Evaluating concordance of bodies of evidence from randomized controlled trials, dietary intake and biomarkers of intake in cohort studies: a meta-epidemiological study

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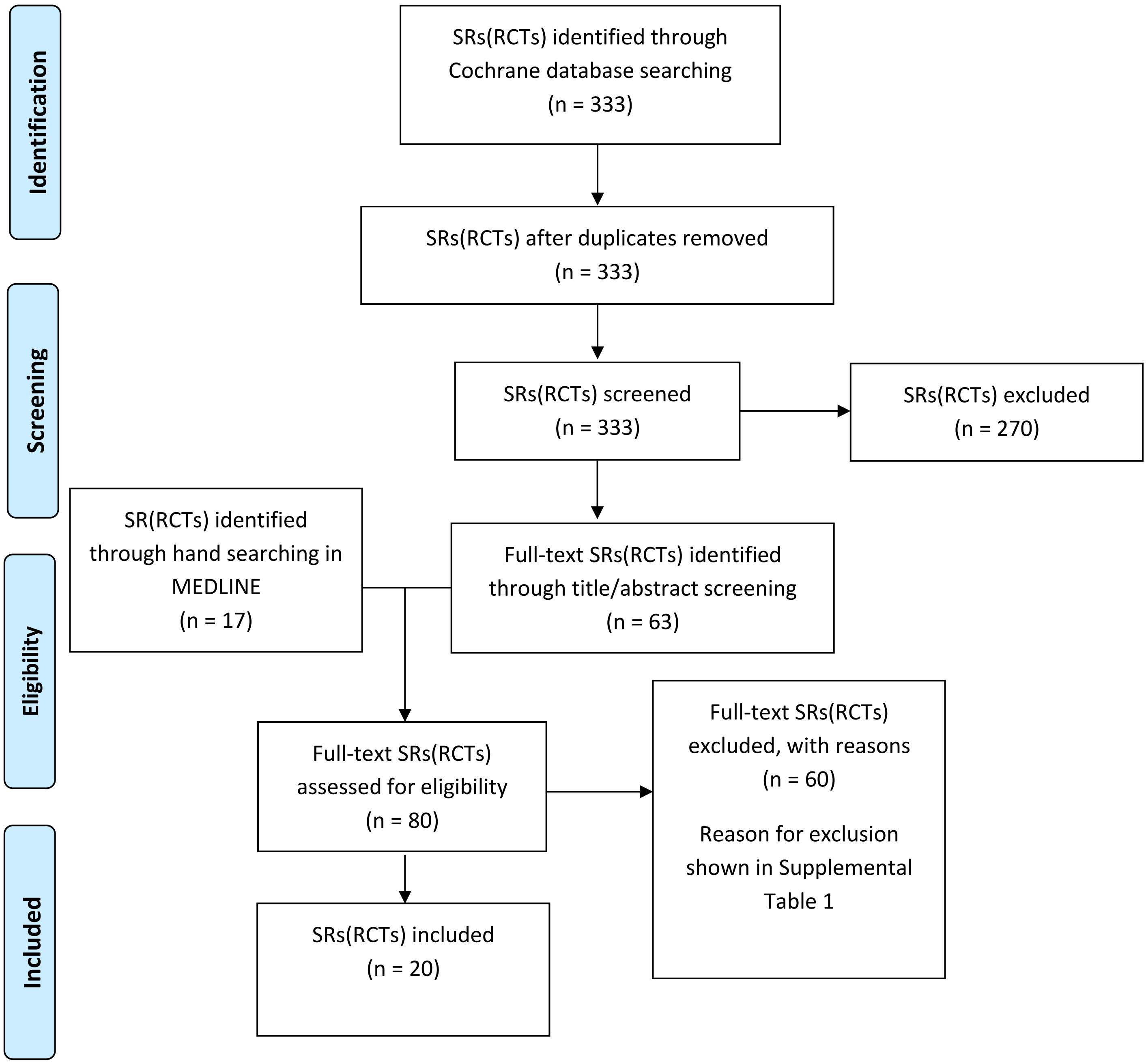
Supplemental Appendix 1: Search strategy for systematic reviews of randomized controlled trials in the Cochrane Database of Systematic Reviews

