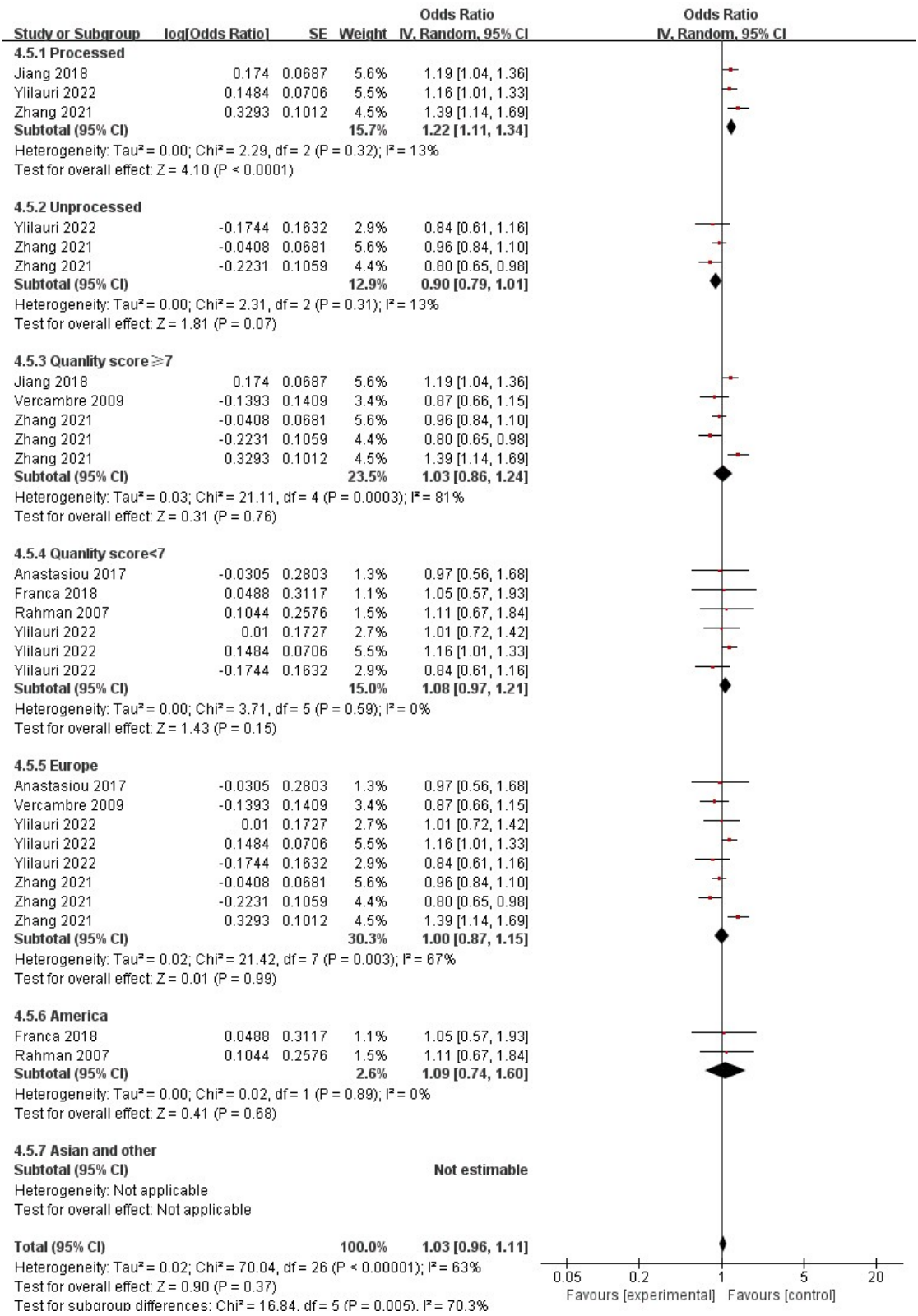
Supplementary Figure 5. Subgroup analysis (stratified by different types of adverse cognitive outcome) for total meat intakes and risk of neurodegenerative cognitive disorders.



