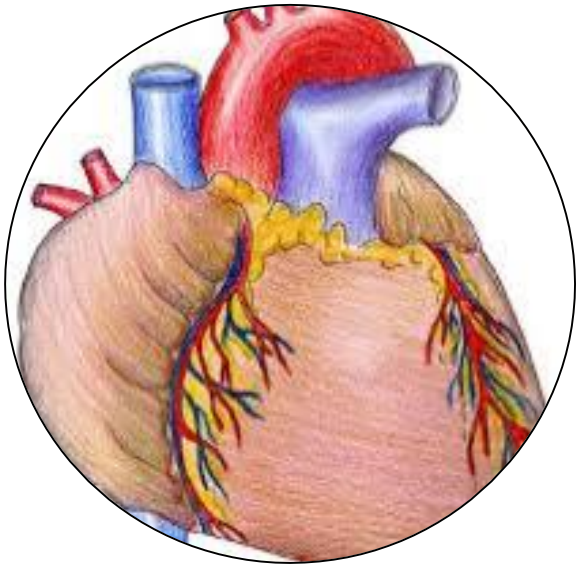
Cardiometabolic health and fermented dairy foods: a review of the evidence

Dr. Sabita S. Soedamah-Muthu

5 April 2017 Dairy Council, Belfast, Northern Ireland



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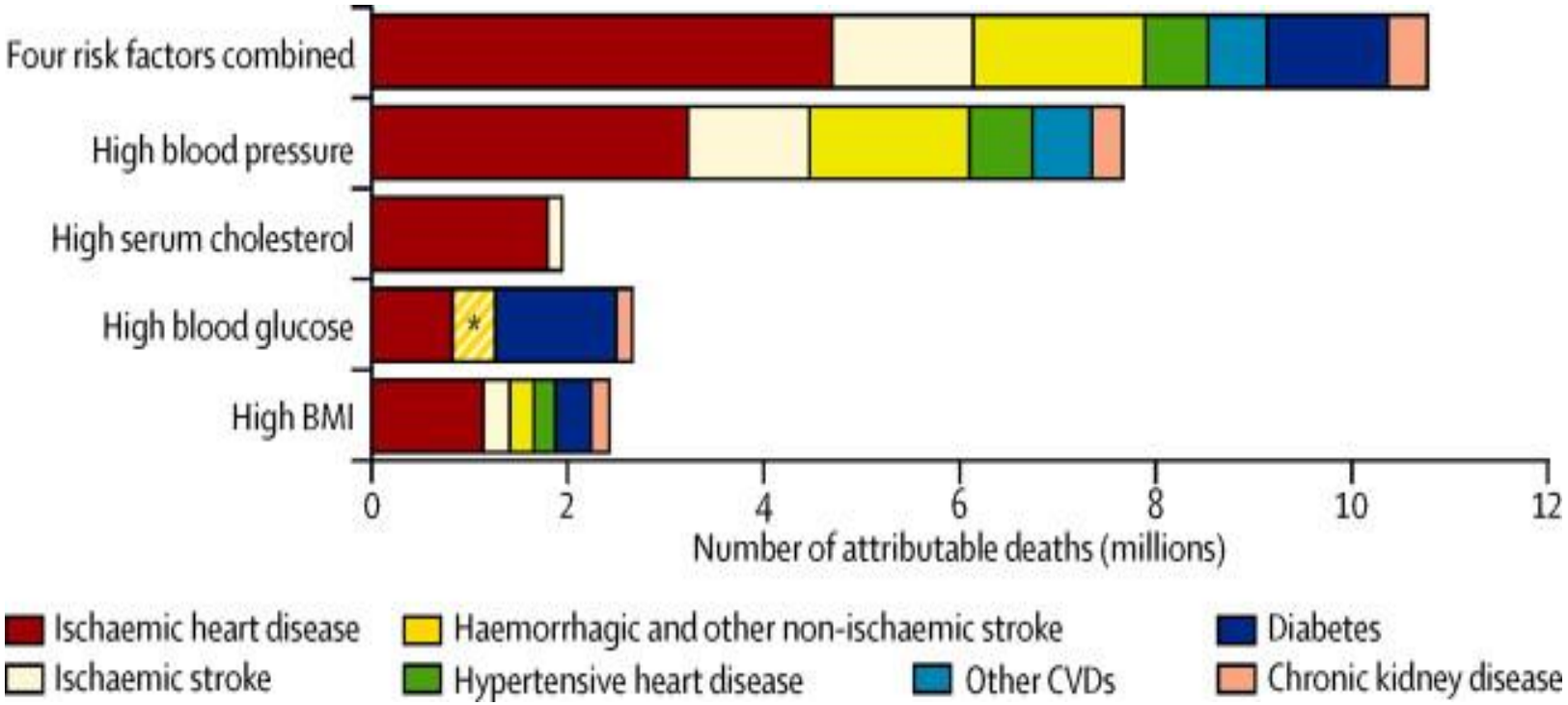
Unrestricted grants for part of the meta-analysis work were received by the Dutch Dairy Association, Global Dairy Platform, The Dairy Research Institute and Dairy Australia

Cardiometabolic Diseases

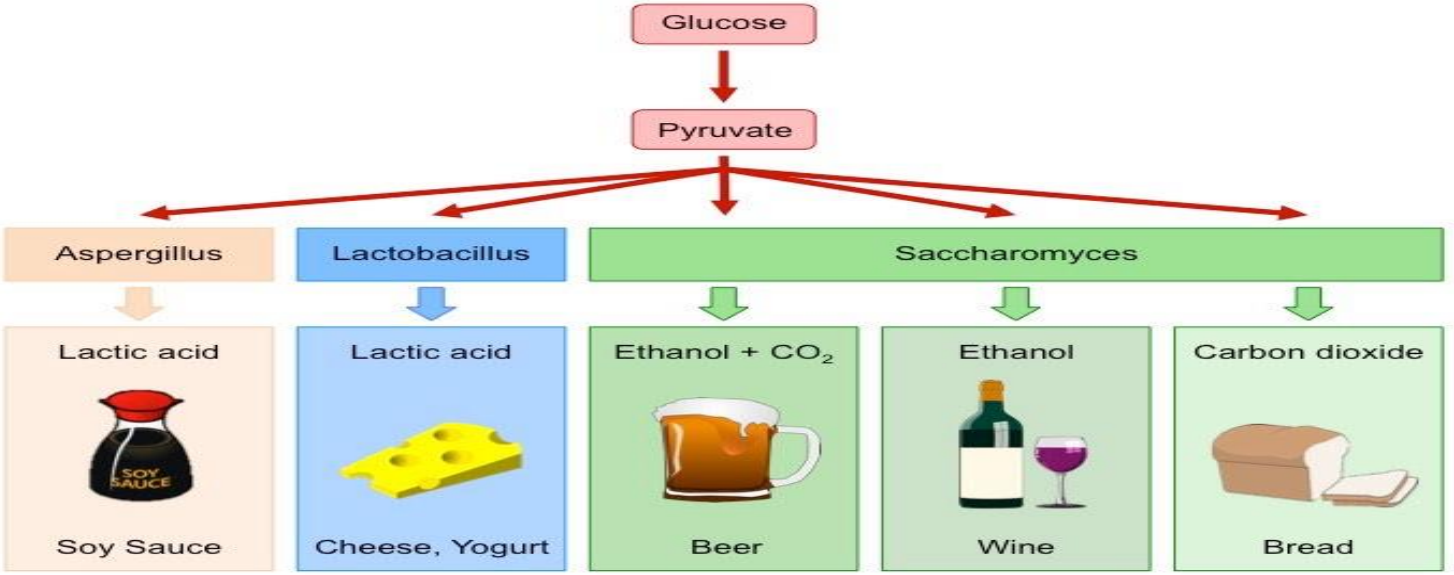


The Global Burden of Metabolic Risk Factors for Chronic Diseases Collaboration Lancet Diabetes Endocrinology 2014

Interpretation The salient features of the cardiometabolic disease and risk factor epidemic at the beginning of the 21st century are high blood pressure and an increasing effect of obesity and diabetes. The mortality burden of cardiometabolic risk factors has shifted from high-income to low-income and middle-income countries. Lowering cardiometabolic risks through dietary, behavioural, and pharmacological interventions should be a part of the global response to non-communicable diseases.

What is fermentation?

- Fermentation in food processing is the process of converting carbohydrates into alcohol, carbon dioxide or organic acids by yeasts, bacteria or a combination.”
- An anaerobic cellular process in which yeasts, bacteria, or other micro-organisms convert organic foods into simpler compounds and chemical energy (ATP) is produced
- The goal of fermentation in these products is to improve preservation, taste, structure or nutrition value of the food



Is it the fermentation?

The relationship between fermented food intake and mortality risk in the European Prospective Investigation into Cancer and Nutrition-Netherlands cohort *British Journal of Nutrition* (2015), **113**, 498–506

	Q1	Q2		Q3		Q4		
	HR	HR	95 % CI	HR	95 % CI	HR	95 % CI	P_{trend}
CVD mortality								
No. of deaths‡	164	184		174		204		
Total fermented foods	1	1·20	0·97, 1·49	1·03	0·82, 1·29	1·04	0·83, 1·30	0·7
Fermented dairy foods	1	0·98	0·79, 1·22	0·98	0·79, 1·22	0·98	0·79, 1·22	0·9
Yogurt	1	1·09	0·88, 1·33	1·09	0·88, 1·35	1·08	0·87, 1·34	0·6
Cheese	1	0·79	0·64, 0·98	0·88	0·72, 1·09	0·80	0·65, 0·99	0·1
Fermented vegetables†	1	0·98	0·80, 1·21	0·89	0·72, 1·11	1·05	0·83, 1·32	0·7
Fermented meat	1	0·94	0·75, 1·18	0·94	0·75, 1·17	1·17	0·95, 1·44	0·034
Stroke mortality								
No. of deaths‡	35	41		34		49		
Total fermented foods	1	1·07	0·68, 1·70	0·72	0·44, 1·17	0·82	0·51, 1·30	0·3
Fermented dairy foods	1	1·05	0·66, 1·69	0·86	0·54, 1·38	0·89	0·56, 1·41	0·5
Yogurt	1	1·27	0·80, 2·02	1·02	0·64, 1·64	0·96	0·60, 1·52	0·5
Cheese	1	0·60	0·39, 0·93	0·62	0·41, 0·96	0·59	0·38, 0·92	0·046
Fermented vegetables†	1	1·15	0·75, 1·78	0·65	0·39, 1·08	1·05	0·65, 1·70	0·9
Fermented meat	1	1·14	0·72, 1·82	1·01	0·63, 1·61	1·07	0·68, 1·68	0·9

Other nutrients in yogurt and cheese?

	Kcal	Prot	SAFA	Chol	Sodium	Potassiu	Ca	Phosphor	Zinc	Vit A	Vit B2	Vit B12	Vit B6
		g	g	mg	mg	mg	mg	mg	mg	µg	µg	µg	µg
Yogurt	58	4	2	9	42	156	143	114	0.5	29	160	0.2	32
Gouda cheese	369	23	20	81	700	86	816	539	4	319	280	2	36
Cheddar	415	25	22	100	670	77	720	490	2	325	400	1	100

