Online Supplemental Material

Online Supplemental Table 1. Exclusion criteria and number of participants who were excluded due to each reason in the three cohorts.

Exclusion reason	HPFS	NHS I	NHS II
Original sample size for the cohort	**51529 (1986)**	**121700 (1976)**	**116671 (1989)**
Diet information not available*	3247	29293	21191
Missing data for red meat or its types	3081	2967	0
Baseline diabetes	1636	2434	4234
Diagnosis date of diabetes during the following up not available, or disease not confirmed	1524	2181	553
Baseline comorbidities (coronary heart disease, stroke, and cancer)	4958	5265	3189
Total number of participants left for the current analysis	**37083**	**79570**	**87504**

HPFS, Health Professionals Follow-up Study; NHS, Nurses' Health Study.

*Not returning diet questionnaire (including participants died before the baseline of the current analysis, 1986 for HPFS, 1980 for NHS I, and 1991 for NHS II), or leaving too many blanks on the diet questionnaire, or unusual total energy intake levels (i.e., daily energy intake <800 or >4200 kcal/d for men, and <500 or >3500 kcal/d for women).

Online Supplemental Methods for Meta-analysis

Literature search

We further conducted an updated meta-analysis incorporating our new results from the three cohorts together with previous publications. The recent two meta-analysis searched literature up to December 2008 (1) or March 2009 (2). Thus, we conducted additional literature search on MEDLINE and EMBASE from March 2009 to April 2011. We searched for all prospective studies that provided effect estimates for potential associations of unprocessed or processed red meat consumption and incidence of T2DM in adults. The two search terms included *meat, meat products, pork, beef, lamb, ham, bacon, sausage, ham, pastrami, salami, deli, animal food*, and *type 2 diabetes*, using MeSH term, key words, title and abstract where appropriate. The detailed search strategy is shown as follows. Our criteria for including studies in our meta-analysis were: prospective cohort study, type 2 diabetes as the endpoint, description of the red meat assessment, presentation of relative risk with a measure of variability, and description of adjustment for potential confounders.

MEDLINE search query

#1

"Meat"[Mesh] OR "Meat Products"[Mesh] OR "Meat*"[tiab] OR "pork"[tiab] OR "beef"[tiab] OR "lamb"[tiab] or "ham"[tiab] OR "bacon" OR "sausage"[tiab] OR "pastrami"[tiab] OR "salami" OR "deli" OR "animal food*"[tiab]

#2

"Diabetes Mellitus"[Mesh] OR "Diabetes Mellitus, Type 2"[Mesh] OR "diabetes*"[tiab] OR "diabetic*"[tiab]

#3

#1 AND #2 AND Limits: Publication Date from 2009/03/01 to 2011/04/01

EMBASE search query

#1

'meat'/exp OR 'meat':ab OR 'meats':ab OR 'pork':ab OR 'beef':ab OR 'lamb':ab OR 'ham':ab OR 'bacon':ab OR 'sausage':ab OR 'pastrami':ab OR 'salami':ab OR 'deli':ab OR 'animal food':ab AND [embase]/lim AND [1-3-2009]/sd NOT [4-1-2011]/sd

#2

'diabetes mellitus'/exp OR 'diabetes':ab OR 'diabetic':ab AND [embase]/lim AND [3-1-2009]/sd NOT [4-1-2011]/sd

#3

#1 AND #2

The literature search resulted in 164 citations from MEDLINE, and 206 citations from EMBASE. After combining the two datasets, 300 citations were left for evaluation, of

which 2 citations met the inclusion criteria and were included in the meta-analysis in addition to the citations in the two previous meta-analyses.