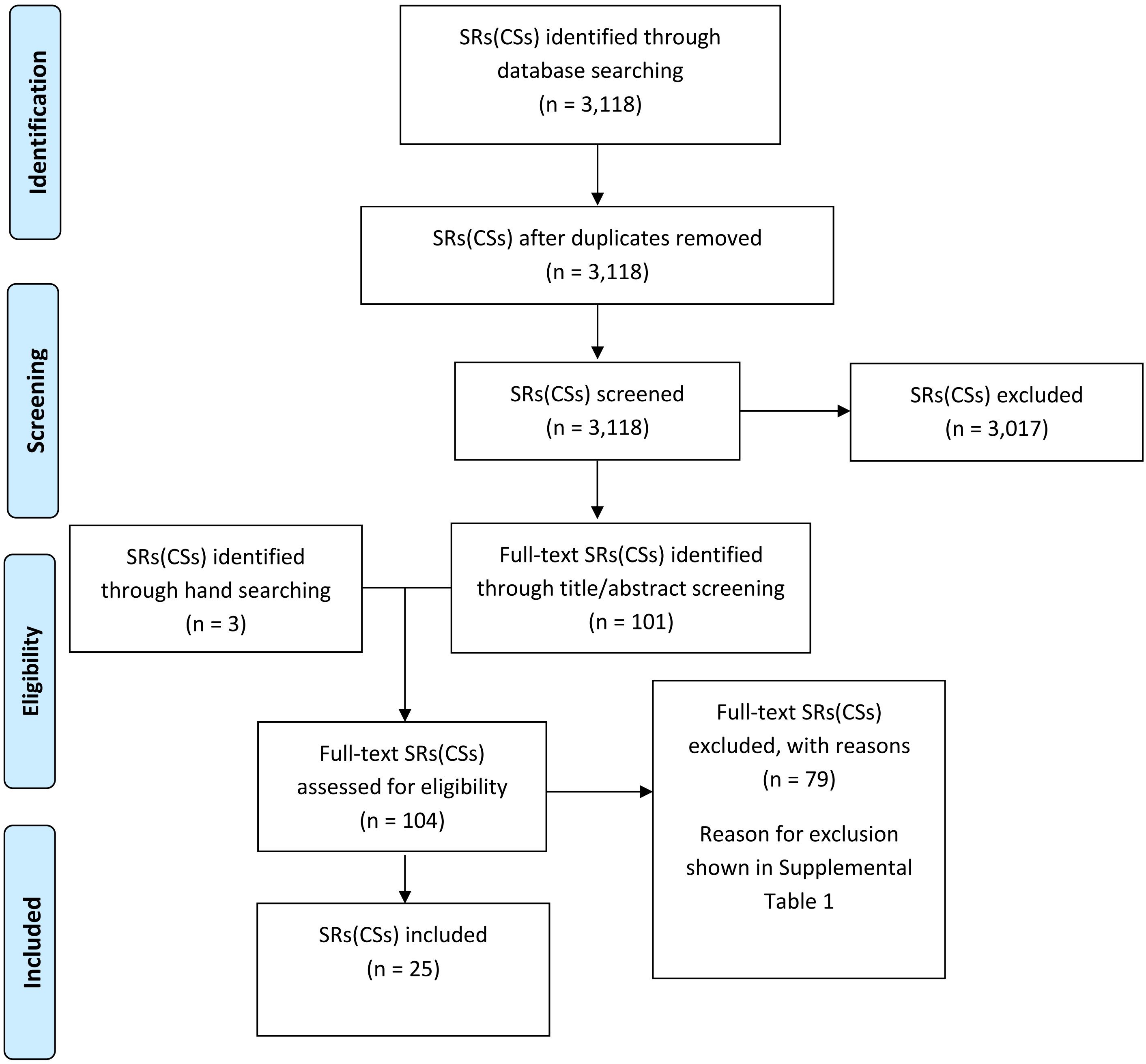
ID	Search	Hits
#1	MeSH descriptor: [Diet, Carbohydrate-Restricted] explode all trees	385
#2	MeSH descriptor: [Healthy Diet] explode all trees	336
#3	MeSH descriptor: [Diet, Mediterranean] this term only	434
#4	MeSH descriptor: [Dietary Approaches To Stop Hypertension] explode all trees	15
#5	MeSH descriptor: [Micronutrients] explode all trees	4,992
#6	MeSH descriptor: [Dietary Supplements] explode all trees	11,620
#7	(mediterranean or dash diet or low-carb* or low-fat* or grain* or vegetable* or fruit* or milk or dairy or meat or processed meat* or fish or eggs or nuts or chocolate or oil*):ti,ab,kw	40,401
#8	(carbohydrate* or fructose or glucose or starch or sucrose or fibre or psyllium or inulin or cellulose or prebiotic* or probiotic* or synbiotic* or n-3 or omega 3 or omega-3 or n3 or n6 or n-6 or omega 6 or omega-6 or unsaturated or monounsaturated or polyunsaturated or EPA or DHA or linoleic acid or protein or amino acid*):ti,ab,kw	167,040
#9	(vitamin* or beta-carot* or ascorbic acid or cholecalciferol* or ergocalciferol or thiamine or riboflavin or niacin or pyridoxine or cobalamin or folic acid or magnesium or calcium or selenium or sodium or potassium or iron or zinc or copper or iodine):ti,ab,kw	118,402
#10	#1 or #2 or #3 or #4 or #5 or #6 or #7 or #8 or #9	283,530
#11	(diet* or nutrition or eat* or consum* or intake):ti,ab,kw	163,651
#12	#10 and #11	83,677
#13	(mortal* or cancer or diabetes or dementia or macular degeneration or body weight or blood pressure or glucose or cholester*):ti,ab,kw	448,002
#14	#12 and #13	48,529
#15	Cochrane Reviews "2010 - 2019"	**333**