Vit K	Vit D	probiotic bacteria
mg	mg	
130	0	
676	300	
149	300	

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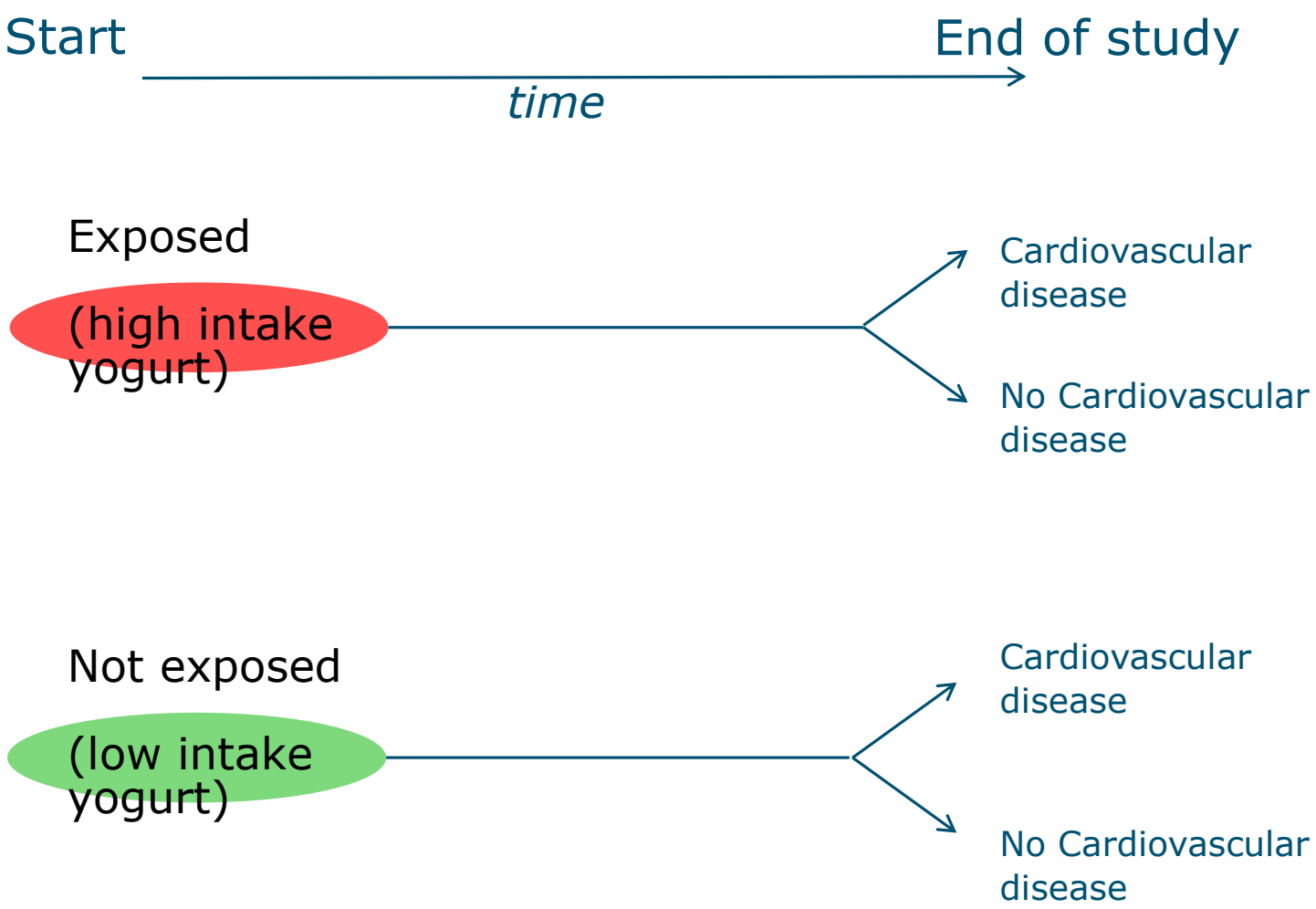
Observational study: Prospective cohort



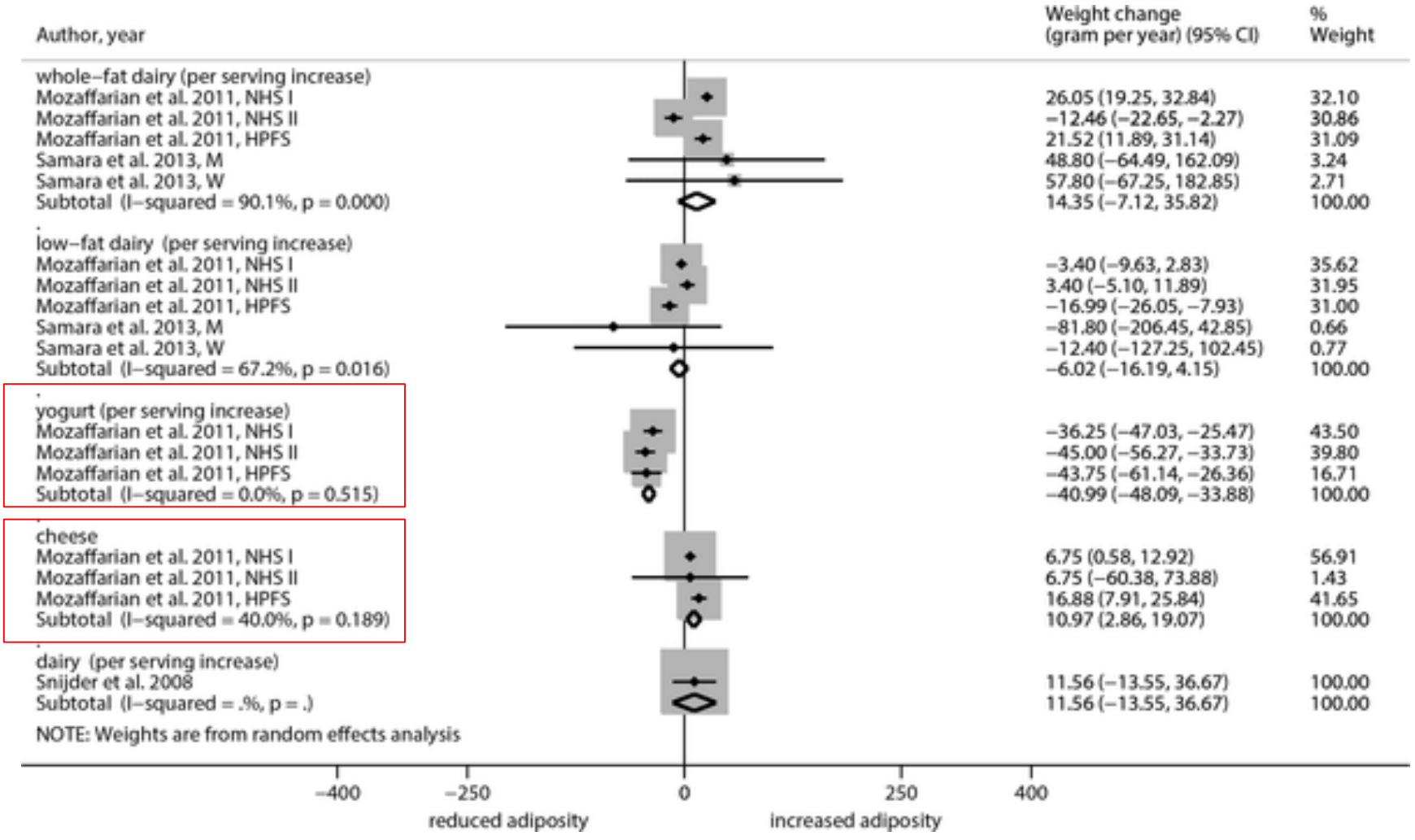
Fermented dairy products and obesity

Obesity- meta analysis of cohort studies

- Meta-analysis of 22 prospective cohort studies
- Inverse association between changes in body weight for each serving's increase of yogurt, and cheese was positively associated
- Highest dairy intake category was associated with a lower risk of abdominal obesity (OR: 0.85; 95% CI, 0.76 to 0.95), and risk of overweight (OR: 0.87; 95% CI, 0.76 to 1.00) compared to the lowest intake category.

Schwingshackl Plos One 2016

Fig 1. Forest plot of associations between changes in body weight (gram/year) and dairy consumption in cohort studies of adults.



Schwingshackl L, Hoffmann G, Schwedhelm C, Kalle-Uhlmann T, Missbach B, et al. (2016) Consumption of Dairy Products in Relation to Changes in Anthropometric Variables in Adult Populations: A Systematic Review and Meta-Analysis of Cohort Studies. PLoS ONE 11(6): e0157461. doi:10.1371/journal.pone.0157461 http://journals.plos.org/plosone/article?id=info:doi/10.1371/journal.pone.0157461

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PLOS ONE

Fermented dairy and Type 2 diabetes

Gijsbers, Soedamah-Muthu Am J Clin Nutrition 2016

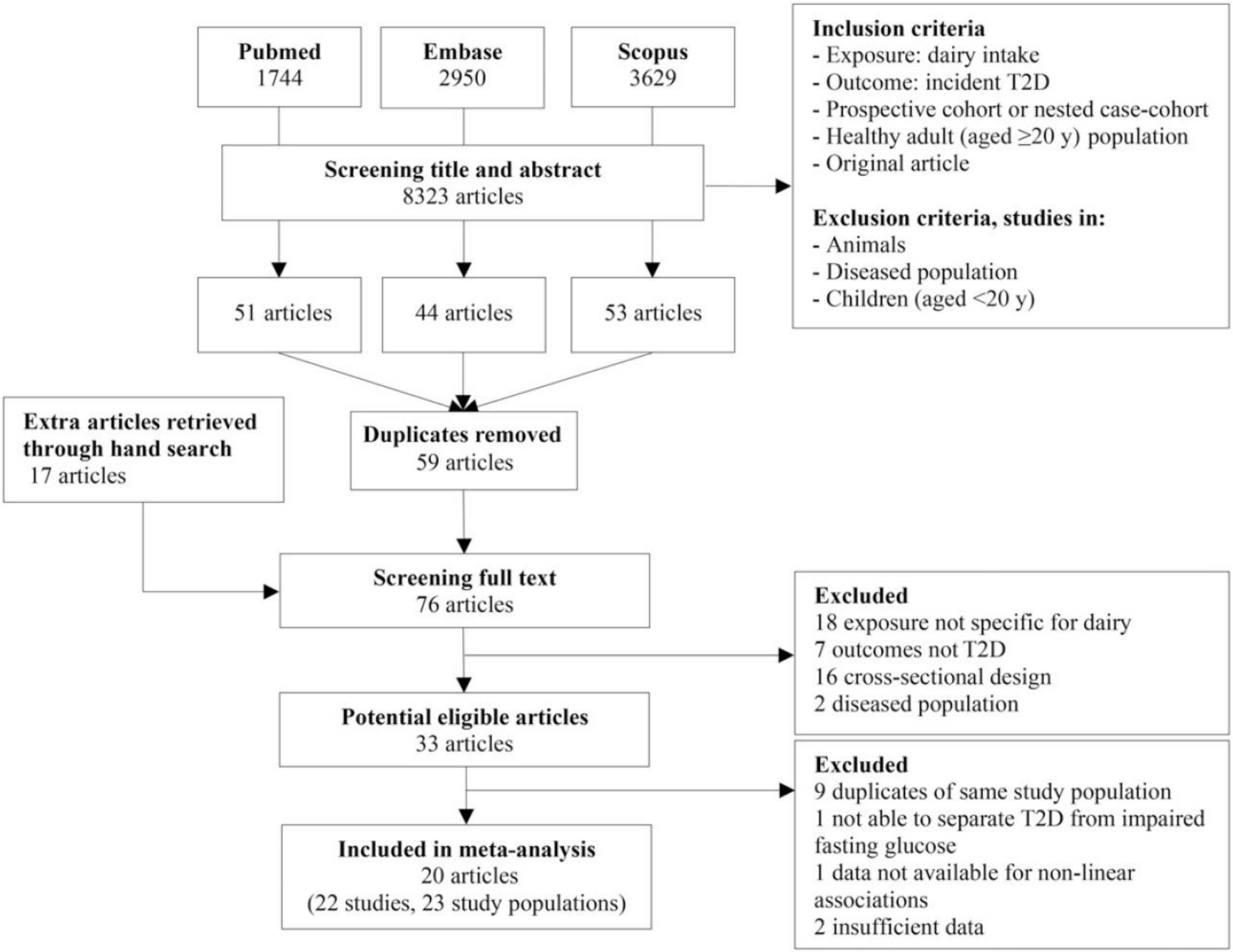
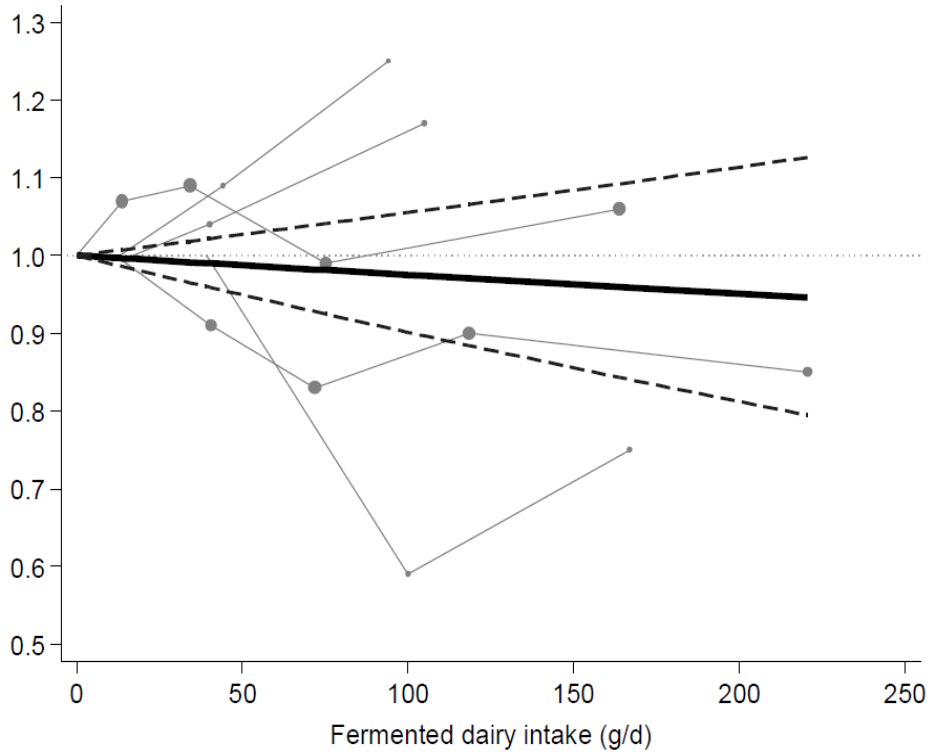