Methods for the meta-analysis

Most of the previous studies reported results in quartiles or quintiles, to obtain the relative risk estimate for 100 grams/d unprocessed red meat and 50 grams of processed red meat, we used the method described by Orsini et al. (3) for the dose–response analysis and computed study-specific slopes across categories of red meat intake using variance-weighted least squares regression. The median or mean level of meat consumption in each category of intake was assigned to the corresponding relative risk for each study. For studies that reported meat consumption by ranges of intake we estimated the mean/median intake in each category by calculating the average of the upper and lower boundaries. When the highest category was open-ended, we assumed the open-ended interval length to be the same as the adjacent interval. When the lowest category was open-ended we set the lower boundary to zero. The relative risks were used as the common measure of association across studies and the hazard ratios and incidence density ratios were considered equivalent to relative risks. The relative risks were pooled using the DerSimonian and Laird random-effects model (4), given that significant heterogeneity was found. Forest plots were produced to visually assess the relative risks and corresponding 95% confidence intervals across studies. Heterogeneity of the relative risks across studies was evaluated by the Cochrane Q test and the I^2 statistic (5, 6). The Cochrane Q test depends on the number of studies and has limited sensitivity, and the I^2 represents the percentage of total variation across studies that is due to between-study heterogeneity rather than chance. I^2 values of approximately 25%, 50% and 75% are considered to indicate low, moderate and high heterogeneity, respectively. The possibility of publication bias was evaluated using the Begg test and visual inspection of a funnel

plot (7, 8). The Duval and Tweedie nonparametric “trim and fill” procedure was used to further assess the possible effect of publication bias in our meta-analysis (9).

Online Supplemental Table 2. Hazard ratio (95% CI) of type 2 diabetes risk according to red meat intake (serving · 1000 $kcal^{-1}$ ·d^{-1}) in the HPFS, NHS I, and NHS II.

	Frequency of consumption (quintiles)					P for	HR for 1
	Q1	Q2	Q3	Q4	Q5	trend	serving·1000$kcal^{-1}$·d^{-1}
HPFS							
Unprocessed red meat							
Cases/person-years	359/130004	409/130529	488/130642	572/130622	604/130535		
Age-adjusted model	1.00	1.15 (1.00, 1.33)	1.38 (1.21, 1.59)	1.62 (1.42, 1.85)	1.73 (1.52, 1.98)	<0.001	2.12 (1.83, 2.46)
Multivariate model[a]	1.00	1.00 (0.87, 1.16)	1.09 (0.95, 1.26)	1.22 (1.06, 1.40)	1.15 (1.00, 1.33)	<0.001	1.28 (1.08, 1.52)
Processed red meat							
Cases/person-years	306/130700	413/130488	479/130620	577/130502	657/130023		
Age-adjusted model	1.00	1.36 (1.17, 1.58)	1.59 (1.38, 1.84)	1.94 (1.69, 2.23)	2.16 (1.88, 2.47)	<0.001	2.77 (2.32, 3.30)
Multivariate model[a]	1.00	1.13 (0.98, 1.32)	1.23 (1.06, 1.43)	1.42 (1.23, 1.64)	1.50 (1.29, 1.73)	<0.001	1.85 (1.49, 2.29)
Total red meat							
Cases/person-years	328/130313	380/130609	487/130618	564/130460	673/130333		
Age-adjusted model	1.00	1.18 (1.01, 1.36)	1.51 (1.31, 1.74)	1.76 (1.53, 2.01)	2.10 (1.84, 2.40)	<0.001	1.97 (1.78, 2.18)
Multivariate model[a]	1.00	1.00 (0.86, 1.16)	1.20 (1.04, 1.39)	1.29 (1.11, 1.49)	1.39 (1.20, 1.61)	<0.001	1.38 (1.22, 1.57)