Supplemental Appendix 2: Search strategy for systematic reviews of cohort studies in Ovid MEDLINE

ID	Search	Hits
#1	(non-randomised or non-randomized or nrs or observational* or cohort or prospective or longitudinal* or follow* or case-cohort or nested case-control or epidemio*).ti,ab,kf.	4,466,200
#2	(meta-analys* or metaanalys* or "systematic review" or systematic-review).ti,ab.	238,477
#3	(Systematic Review or Meta-Analysis).pt.	177,170
#4	#1 and (#2 or #3)	104,427
#5	Diet, Mediterranean/ or Diet, Carbohydrate-Restricted/ or Healthy Diet/ or Dietary Abbroach to Stop Hypertension/ or Micronutrients/ or Dietary Supplements/	65,391
#6	(mediterranean or dash diet or low-carb* or low-fat* or grain* or vegetable* or fruit* or milk or dairy or meat or processed meat* or fish or eggs or nuts or chocolate or oil*).ti,ab.	733,079
#7	(carbohydrate* or fructose or glucose or starch or sucrose or fibre or psyllium or inulin or cellulose or prebiotic* or probiotic* or synbiotic* or n-3 or omega 3 or omega-3 or n3 or n6 or n-6 or omega 6 or omega-6 or unsaturated or monounsaturated or polyunsaturated or EPA or DHA or linoleic acid or protein or amino acid*).ti,ab.	3,445,283
#8	(vitamin* or beta-carot* or ascorbic acid or cholecalciferol* or ergocalciferol or thiamine or riboflavin or niacin or pyridoxine or cobalamin or folic acid or magnesium or calcium or selenium or sodium or potassium or iron or zinc or copper or iodine).ti,ab.	1,391,454
#9	(diet* or nutrition or eat* or consum* or intake).ti,ab.	1,173,600
#10	(#5 or #6 or #7 or #8) and #9	502,160
#11	#4 and #10	3,809
#12	limit #11 to yr="2010 - 2019"	**3,118**



Supplemental Figure 1: Flow diagram showing study selection process for systematic reviews (SRs) of randomized controlled trials (RCTs).