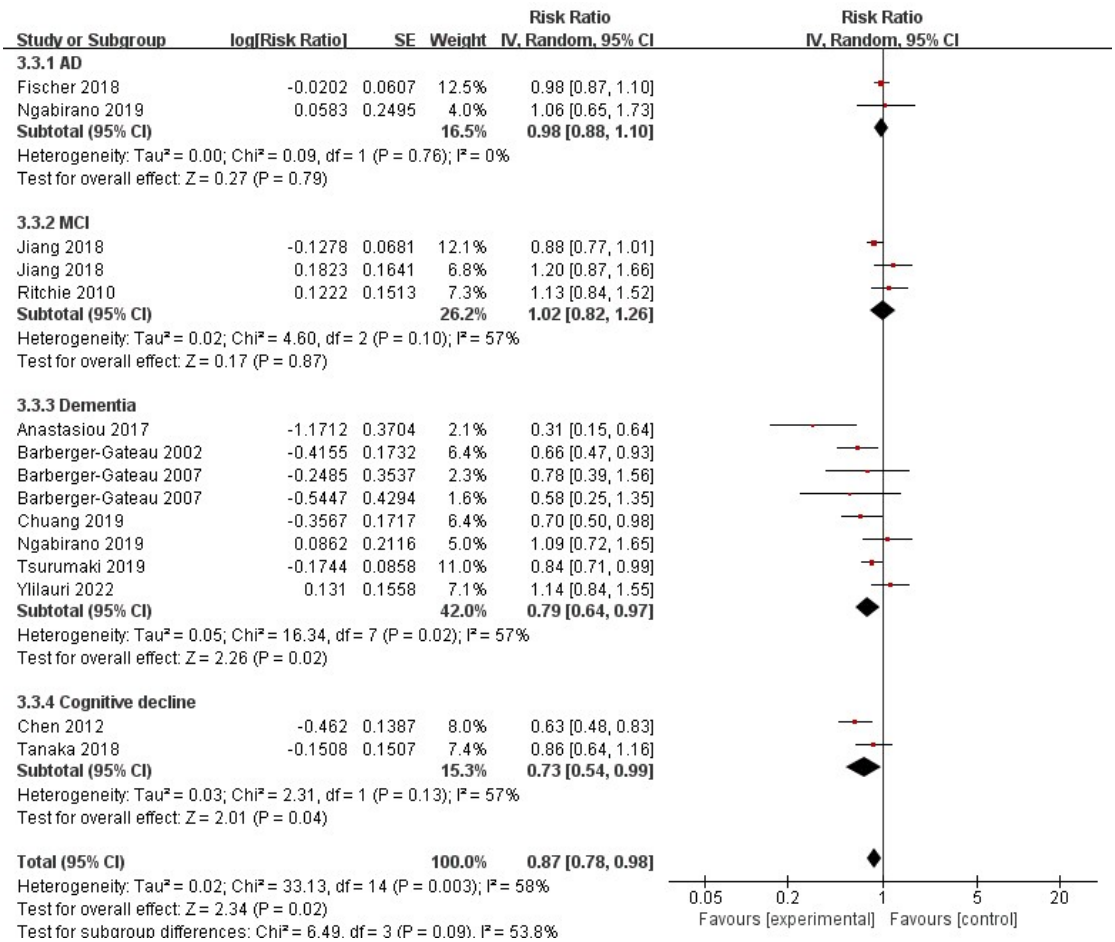
Supplementary Figure 6. Subgroup analysis (stratified by processing method of meat, location and quality score of studies) for total meat intakes and risk of neurodegenerative cognitive disorders.