NHS I							
Unprocessed red meat							
Cases/person-years	1359/402023	1520/403026	1673/403421	1813/403209	1888/402493		
Age-adjusted model	1.00	1.14 (1.06, 1.26)	1.26 (1.17, 1.35)	1.36 (1.27, 1.46)	1.42 (1.32, 1.52)	<0.001	1.39 (1.30, 1.49)
Multivariate model[a]	1.00	1.00 (0.92, 1.07)	1.06 (0.98, 1.14)	1.09 (1.01, 1.17)	1.12 (1.04, 1.21)	<0.001	1.14 (1.05, 1.24)
Processed red meat							
Cases/person-years	1157/402791	1478/402718	1694/403050	1835/403190	2089/402423		
Age-adjusted model	1.00	1.31 (1.22, 1.42)	1.53 (1.42, 1.64)	1.67 (1.55, 1.80)	1.90 (1.77, 2.04)	<0.001	2.57 (2.30, 2.86)
Multivariate model[a]	1.00	1.11 (1.02, 1.19)	1.22 (1.13, 1.32)	1.22 (1.13, 1.32)	1.30 (1.21, 1.40)	<0.001	1.52 (1.33, 1.73)
Total red meat							
Cases/person-years	1227/402436	1456/402973	1732/403118	1823/403301	2015/402344		
Age-adjusted model	1.00	1.21 (1.12, 1.31)	1.45 (1.35, 1.56)	1.53 (1.43, 1.65)	1.70 (1.58, 1.82)	<0.001	1.49 (1.41, 1.58)
Multivariate model[a]	1.00	1.04 (0.96, 1.12)	1.16 (1.08, 1.25)	1.18 (1.10, 1.27)	1.25 (1.16, 1.35)	<0.001	1.20 (1.12, 1.28)
NHS II							
Unprocessed red meat							
Cases/person-years	361/271079	495/272534	587/273548	732/274336	893/274678		
Age-adjusted model	1.00	1.39 (1.21, 1.59)	1.63 (1.43, 1.85)	2.00 (1.76, 2.27)	2.40 (2.12, 2.71)	<0.001	2.68 (2.39, 2.99)
Multivariate model[a]	1.00	1.10 (0.96, 1.26)	1.11 (0.97, 1.27)	1.21 (1.06, 1.38)	1.26 (1.11, 1.44)	<0.001	1.36 (1.17, 1.58)

Processed red meat							
Cases/person-years	405/271903	459/272498	597/273347	691/273829	916/274599		
Age-adjusted model	1.00	1.18 (1.03, 1.35)	1.56 (1.38, 1.77)	1.82 (1.61, 2.05)	2.42 (2.15, 2.72)	<0.001	4.58 (4.00, 5.24)
Multivariate model[a]	1.00	0.84 (0.73, 0.96)	1.02 (0.90, 1.16)	1.04 (0.91, 1.18)	1.11 (0.98, 1.26)	<0.001	1.91 (1.50, 2.43)
Total red meat							
Cases/person-years	333/271598	449/272454	598/273505	679/274158	1011/274460		
Age-adjusted model	1.00	1.37 (1.19, 1.58)	1.81 (1.58, 2.07)	2.05 (1.80, 2.34)	3.02 (2.67, 3.42)	<0.001	2.73 (2.50, 2.98)
Multivariate model[a]	1.00	1.01 (0.88, 1.16)	1.11 (0.96, 1.27)	1.11 (0.97, 1.27)	1.33 (1.16, 1.51)	<0.001	1.37 (1.22, 1.54)
Pooled results[b]							
Unprocessed red meat	1.00	1.02 (0.96, 1.07)	1.07 (1.01, 1.14)	1.13 (1.07, 1.20)	1.15 (1.08, 1.23)	<0.001	1.20 (1.12, 1.29)
Processed red meat	1.00	1.02 (0.85, 1.22)	1.17 (1.10, 1.25)	1.21 (1.04, 1.41)	1.29 (1.12, 1.49)	<0.001	1.65 (1.49, 1.83)
Total red meat	1.00	1.03 (0.97, 1.09)	1.16 (1.09, 1.23)	1.18 (1.12, 1.26)	1.29 (1.21, 1.37)	<0.001	1.26 (1.20, 1.33)

[a]Multivariate model: adjusted for age (continuous), BMI category (<23, 23-24.9, 25-29.9, 30-34.9, ≥35 kg/m^2), alcohol consumption (0, 0.1-4.9, 5.0-14.9, ≥15 g/d), physical activity level (<3, 3-8.9, 9-17.9, 18.26.9, ≥27 MET-hrs/wk), smoking status (never, past, current 1-14 cigarettes/d, current 15-24 cigarettes/d, current ≥24 cigarettes/d), race (white/non-white), menopausal status and hormone use in women (premenopausal, postmenopausal never users, postmenopausal past users, postmenopausal current users), family history of diabetes, history of hypertension and hypercholesterolemia, quintiles of total calorie, and dietary score;

[b]Results from multivariate model were combined using fix effect model given than all the test for heterogeneity P >0.15.