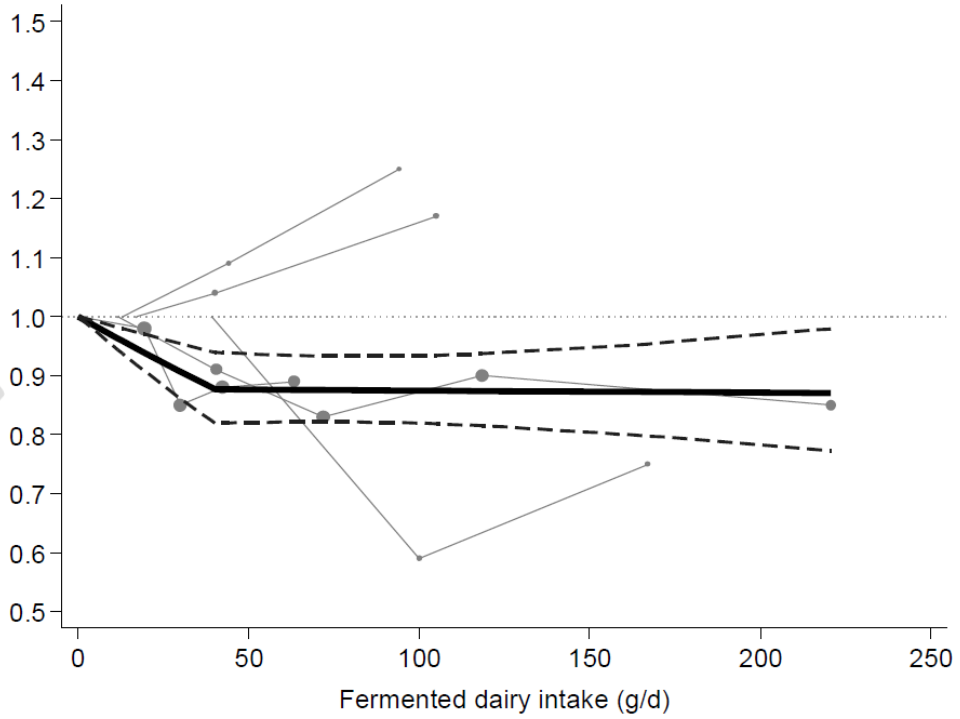
FIGURE 1 Flowchart of literature search for meta-analysis on dairy intake and incident T2D. T2D, type 2 diabetes.

Dairy products and Type 2 diabetes

Exposure	N Studies	Total N	N cases	Mean follow-up (years)	Men (%)	Mean age (years)	Mean BMI (kg/m^2)	Range median intake (g/d)
Total dairy	16[1]	489 113	38 993	11.4	39.0	53.5	25.7[2]	71 - 400
Low-fat dairy	13	405 667	27 597	12.1	33.0	54.1	26.3	65 - 294
High-fat dairy	13	327 895	24 034	13.2	37.1	53.2	26.3	17 - 135
Total milk	11[1]	145 472	17241	8.8	56.9	56.1	25.5[2]	62 - 442
Low-fat milk	7	267 607	20 098	15.0	31.7	52.2	25.9[2]	34 - 237
High-fat milk	9	336 102	21 995	15.0	30.6	52.0	25.7[2]	6 - 568
Fermented dairy	5	64 277	14 311	9.0	46.9	55.8	26.8	40 - 100
Cheese	12[1]	369 697	32 936	12.2	41.6	53.7	25.4[2]	2 - 40
Yogurt	11[1]	438 140	36 125	12.1	36.0	54.2	25.6[2]	17 - 71
Cream	5	258 571	19 730	19.2	71.3	49.6	25.2	2 - 11
Ice cream	5	258 571	19 730	19.2	71.3	49.6	25.2	6 - 10
Sherbet	4	231 641	16 759	20.5	75.0	47.5	24.9	6 - 8

Fermented dairy and Diabetes





Including low-fat fermented data of Ericson
RR=0.98 per 100 g/d, 95%CI 0.90, 1.06

Including high-fat fermented data of Ericson
RR=0.88 at 40 g/d, 95%CI 0.82, 0.94

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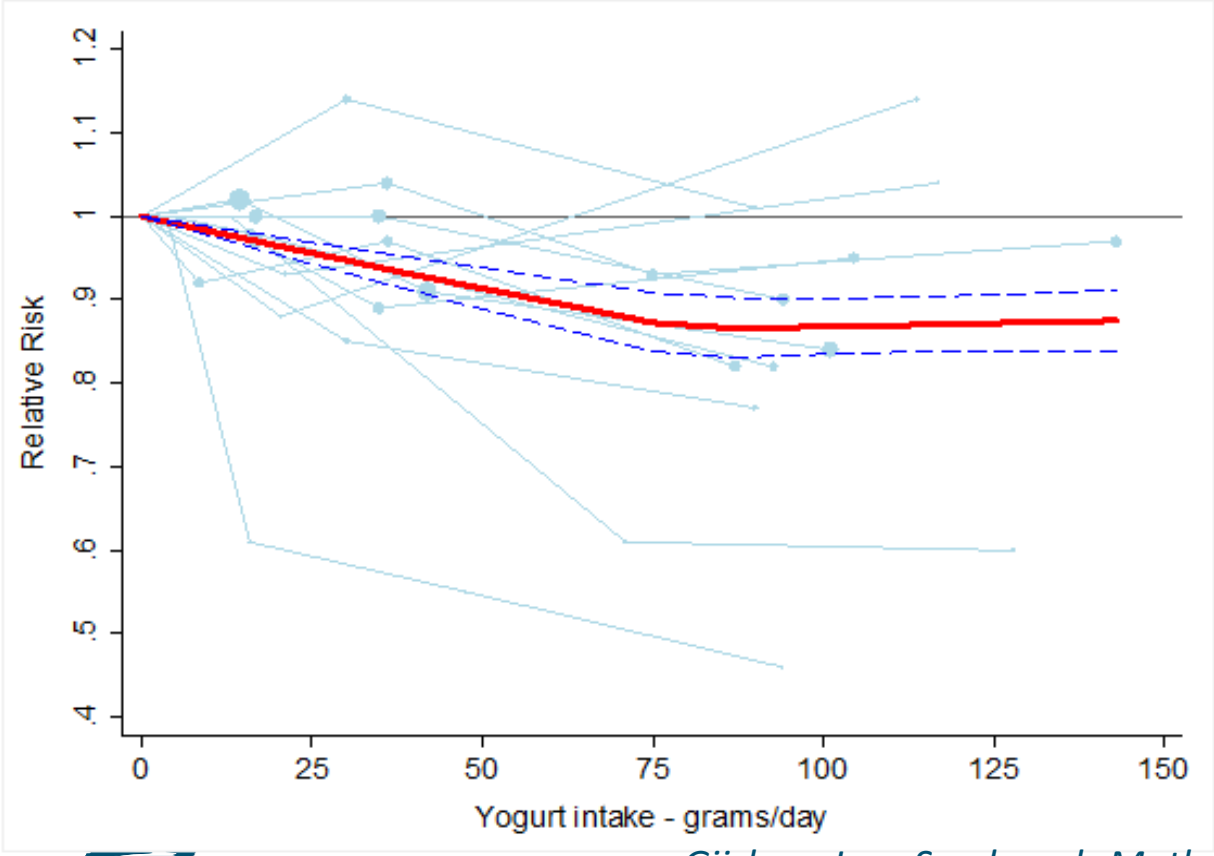
Results for relation Dairy-Diabetes in a nutshell

- 22 prospective cohort studies >500,000 people
- Cheese, RR=1.00 per 10 g/d, 95%CI 0.99-1.02
- Yogurt: 15% lower risk (RR=0.86 at 80 g/d, 95% CI 0.83 to 0.90; P<0.001)



Gijsbers-L, ... Soedamah-Muthu SS. Am J Clin Nutrition 2016

Fermented dairy and Hypertension

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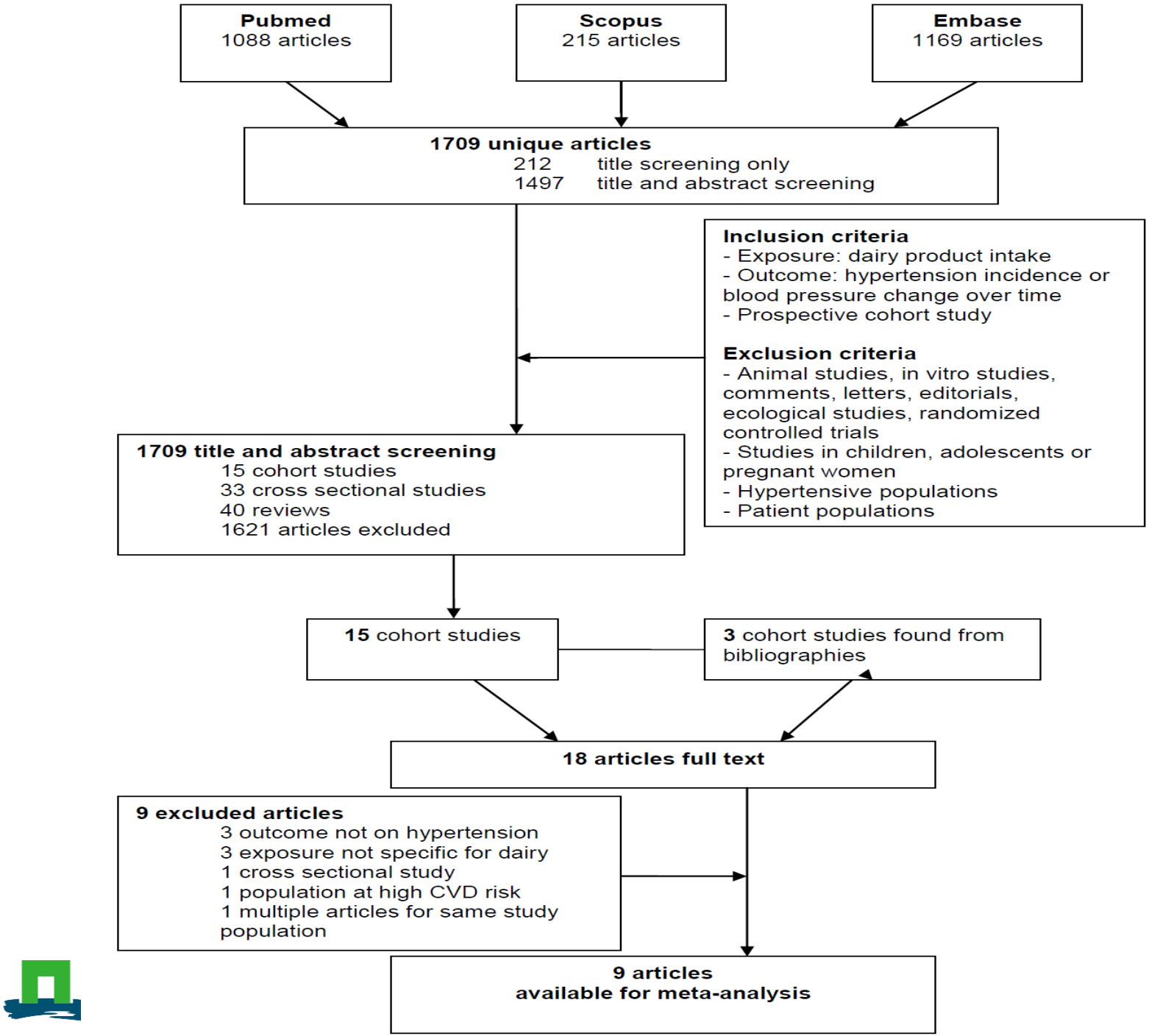
Soedamah-Muthu Hypertension 2012: 60(5):1131-7