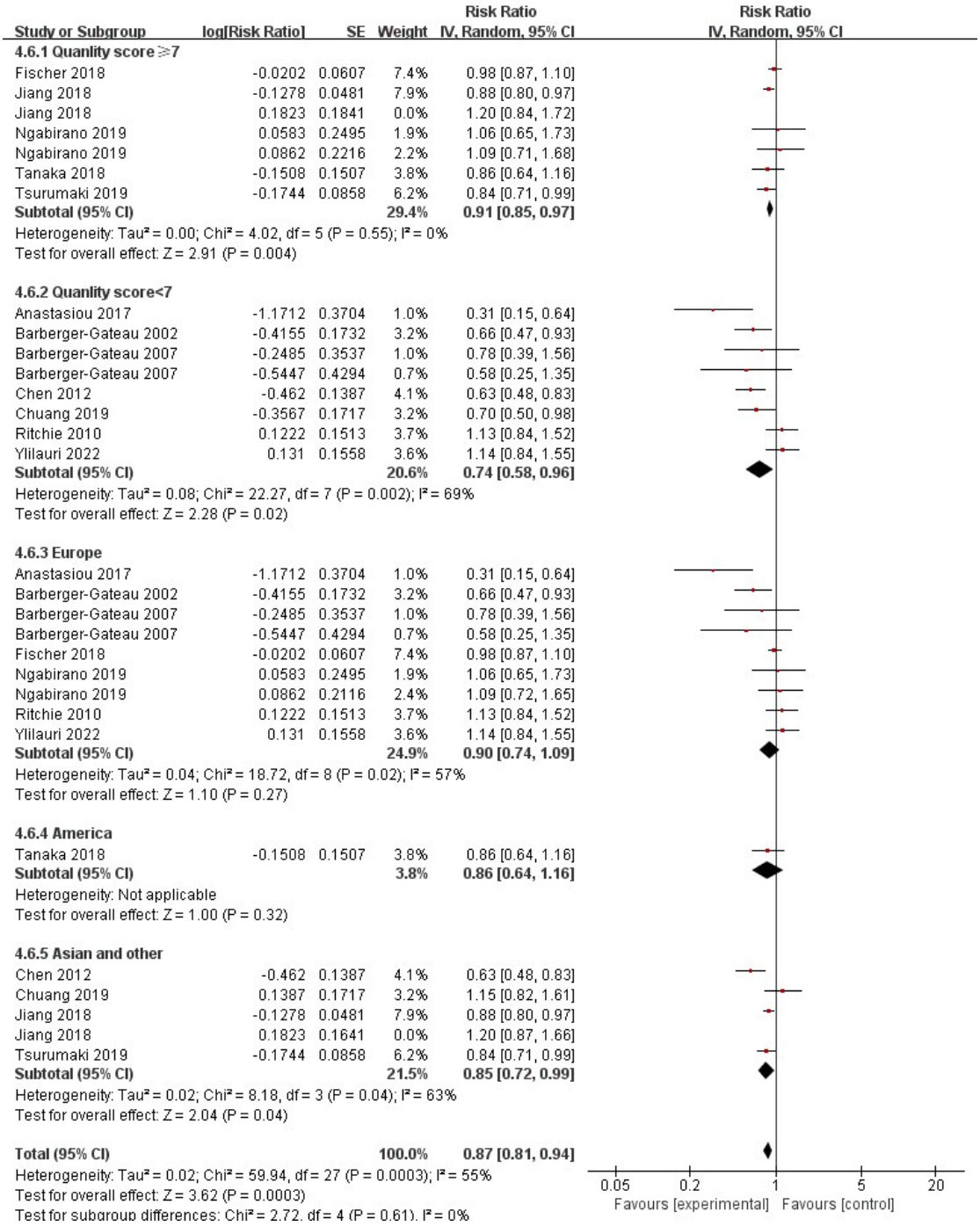
Supplementary Figure 7. Subgroup analysis (stratified by different types of adverse cognitive outcome) for read meat intakes and risk of neurodegenerative cognitive disorders.



Supplementary Figure 8. Subgroup analysis (stratified by processing method of meat, location and quality score of studies) for read meat intakes and risk of neurodegenerative cognitive disorders.



Supplementary Figure 9. Subgroup analysis (stratified by different types of adverse cognitive outcome) for fish intakes and risk of neurodegenerative cognitive disorders.



Supplementary Figure 10. Subgroup analysis (stratified by processing method of meat, location and quality score of studies) for fish intakes and risk of neurodegenerative cognitive disorders.