Online Supplemental Table 3. Hazard ratio (95% CI) of type 2 diabetes risk according to red meat intake in the HPFS, NHS I, and NHS II.

	Frequency of consumption					P for trend	HR for 1 serving/d
Unprocessed red meat							
	<1/wk	**1/wk**	**2-4/wk**	**5-6/wk**	**≥1/d**		
HPFS							
Cases/person-years	122/48444	459/147266	694/189831	337/86962	818/179801		
Age-adjusted model	1.00	1.22 (1.00, 1.49)	1.42 (1.17, 1.72)	1.54 (1.25, 1.90)	1.91 (1.57, 2.30)	<0.001	1.38 (1.29, 1.48)
Multivariate model[a]	1.00	1.03 (0.84, 1.26)	1.07 (0.88, 1.21)	1.11 (0.89, 1.38)	1.26 (1.02, 1.56)	<0.001	1.16 (1.06, 1.26)
NHS I							
Cases/person-years	79/33878	851/240276	2622/644637	1466/319173	3235/776209		
Age-adjusted model	1.00	1.47 (1.17, 1.85)	1.74 (1.39, 2.17)	1.96 (1.56, 2.46)	2.27 (1.82, 2.84)	<0.001	1.29 (1.24, 1.34)
Multivariate model[a]	1.00	1.10 (0.87, 1.39)	1.18 (0.94, 1.48)	1.22 (0.97, 1.54)	1.31 (1.05, 1.65)	<0.001	1.09 (1.04, 1.14)
NHS II							
Cases/person-years	106/106217	506/321795	1029/487376	440/162034	987/288754		
Age-adjusted model	1.00	1.54 (1.24, 1.89)	2.02 (1.65, 2.46)	2.45 (1.98, 3.03)	3.50 (2.87, 4.28)	<0.001	1.88 (1.77, 1.99)
Multivariate model[a]	1.00	1.05 (0.85, 1.29)	1.16 (0.94, 1.42)	1.12 (0.90, 1.39)	1.33 (1.07, 1.64)	<0.001	1.18 (1.09, 1.28)

Pooled results[b]							
Multivariate model[a]	1.00	1.06 (0.93, 1.19)	1.11 (1.01, 1.22)	1.15 (1.01, 1.30)	1.30 (1.15, 1.47)	<0.001	1.12 (1.08, 1.16)
Processed red meat							
	<1/wk	**1/wk**	**2-4/wk**	**≥5/wk**			
HPFS							
Cases/person-years	681/241861	953/247149	498/109159	298/54135			
Age-adjusted model	1.00	1.39 (1.26, 1.53)	1.66 (1.48, 1.87)	2.10 (1.83, 2.41)		<0.001	1.55 (1.43, 1.68)
Multivariate model[a]	1.00	1.17 (1.05, 1.29)	1.33 (1.17, 1.50)	1.64 (1.41, 1.91)		<0.001	1.34 (1.21, 1.48)
NHS I							
Cases/person-years	1689/518708	4442/1045500	1601/338619	521/111345			
Age-adjusted model	1.00	1.43 (1.35, 1.51)	1.74 (1.63, 1.87)	2.10 (1.90, 2.32)		<0.001	1.85 (1.74, 1.97)
Multivariate model[a]	1.00	1.16 (1.10, 1.23)	1.23 (1.14, 1.32)	1.34 (1.21, 1.49)		<0.001	1.30 (1.21, 1.41)
NHS II							
Cases/person-years	1085/664249	1348/533124	473/134105	162/34698			
Age-adjusted model	1.00	1.55 (1.43, 1.68)	2.33 (2.09, 2.59)	3.58 (3.04, 4.23)		<0.001	2.53 (2.34, 2.73)
Multivariate model[a]	1.00	1.09 (1.00, 1.19)	1.22 (1.08, 1.36)	1.44 (1.21, 1.71)		<0.001	1.37 (1.21, 1.55)
Pooled results[b]							
Multivariate model[a]	1.00	1.14 (1.10, 1.20)	1.25 (1.18, 1.31)	1.43 (1.33, 1.55)		<0.001	1.32 (1.25, 1.40)