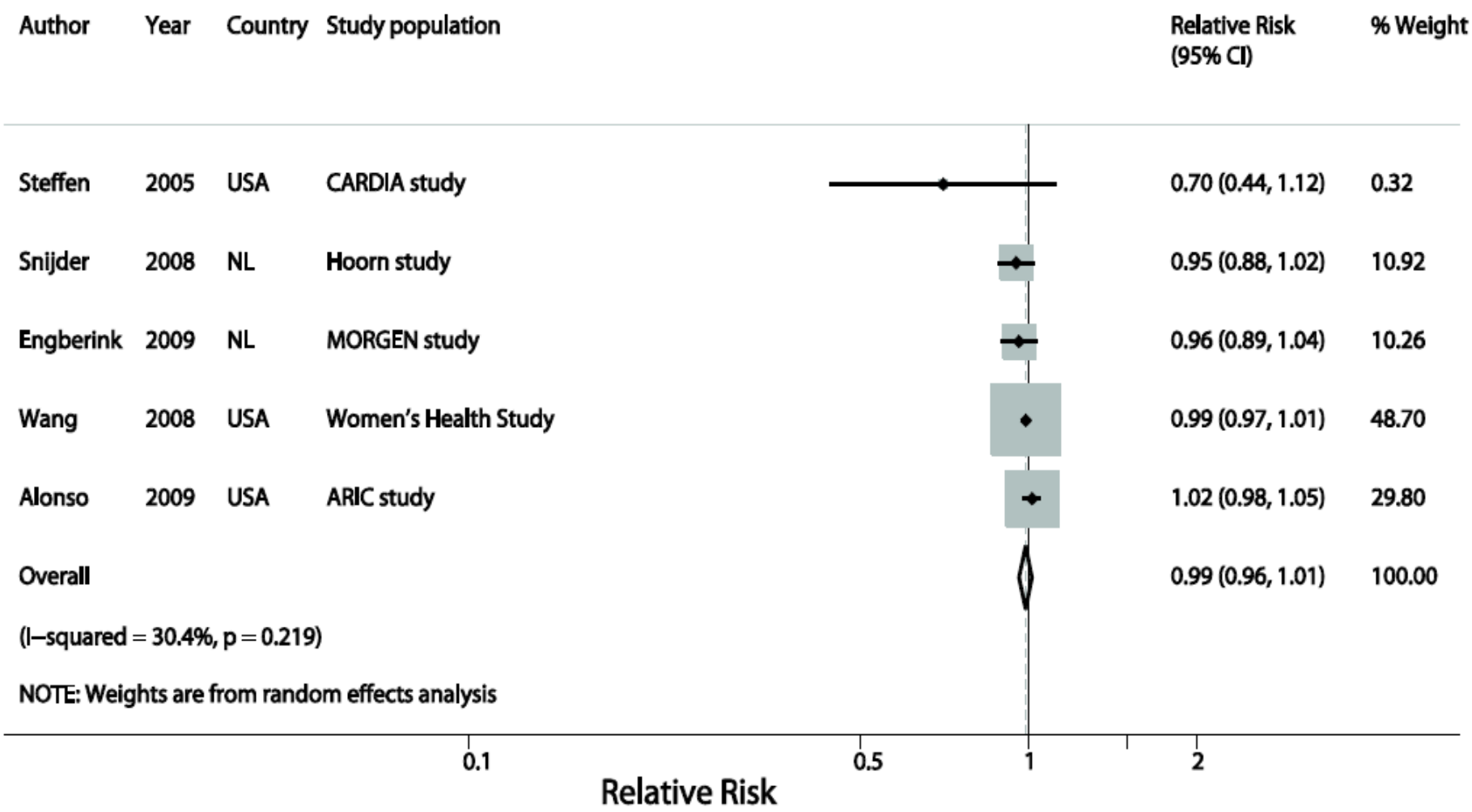

Pubmed
1088 articles
Scopus
215 articles
Embase
1169 articles
1709 unique articles
212 title screening only
1497 title and abstract screening
Inclusion criteria
- Exposure: dairy product intake
- Outcome: hypertension incidence or blood pressure change over time
- Prospective cohort study
Exclusion criteria
- Animal studies, in vitro studies, comments, letters, editorials, ecological studies, randomized controlled trials
- Studies in children, adolescents or pregnant women
- Hypertensive populations
- Patient populations
1709 title and abstract screening
15 cohort studies
33 cross sectional studies
40 reviews
1621 articles excluded
15 cohort studies
3 cohort studies found from bibliographies
18 articles full text
9 excluded articles
3 outcome not on hypertension
3 exposure not specific for dairy
1 cross sectional study
1 population at high CVD risk
1 multiple articles for same study population
9 articles
available for meta-analysis

Relation between fermented dairy and hypertension

Table S3 Characteristics of separate meta-analyses, per dairy category

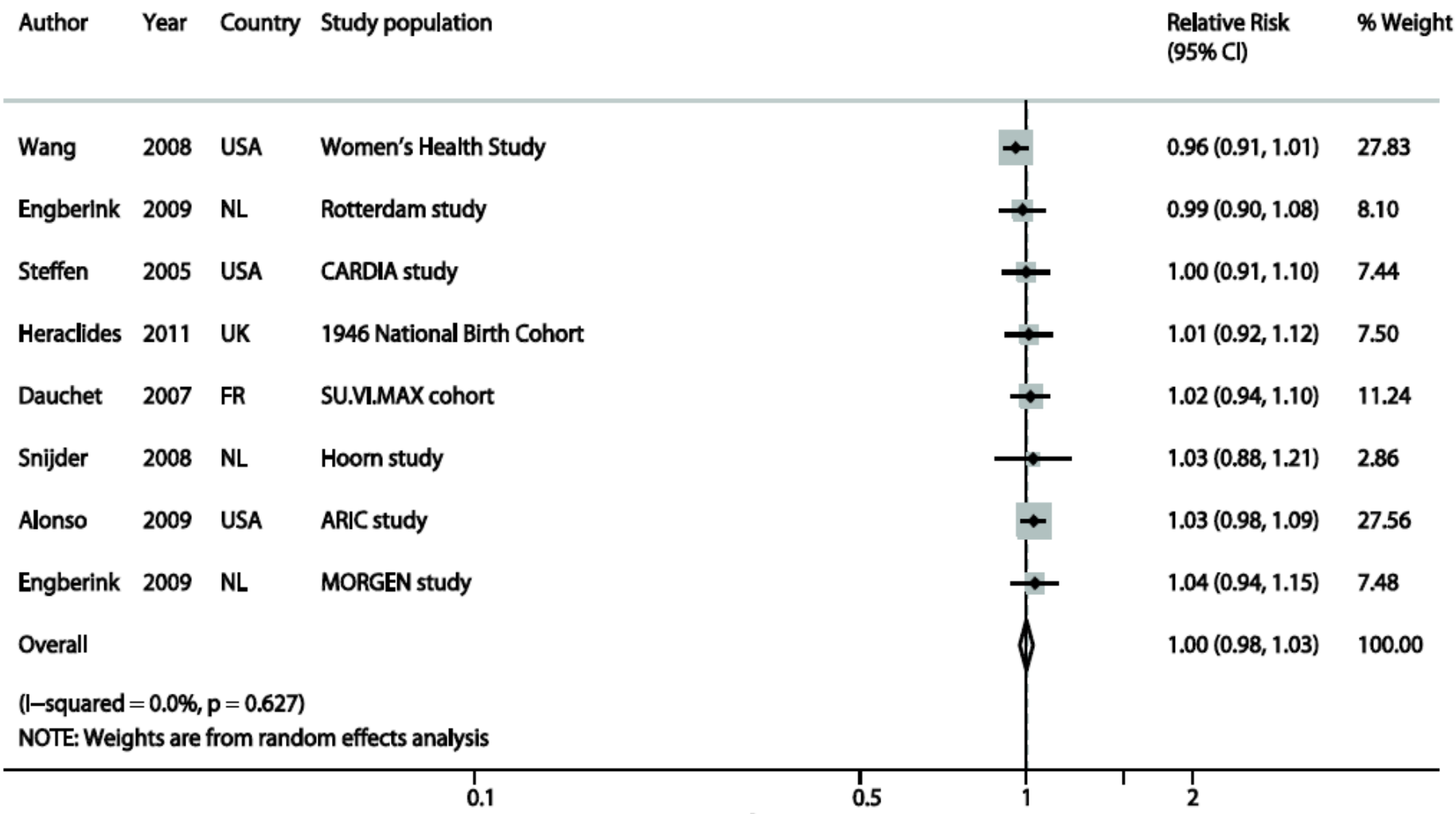
Dairy group	Number of studies	Follow-up time (y)	Men (%)	Age (y)	BMI (kg/m^2)
Total dairy	9	8 (4)	38 (15)	48 (12)	25.0 (0.9)
Low-fat dairy	6	7 (3)	37 (18)	51 (10)	24.8 (0.9)
High-fat dairy	6	7 (3)	37 (18)	51 (10)	24.8 (0.9)
Fermented dairy	4	7 (2)	45 (2)	54 (10)	25.2 (0.4)
Cheese	8	8 (3)	38 (16)	50 (12)	25.3 (0.5)
Milk	7	9 (4)	37 (17)	50 (11)	25.3 (0.2)
Yogurt	5	9 (4)	35 (20)	48 (13)	24.4 (0.6)

Figure S5, Panel A. Forest plot for the linear dose-response relationship between yogurt intake (per increment of 50 g/d) and HTN incidence from 5 studies.



45088 individuals , 12959 Hypertension cases

Figure S6, Panel A. Forest plot for the linear dose-response relationship between cheese intake (per increment of 30 g/d) and HTN incidence from 8 studies.