Total red meat							
	≤1/wk	**2-4/wk**	**5-6/wk**	**1/d**	**≥2/d**		
HPFS							
Cases/person-years	320/121961	454/144046	305/81192	1000/235758	351/69347		
Age-adjusted model	1.00	1.21 (1.05, 1.40)	1.44 (1.23, 1.69)	1.66 (1.47, 1.89)	2.12 (1.82, 2.47)	<0.001	1.33 (1.27, 1.39)
Multivariate model[a]	1.00	1.05 (0.90, 1.21)	1.17 (0.99, 1.38)	1.28 (1.11, 1.48)	1.51 (1.26, 1.81)	<0.001	1.19 (1.12, 1.27)
NHS I							
Cases/person-years	424/141283	1515/405095	1196/294675	4131/917399	987/255720		
Age-adjusted model	1.00	1.28 (1.15, 1.42)	1.42 (1.27, 1.58)	1.77 (1.60, 1.96)	2.12 (1.88, 2.38)	<0.001	1.32 (1.28, 1.36)
Multivariate model[a]	1.00	1.07 (0.95, 1.19)	1.08 (0.97, 1.22)	1.23 (1.10, 1.36)	1.29 (1.14, 1.46)	<0.001	1.13 (1.08, 1.17)
NHS II							
Cases/person-years	227/191417	581/344902	442/218343	1441/520046	377/91468		
Age-adjusted model	1.00	1.42 (1.22, 1.65)	1.77 (1.50, 2.07)	2.59 (2.25, 2.98)	4.54 (3.85, 5.35)	<0.001	1.82 (1.74, 1.91)
Multivariate model[a]	1.00	1.00 (0.85, 1.16)	1.06 (0.90, 1.25)	1.18 (1.02, 1.37)	1.39 (1.16, 1.67)	<0.001	1.18 (1.11, 1.26)
Pooled results[b]							
Multivariate model[a]	1.00	1.05 (0.97, 1.13)	1.10 (1.01, 1.19)	1.23 (1.14, 1.32)	1.36 (1.25, 1.49)	<0.001	1.14 (1.10, 1.18)

[a]Multivariate model: adjusted for age (continuous), BMI category (<23, 23-24.9, 25-29.9, 30-34.9, ≥35 kg/m^2), alcohol consumption (0, 0.1-4.9, 5.0-14.9, ≥15 g/d), physical activity level (<3, 3-8.9, 9-17.9, 18.26.9, ≥27 MET-hrs/wk), smoking status (never, past, current 1-14 cigarettes/d, current 15-24 cigarettes/d, current ≥24 cigarettes/d), race (white/non-white), menopausal status and hormone use in women (premenopausal, postmenopausal never users, postmenopausal past users, postmenopausal current users), family history of diabetes, history of hypertension and hypercholesterolemia, quintiles of total calorie, and dietary score;

[b]Results from multivariate model were combined using fix effect model given than all the test for heterogeneity $P > 0.15$.

Online Supplemental Table 4. List of papers included in previous two meta-analyses and the newly found 2 papers.

Study	Included in the current meta-analysis	Reason for exclusion
van Dam et al. 2002 (10)	No	Previous publication in the Health Professionals Follow-up Study
Schulze et al. 2003 (11)	No	Previous publication in Nurses' Health Study II
Fung et al. 2004 (12)	No	Previous publication in Nurses' Health Study I
Simmons et al. 2007 (13)	No	≥1 portion/d vs. <1 portion/d, crude analysis without adjustment for other covariates, data could not be extracted
Meyer et al. 2001. (14)	No	No continuous data available.
Lee et al. 2004 (15)	No	Same cohort as Meyer's paper. No continuous data available.
Song et al. 2004 (16)	Yes	
Montonen et al. 2005 (17)	Yes	

Villegas et al. 2006 (18)	Yes	Only in the unprocessed red meat analysis. Data could not be extracted for processed red meat analysis.
Hodge et al. 2007 (19)	No	Dietary pattern analysis.
Schulze et al. 2007 (20)	Yes	The authors provided unpublished data. Kroger J et al., 2011, unpublished data.
Steinbrecher et al. 2010 (21)	Yes	
Männistö et al. 2010 (22)	Yes	