51007 individuals, 15 066 Hypertension cases

Fermented dairy products and Stroke

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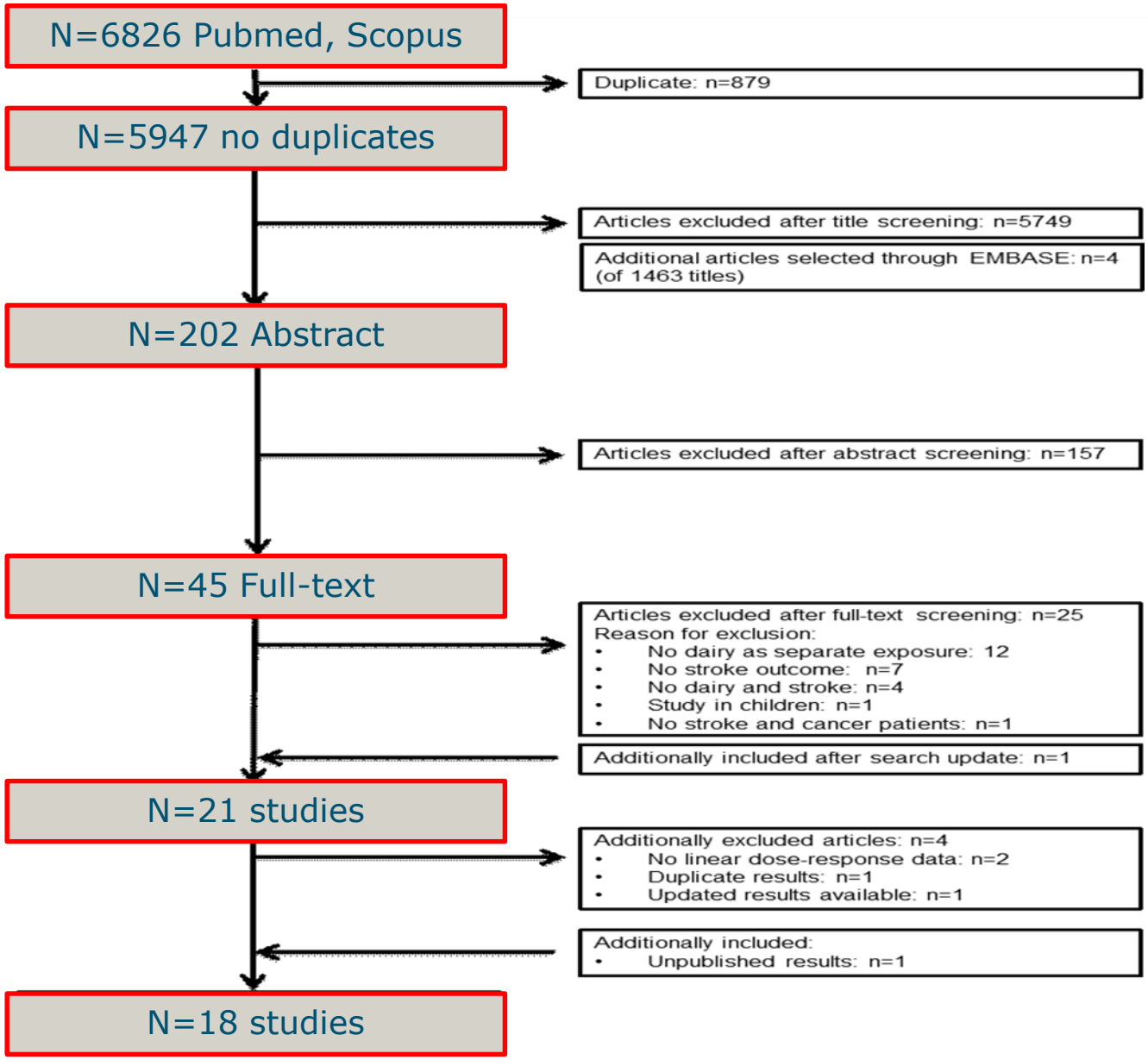
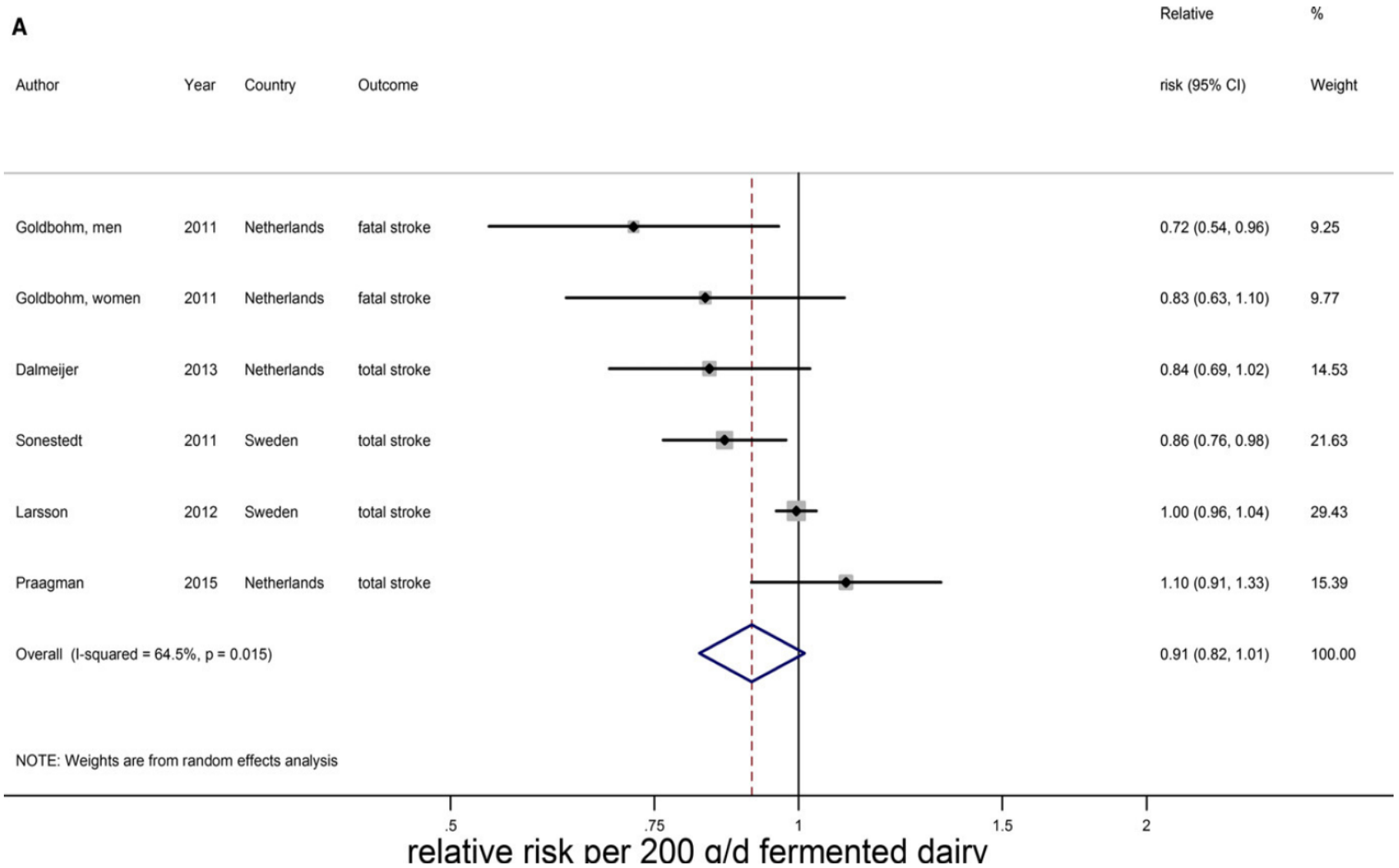
De Goede, Soedamah-Muthu et al.. JAHA 2016

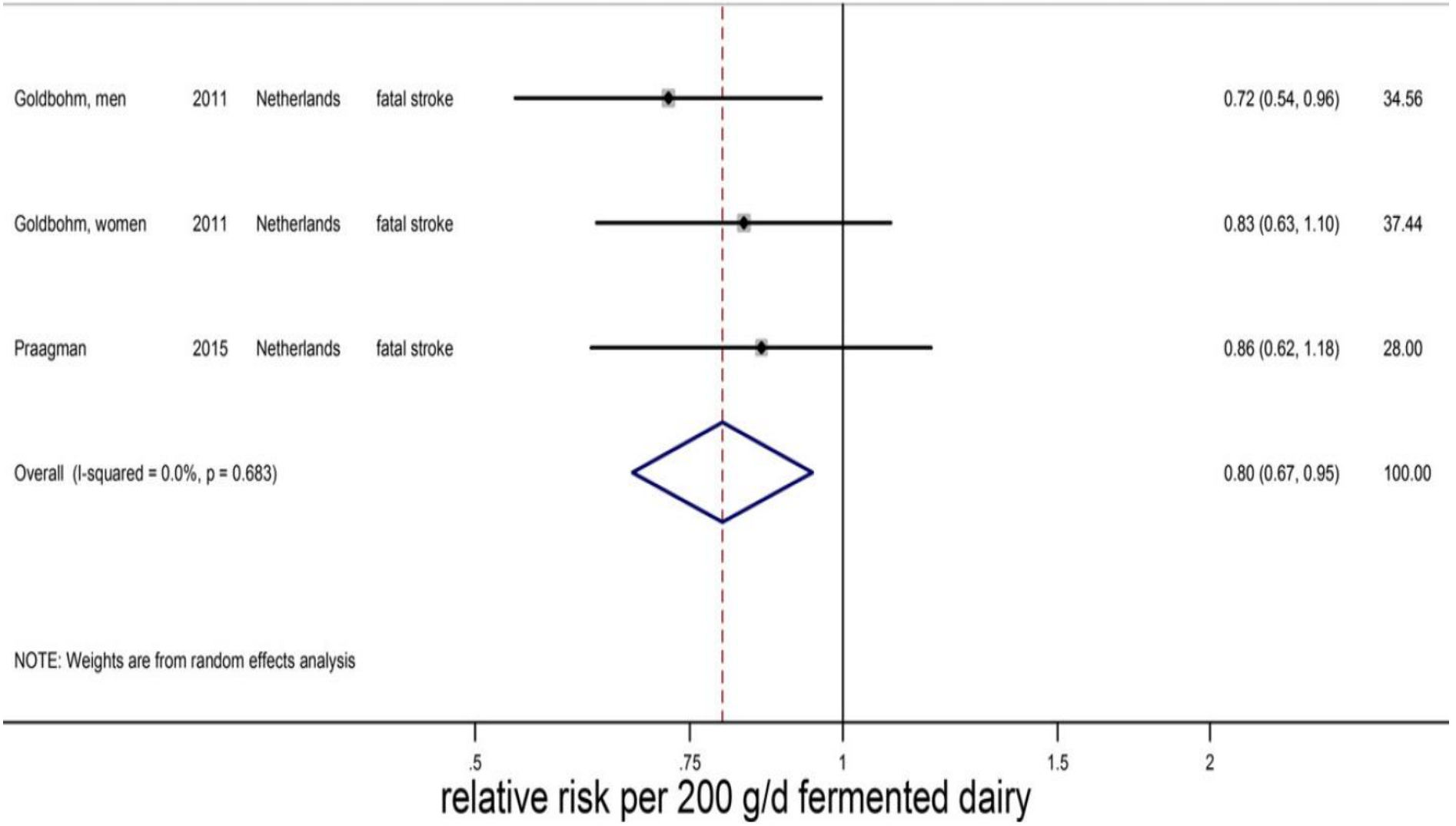
Flowchart


N=6826 Pubmed, Scopus
Duplicate: n=879
N=5947 no duplicates
Articles excluded after title screening: n=5749
Additional articles selected through EMBASE: n=4 (of 1463 titles)
N=202 Abstract
Articles excluded after abstract screening: n=157
N=45 Full-text
Articles excluded after full-text screening: n=25
Reason for exclusion:
• No dairy as separate exposure: 12
• No stroke outcome: n=7
• No dairy and stroke: n=4
• Study in children: n=1
• No stroke and cancer patients: n=1
Additionally included after search update: n=1
N=21 studies
Additionally excluded articles: n=4
• No linear dose-response data: n=2
• Duplicate results: n=1
• Updated results available: n=1
Additionally included:
• Unpublished results: n=1
N=18 studies

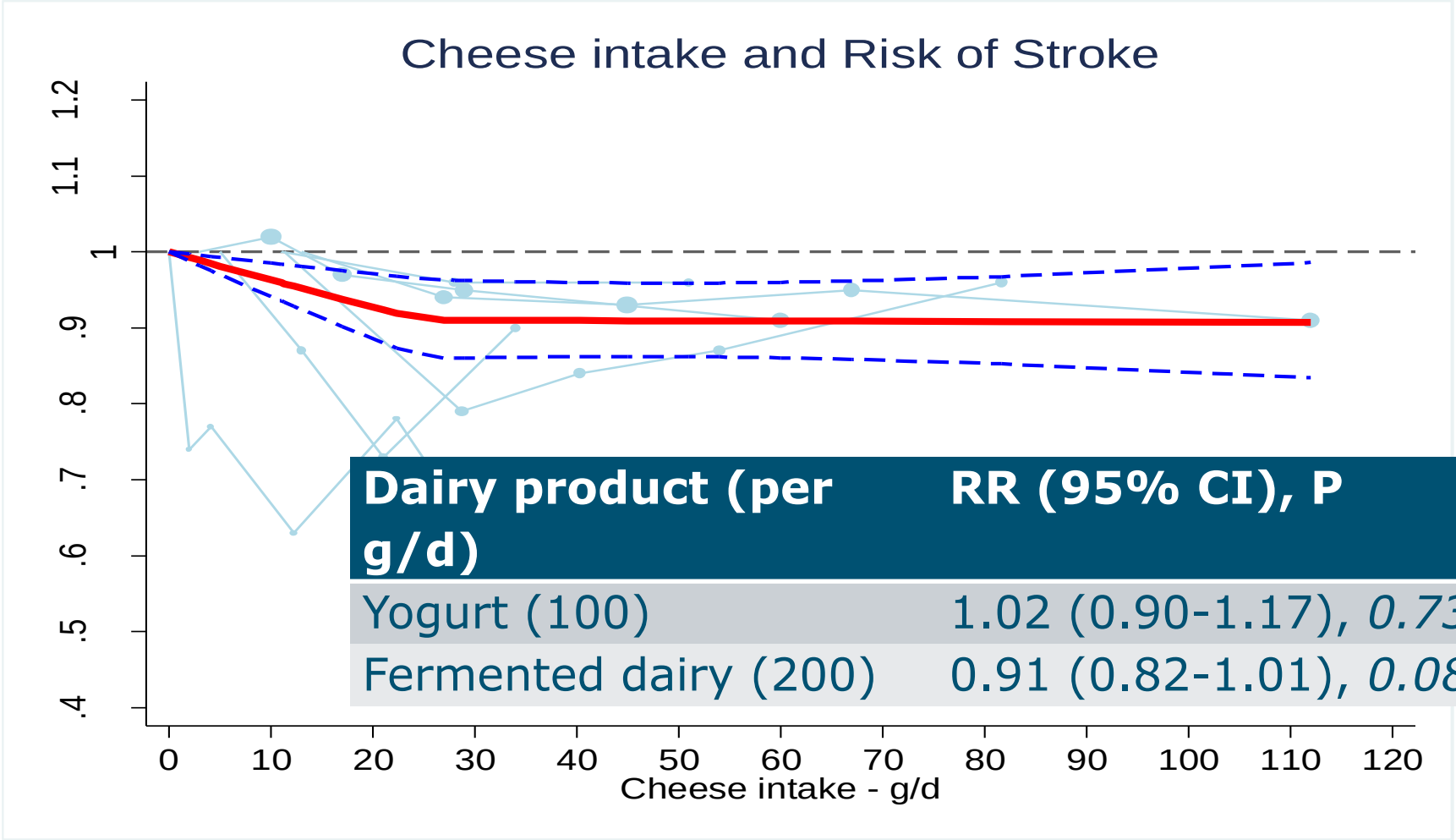
Fermented dairy and total stroke



Fermented dairy and fatal stroke



Spaghetti plot cheese intake and stroke



Dairy product (per g/d)	RR (95% CI), P
Yogurt (100)	1.02 (0.90-1.17), *0.73*
Fermented dairy (200)	0.91 (0.82-1.01), *0.08*