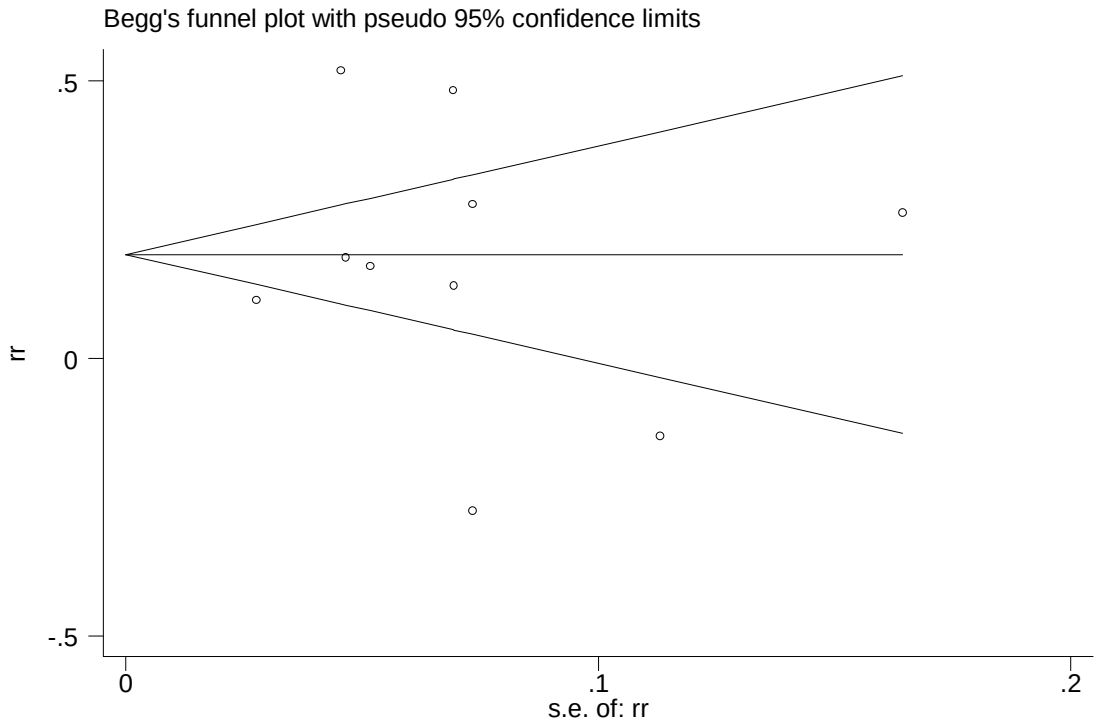
Online Supplemental Table 5. Characteristics of the prospective studies included in the current meta-analysis.

References	Cohort name	Total No. of cases and participants	Follow-up years	Age at baseline	Sex	Diet assessment	Diabetes assessment	Adjusted covariates
Song et al. 2004 (16)	Women's Health Study, USA	1558 cases, 37309 participants	1993-2003, 8.8 years	≥45	Female	Baseline validated FFQ	Self-report + Appendix questionnaires	Age, body mass index, smoking status, alcohol intake, physical activity, family history of diabetes, total energy intake, dietary intakes of fiber intake, glycemic load, magnesium, and total fat
Montonen et al. 2005 (17)	Finnish Mobile Clinic Health Examination Survey, Finland	383 cases, 4304 participants	1967/1972-1990, 23 years	40-69	Both	Dietary history interview	Drug reimbursement register	Age, sex, body mass index, smoking status, family history of diabetes, geographic area and total energy intake
Villegas et al. 2006 (18)	Shanghai Women's Health Study, China	1972 cases, 70609 participants	1997-2004, 4.6 years	40-70	Female	Updated validated FFQ	Self-report, but results were also confirmed in cases who met ADA criteria	Age, body mass index, waist to hip ratio, smoking status, alcohol intake, physical activity, income level, education level, occupation status, history of hypertension and chronic disease at baseline, total energy intake and vegetable intake
Schulze et al. 2007 (20)	EPIC-Potsdam Study, Germany	849 cases, 25167 participants	1994/1998-2005, 7.0 years	35–65	Both	Baseline validated FFQ	Self-report, but validated according to ICD-10	Age, sex, body mass index, waist circumference, smoking status, education, occupational activity, sports activity, cycling, alcohol intake, total energy intake, magnesium, fiber, coffee, fruit and vegetable

								intake
Steinbrecher et al. 2010 (21)	Multiethnic Cohort, USA	4555 cases, 36256 participants	1993/1996-2007, 13.5 years	45–75	Male	Baseline validated FFQ	Self-report, medication questionnaire, health plan linkage	Age, ethnicity, body mass index, physical activity, education and total energy intake.
Steinbrecher et al. 2010 (21)	Multiethnic Cohort, USA	4032 cases, 39256 participants	1993/1996-2007, 13.5 years	45–75	Female	Baseline validated FFQ	Self-report, medication questionnaire, health plan linkage	Age, ethnicity, body mass index, physical activity, education and total energy intake.
Männistö et al. 2010 (22)	Alpha-Tocopherol, Beta-Carotene Cancer Prevention study, Finland	1098 cases, 24854 participants	1985/1988-1997, 12 years	50-69	Male	Baseline validated FFQ	Drug reimbursement register	Age, intervention groups, body mass index, number of cigarettes smoked daily, smoking years, alcohol intake, leisure-time physical activity, systolic blood pressure, diastolic blood pressure, serum total cholesterol and serum HDL cholesterol, total energy intake, fruits, vegetables, rye, milk and coffee intake
Pan et al. 2011	Health Professionals Follow-up Study, USA	2,460 cases, 37,272 participants	1986-2006, 20 years	40-75	Male	Updated validated FFQ	Self-report + Appendix questionnaires	Age, ethnicity, smoking status, alcohol intake, physical activity, history of hypertension and hypercholesterolemia, and a family history of

								diabetes, total energy intake and diabetes dietary score
Pan et al. 2011	Nurses' Health Study I, USA	8,253 cases, 79,570 participants	1980-2008, 28 years	34-59	Female	Updated validated FFQ	Self-report + Appendix questionnaires	Same as above plus postmenopausal status and menopausal hormone use
Pan et al. 2011	Nurses' Health Study II, USA	3,068 cases, 87,504 participants	1991-2005, 14 years	27-44	Female	Updated validated FFQ	Self-report + Appendix questionnaires	Same as above plus postmenopausal status, menopausal hormone use, and oral contraceptive use

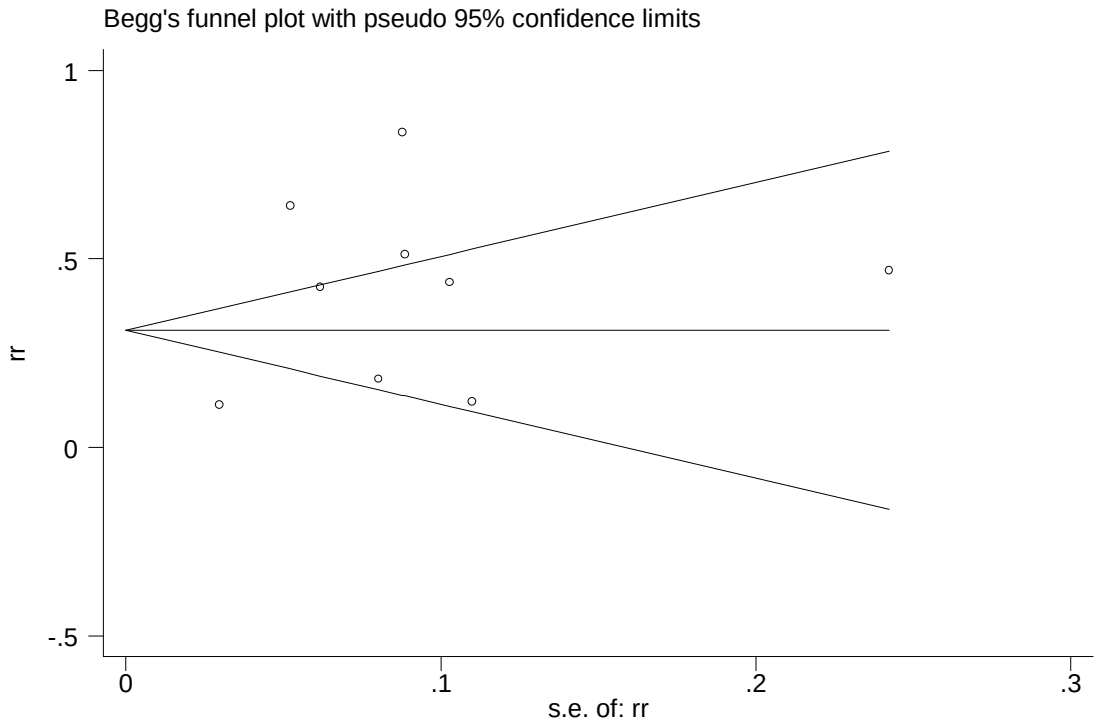
Online Supplemental Figure 1. Publication bias test for unprocessed red meat and risk of type 2 diabetes.