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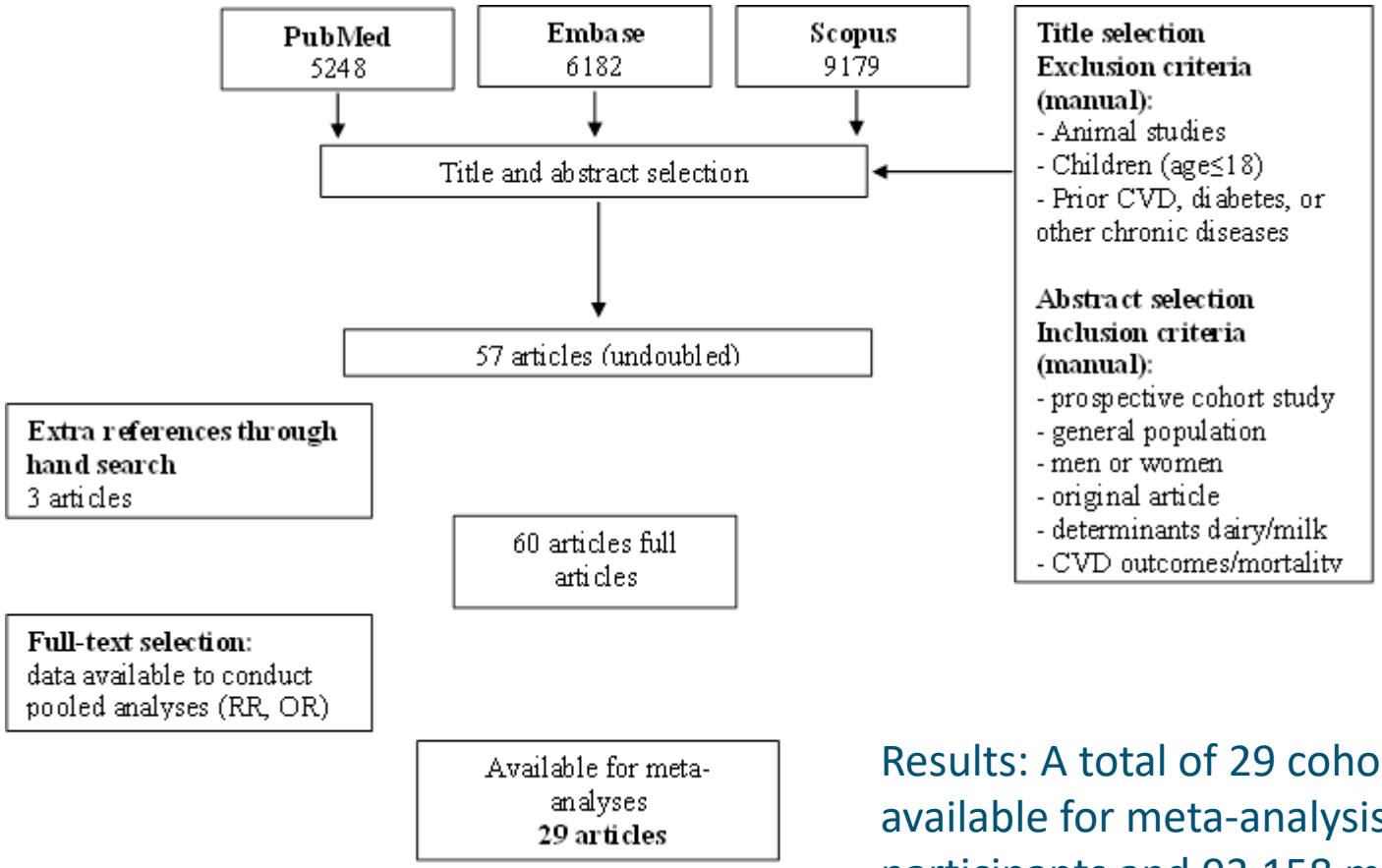
For quality of life

0.91; 95% CI 0.86–0.96;

Fermented dairy products and mortality

Jing Guo Eur J Epi 2017

Flowchart Meta-analysis Dairy-CVD/mortality



Results: A total of 29 cohort studies were available for meta-analysis, with 938,465 participants and 93,158 mortality, 28,419 total CHD and 25,416 total CVD cases.

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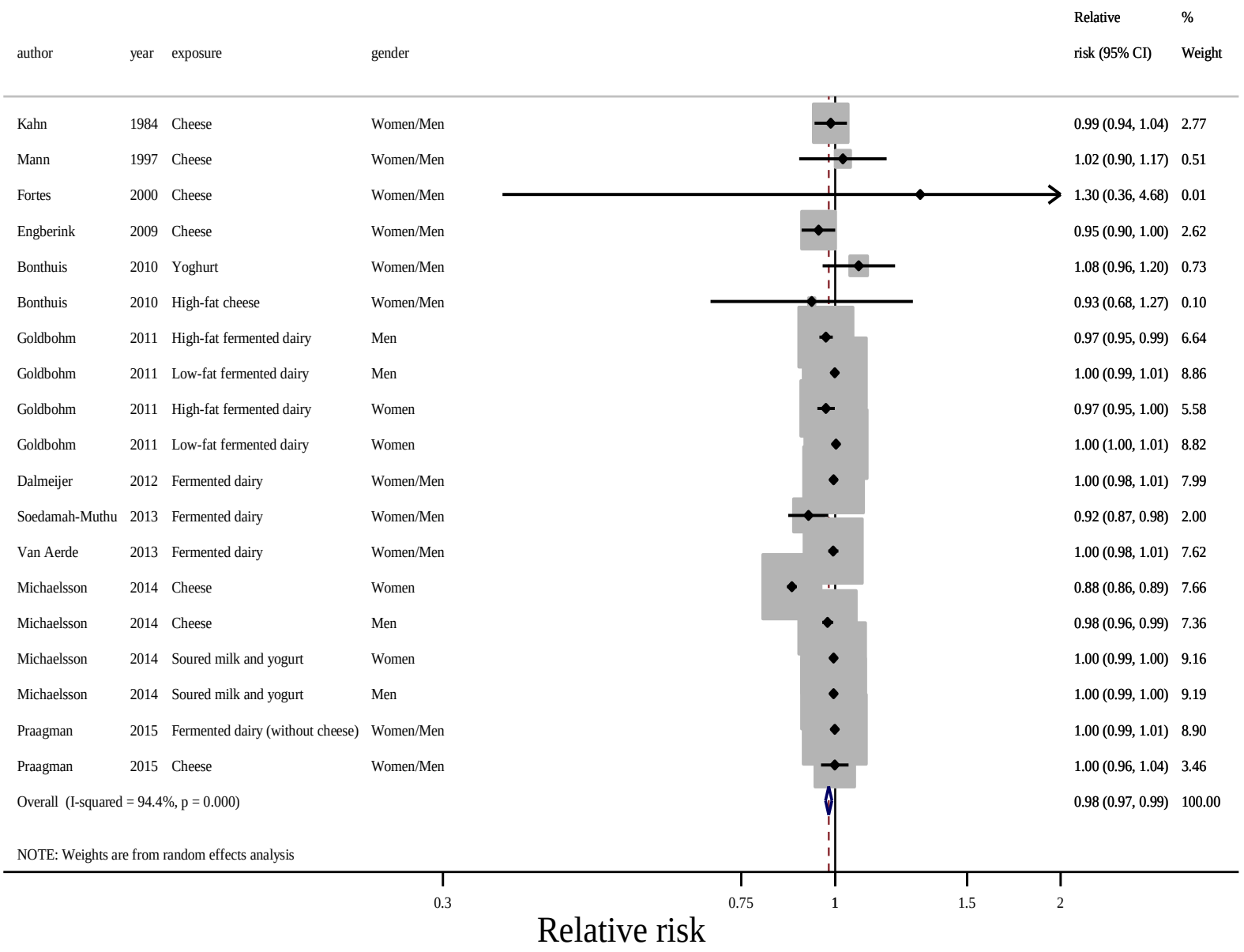
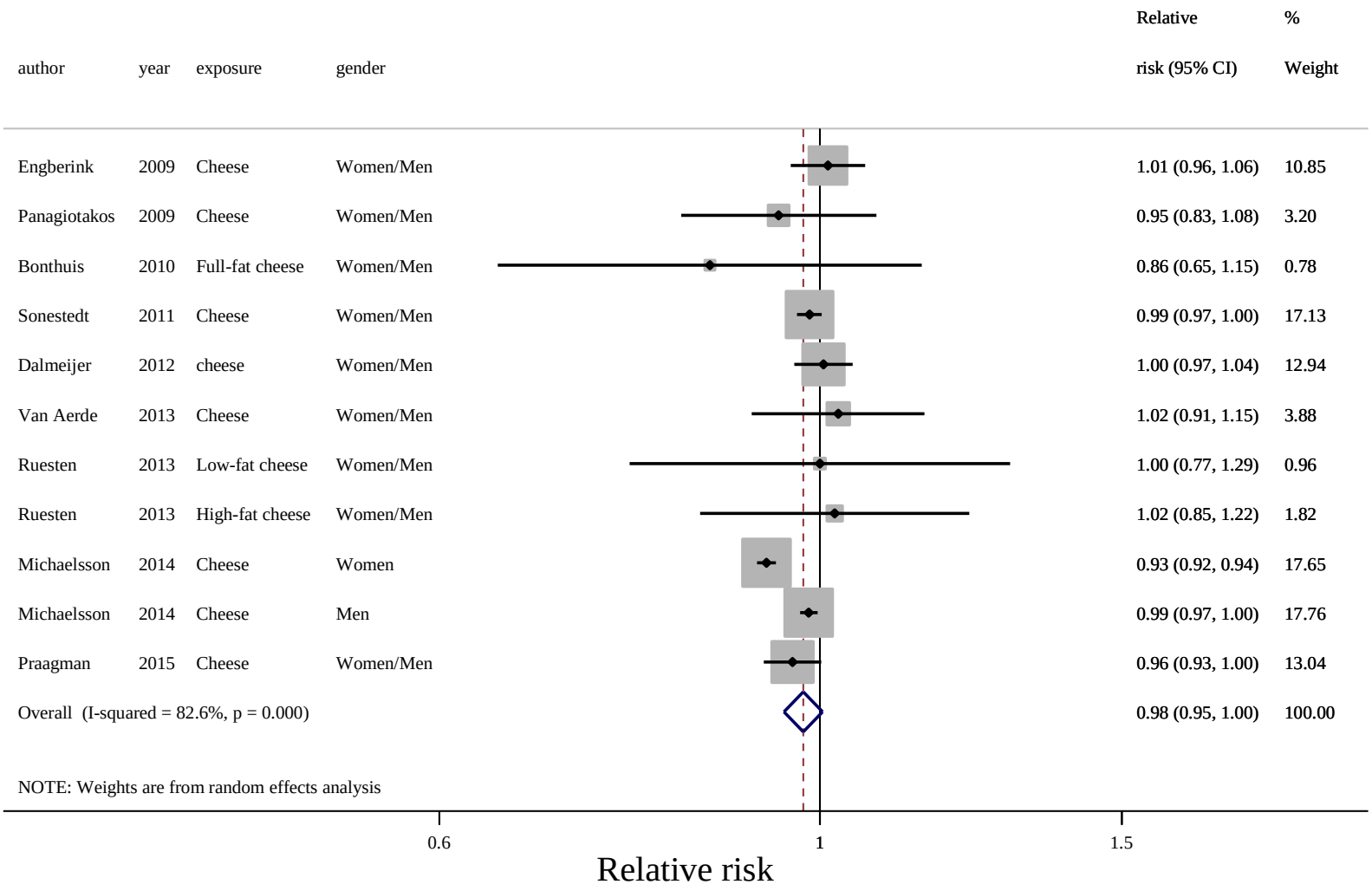
Jing Guo Eur J Epi 2017 just accepted

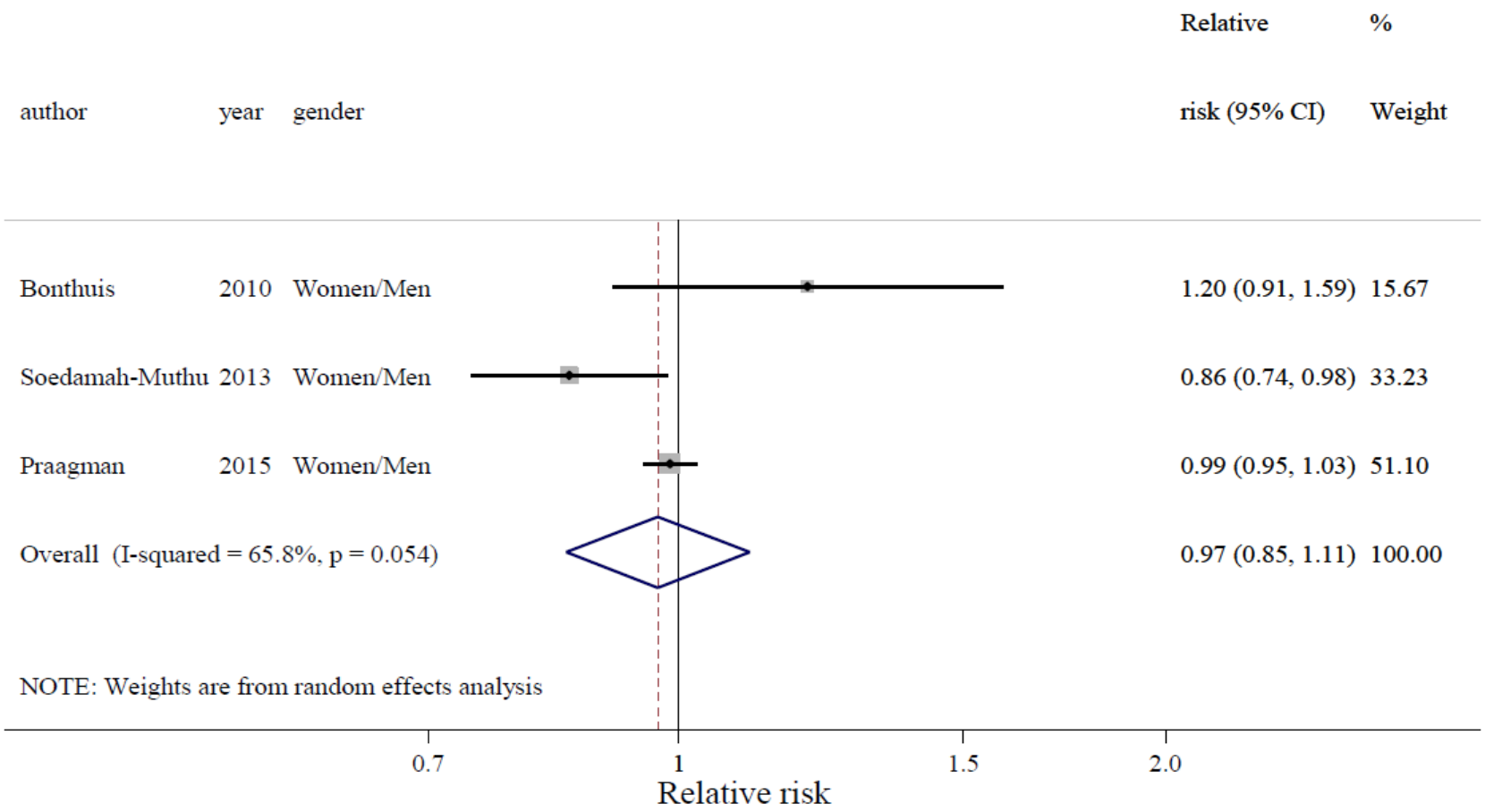
Fermented dairy and all-cause mortality



Cheese and CVD mortality



Yogurt and all-cause mortality



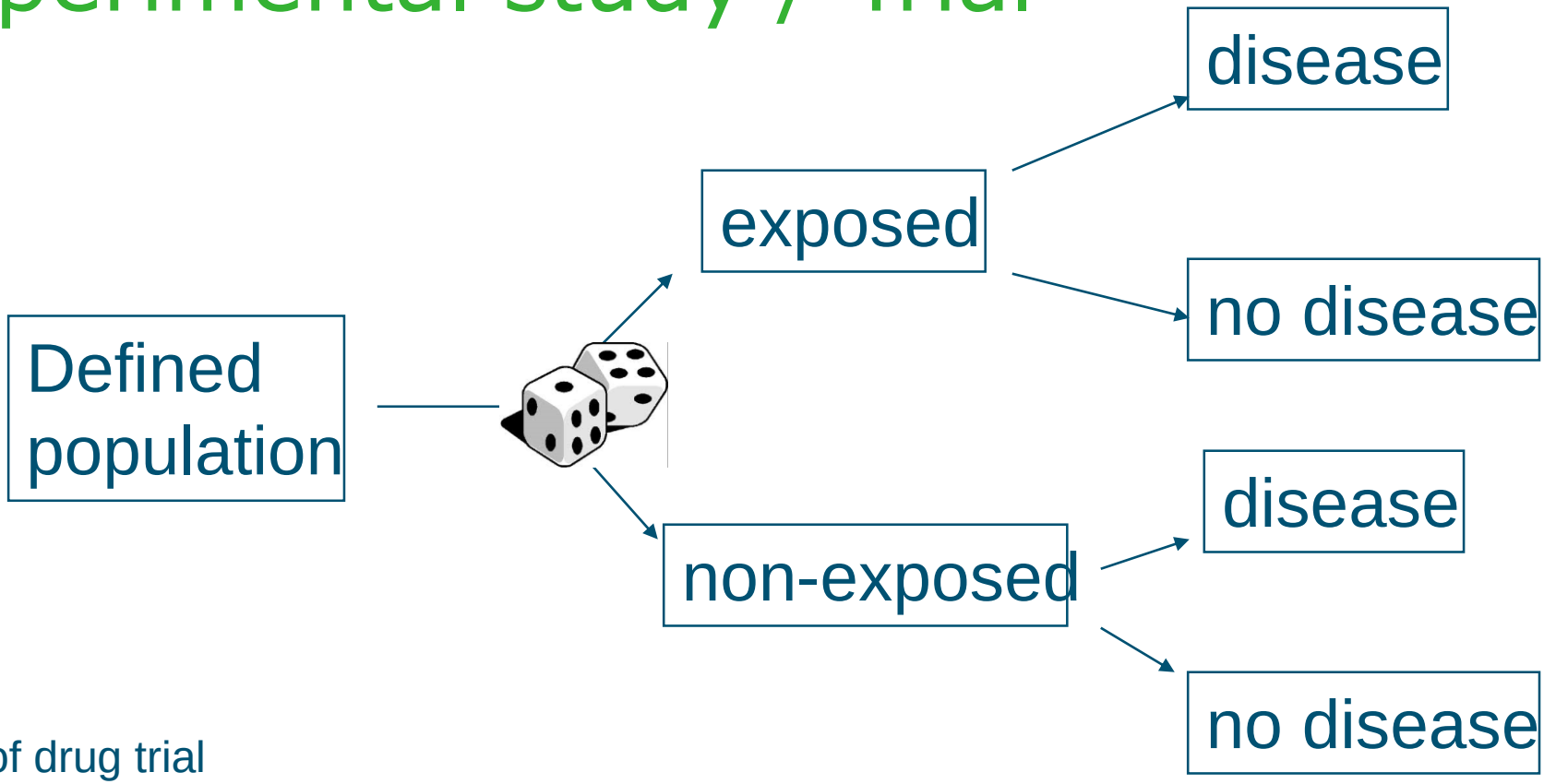
Conclusions

- Cheese per 10 g/d was possibly associated with a 2% lower risk of CVD mortality (RR 0.98, 95% CI: 0.95-1.00; I2=82.6%), but not yogurt.
- All of these marginally inverse associations were attenuated in sensitivity analyses by removing one large Swedish study.
- This meta-analysis combining data from 29 prospective cohort studies demonstrated neutral associations between fermented dairy products and cardiovascular and all-cause mortality

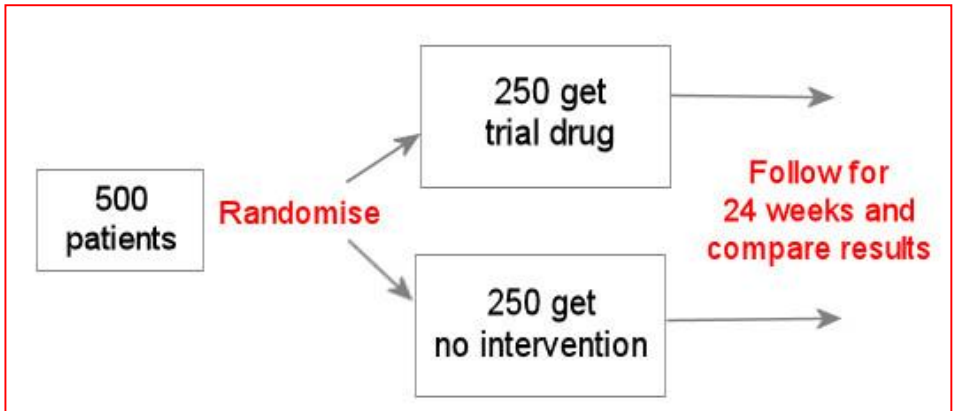
Final conclusions

- There is a possible role for fermented dairy foods in the prevention of cardiometabolic diseases.
  - Yogurt inversely associated with diabetes
  - Not with hypertension
  - Possibly cheese with stroke and CVD risk
- Effect estimates were generally weak and results should be considered in the context of the observed heterogeneity.
- Future epidemiological studies should provide more details about dairy types, including fat content.

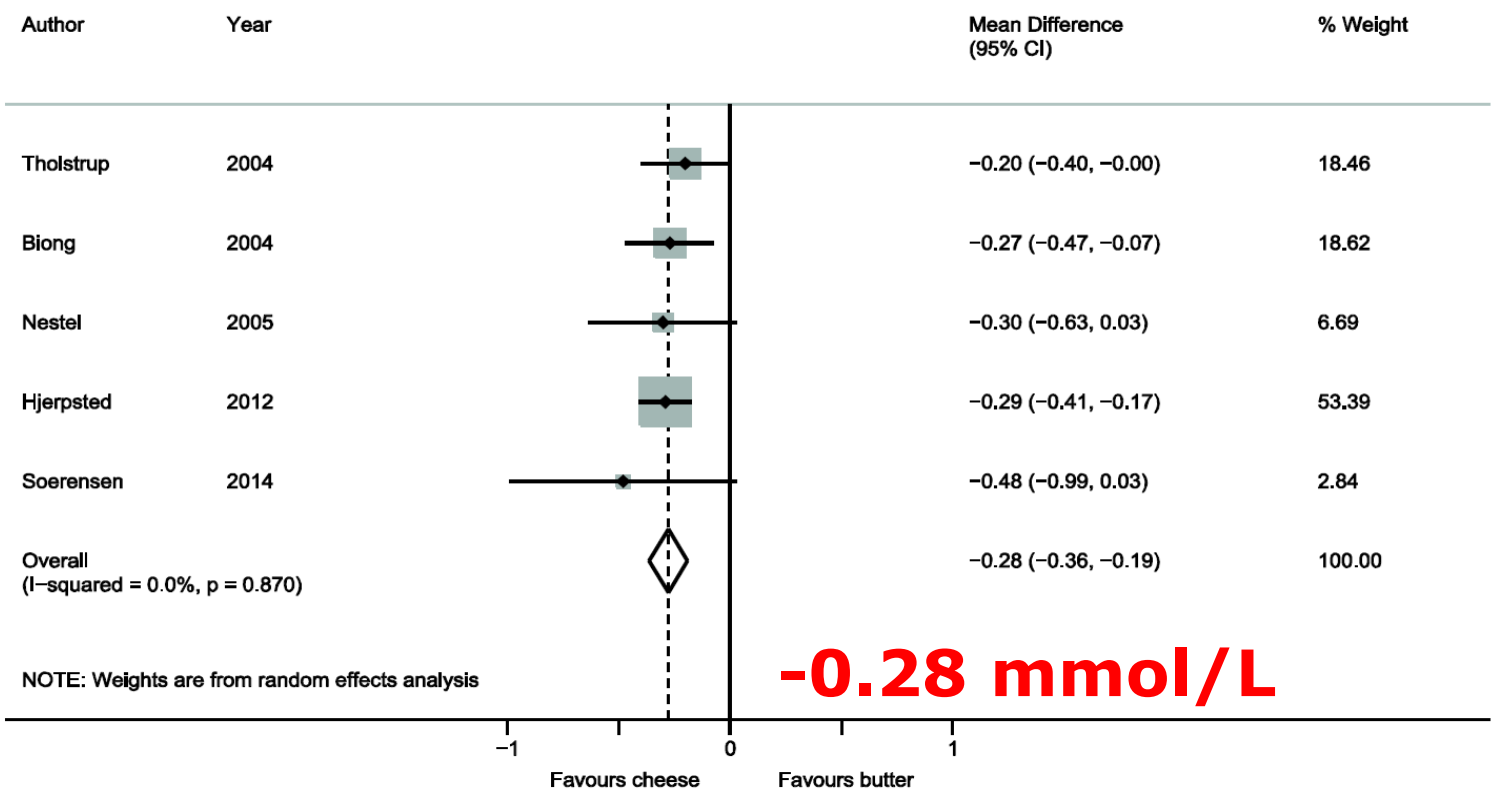
Experimental study / Trial



Example of drug trial



Meta-analysis of trials with effects of cheese vs. butter on total cholesterol *(Nutr Rev 2015: dr. J. de Goede)*



-0.28 mmol/L

Cheese intake (mean:145 g/d)

-lowering of HDL-cholesterol -0.05 mmol/l (95% CI: -0.09 ; -0.02)

-no effect on triglycerides (0.01 mmol/l; 95% CI: -0.06 ; 0.05).