Tests for Publication Bias

Begg's Test, $P = 0.66$; Egger's Test, $P = 0.35$.

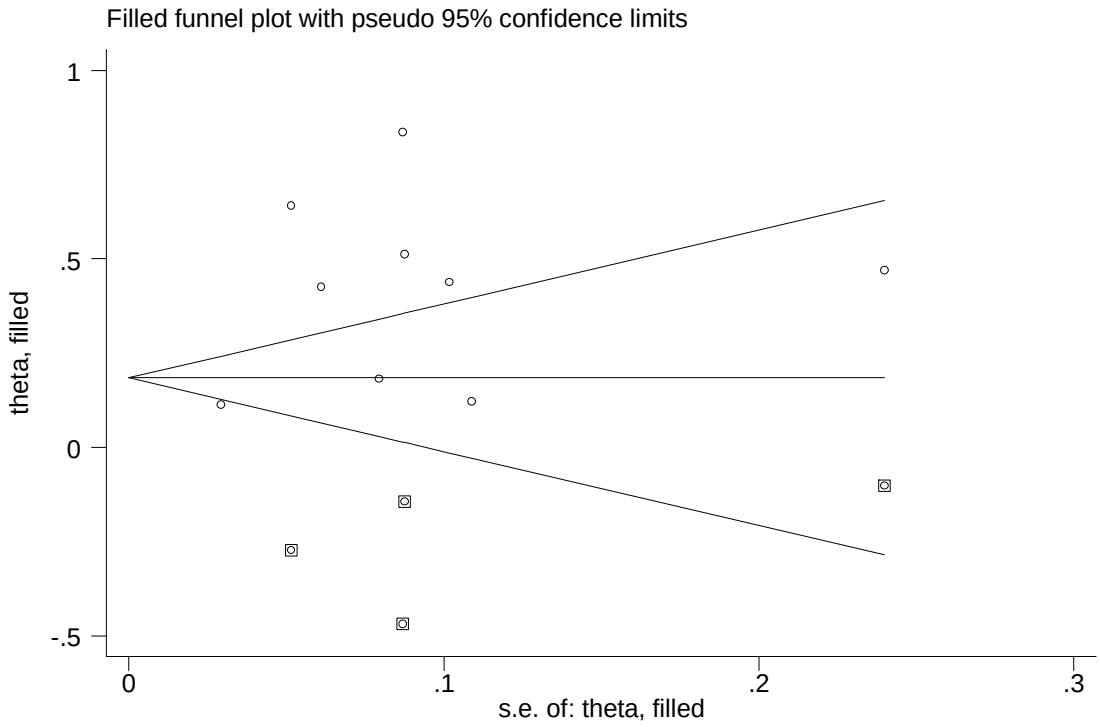
Online Supplemental Figure 2. Publication bias test for processed red meat and risk of type 2 diabetes.



Tests for Publication Bias

Begg's Test, $P = 0.35$; Egger's Test, $P = 0.03$.

Online Supplemental Figure 3. Publication bias test for the association between processed red meat intake and risk of type 2 diabetes after using trim and fill method.



References for the Online Supplemental Materials

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