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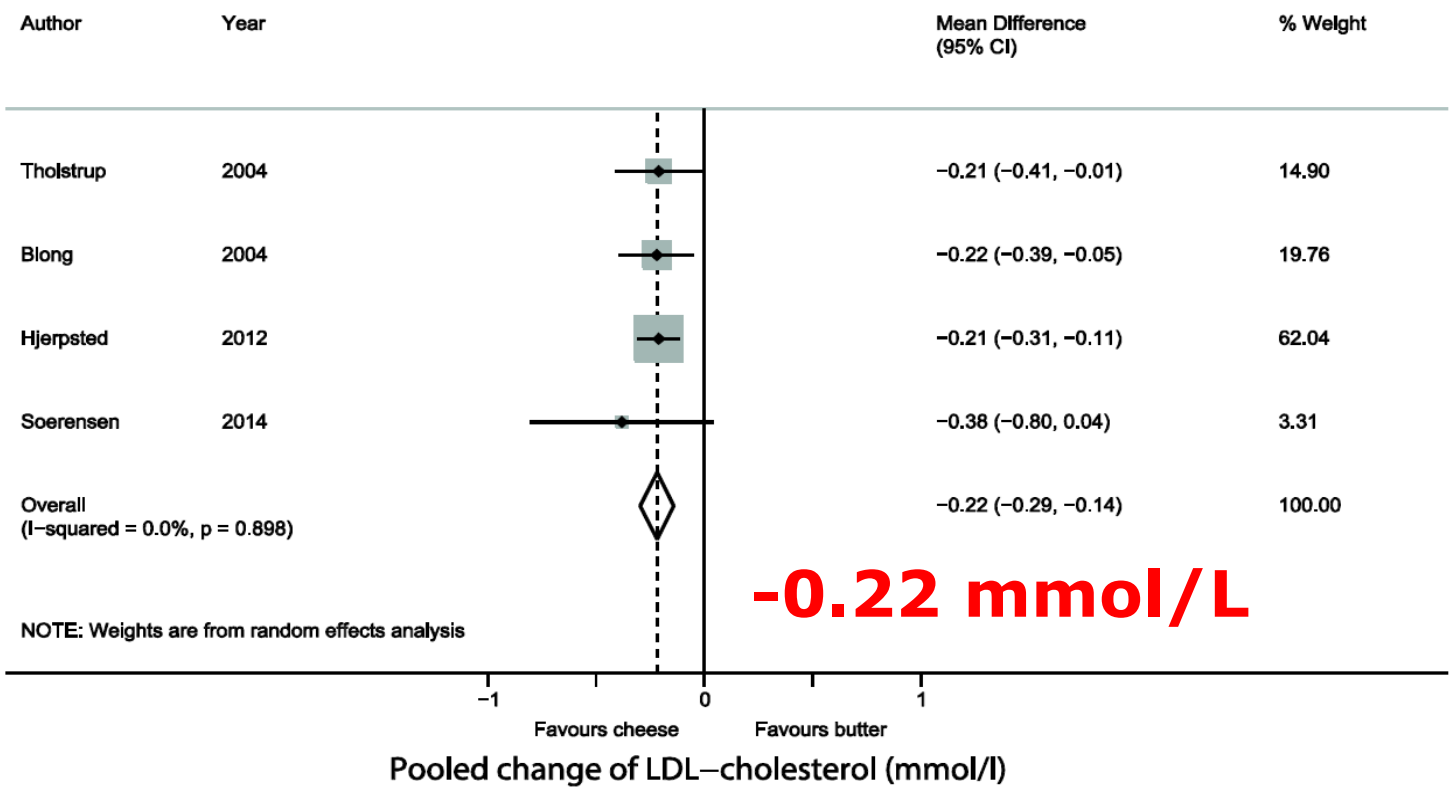
Effects of cheese vs. butter on LDL-cholesterol



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Cheese intake (mean:145 g/d)

Comparisons

Cheese - butter comparisons

Author	Intervention	Cross over design	Study participants
Tholstrup	205 g/d Samso (hard) cheese vs. 64 g/d butter 3 wk	Completely controlled diet	14 healthy males Denmark
Biong	150 g/d Jarlsberg (hard) cheese vs. 52 g/d butter 3 wk	Completely controlled diet	22 healthy males/females Norway
Nestel	120 g/d Cheddar (hard) cheese vs. 40 g/d butter 4 wk	Diet based on selection of predefined set of foods	19 males/females with moderately elevated LDL-c Australia
Hjerpsted	143 g/d Samso (hard) cheese vs. 47 g/d butter 6 wk	Diet based on self-selection	49 healthy males/females Denmark
Soerensen	120 g/d Klovborg (semi-hard) cheese vs. butter 2 wk	Completely controlled diet	15 healthy males Denmark

Same P/S ratio for butter vs. cheese comparison

Comprehensive Review of the Impact of Dairy Foods and Dairy Fat on Cardiometabolic Risk[1–3]

Jean-Philippe Drouin-Chartier,[4] Julie Anne Côté,[6] Marie-Ève Labonté,[7] Didier Brassard,[4] Maude Tessier-Grenier,[4] Sophie Desroches,[4] Patrick Couture,[4,5] and Benoît Lamarche[4]*

comprehensive assessment of evidence from RCTs suggests that there is no apparent risk of potential harmful effects of dairy consumption, irrespective of the content of dairy fat, on a large array of cardiometabolic variables, including lipid-related risk factors, blood pressure, inflammation, insulin resistance, and vascular function. This suggests that the purported detrimental effects of SFAs on cardiometabolic health may in fact be nullified when they are consumed as part of complex food matrices such as those in cheese and other dairy foods. Thus, the focus on low-fat dairy products in current guidelines apparently is not entirely supported by the existing literature and may need to be revisited on the basis of this evidence. Future studies addressing key research gaps in this area will be extremely informative to better appreciate the impact of dairy food matrices, as well as dairy fat specifically, on cardiometabolic health. *Adv Nutr* 2016;7:1041–51.

Review by Drouin-Chartier 2016

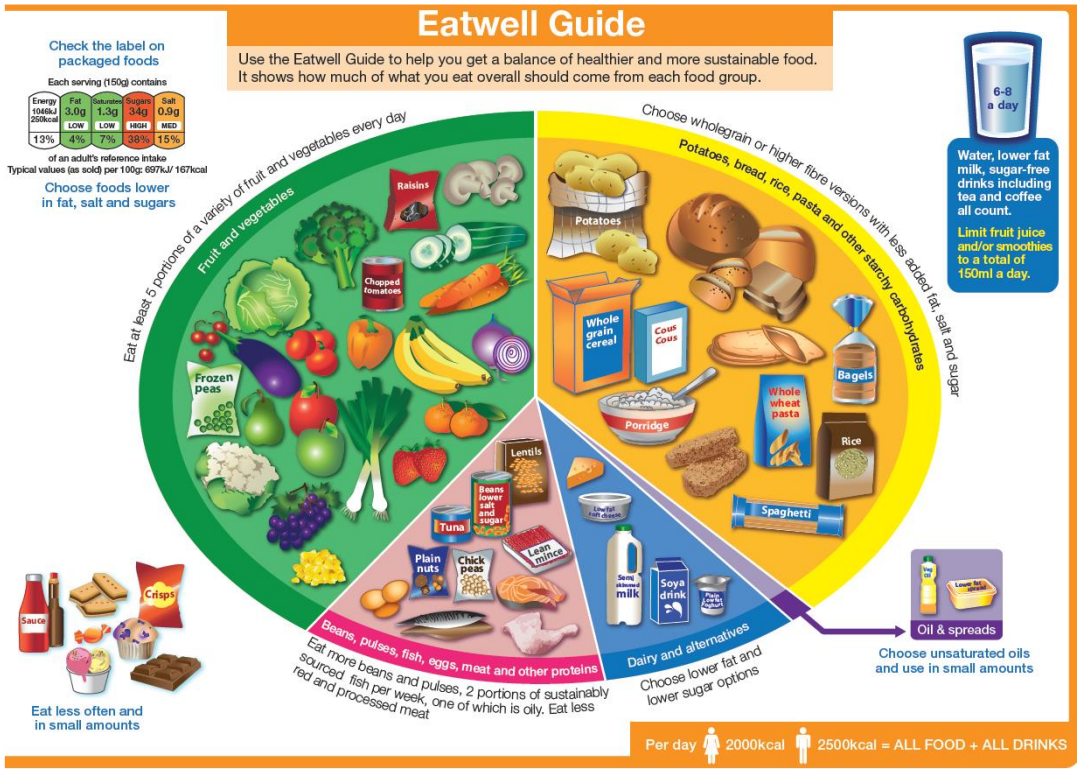
	Cheese	Yogurt
LDL cholesterol	No effect[§]	No effect[§]
HDL cholesterol	Uncertain[‡]	No effect[§]
Fasting TGs	No effect[§]	No effect[§]
Postprandial TGs	No effect[§]	Undetermined[#]
LDL size	Undetermined[#]	Undetermined[#]
apoB	No effect[§]	Undetermined[#]
Non-HDL cholesterol	Undetermined[#]	Undetermined[#]
Cholesterol ratios	No effect[§]	Reduced[§]
Inflammation	Undetermined[#]	Undetermined[#]
Insulin resistance	No effect[§]	Undetermined[#]
Blood pressure	Undetermined[#]	Undetermined[#]
Vascular function	Undetermined[#]	Undetermined[#]

[#] No randomized controlled trials on this topic.

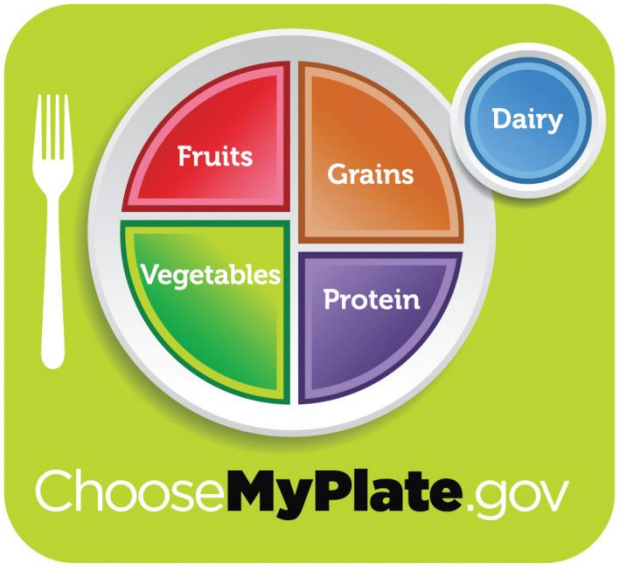
[§] Reported in <3 randomized controlled trials; data need to be interpreted with caution

Thank you for your attention

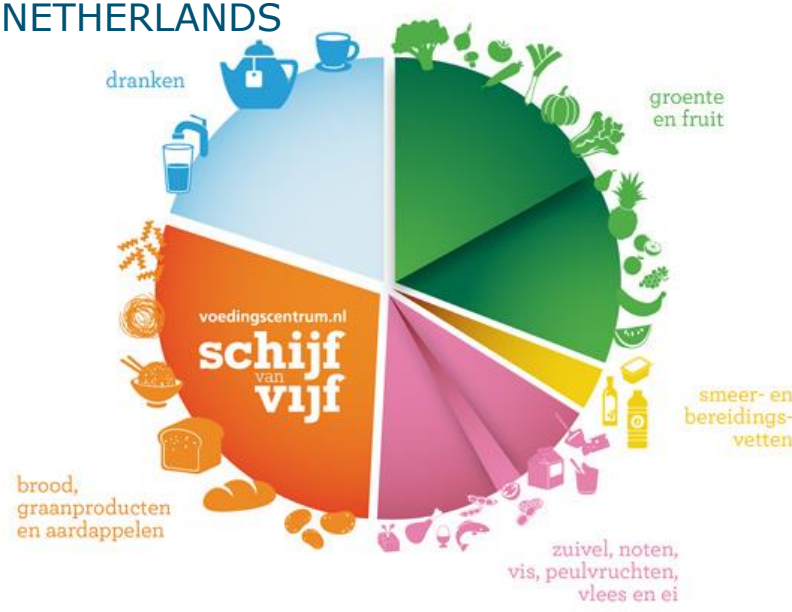
UK



US



NETHERLANDS



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