Supplemental Figure 2: Flow diagram showing study selection process for systematic reviews (SRs) of cohort studies (CSs).

Supplemental Table 1: Reason for exclusion

Reference	**Reason for exclusion**
Systematic reviews of randomized controlled trials	
(1-16)	Did not fulfil PICO inclusion criteria (see PICO criteria Table 1).
(17-54)	No corresponding systematic review of cohort studies on dietary intake and biomarker was available.
(55-60)	More recent or appropriate systematic review of randomized controlled trials available (e.g. higher number of included studies, better matching PICO).
Systematic reviews of cohort studies	
(61-64)	Did not fulfil PECO inclusion criteria (see PECO criteria Table 1).
(65-91)	Corresponding systematic review only on dietary intake.
(92-104)	Corresponding systematic review only on biomarker or status.
(105-113)	More recent or appropriate systematic review of cohort studies available (e.g. higher number of included studies, better matching PECO).
(114-139)	No body of randomized controlled trials available.

PI/ECO: population, intervention/exposure, comparator, outcome.

Supplemental Table 2: Characteristics of included systematic reviews of randomized controlled trials

Reference	Intervention (as defined by the authors)	Outcome (as defined by the authors)	Population: Mixed[1] or General[2]	Studies, n	Participants	Cases	Estimate	Effect	95% CI	
Abdelhamid et al. 2018 (140)	Long-chain Omega-3 supplements + intake	Cardiovascular disease	Mixed	38	90,378	14,737	RR	0.99	0.94	1.04
Abdelhamid et al. 2018 (140)	Long-chain Omega-3 supplements + intake	Cardiovascular mortality	Mixed	25	67,772	4,544	RR	0.95	0.87	1.03
Abdelhamid et al. 2018 (140)	α-Linolenic acid supplements + intake	Cardiovascular disease	Mixed	5	19,327	884	RR	0.95	0.83	1.07
Adler et al. 2014 (141)	Low sodium intake	All-cause mortality	Mixed	7	6,603	625	RR	0.96	0.83	1.10
Adler et al. 2014 (141)	Low sodium intake	Cardiovascular disease	Mixed	4	3,397	194	RR	0.76	0.57	1.01
Adler et al. 2014 (141)	Low sodium intake	Cardiovascular mortality	Mixed	3	2,656	106	RR	0.67	0.45	1.01
Bjelakovic et al. 2012 (142)	Vitamin C supplements	All-cause mortality	Mixed	41	90,191	8,020	RR	1.01	0.97	1.05
Bjelakovic et al. 2012 (142)	Vitamin E supplements	All-cause mortality	Mixed	64	211,957	22,058	RR	1.02	0.99	1.04
Bjelakovic et al. 2012 (142)	β-carotene supplements	All-cause mortality	Mixed	31	195,503	23,182	RR	1.02	0.98	1.07
Bjelakovic et al. 2014 (143)	Vitamin D3 supplements	Breast cancer	Mixed	7	43,669	1,135	RR	0.97	0.86	1.09
Bjelakovic et al. 2014 (143)	Vitamin D3 supplements	Colorectal cancer	Mixed	5	45,598	436	RR	1.11	0.92	1.34
Bjelakovic et al. 2014 (143)	Vitamin D3 supplements	Lung cancer	Mixed	5	45,509	329	RR	0.86	0.69	1.07
Brown et al. 2019 (144)	Long-chain Omega-3 supplements + intake	Type 2 diabetes	Mixed	17	58,643	2,196	RR	1.00	0.85	1.17
Brown et al. 2019 (144)	α-Linolenic acid supplements + intake	Type 2 diabetes	Mixed	2	18,243	230	RR	0.68	0.33	1.39
Chowdhury et al. 2012 (145)	Long-chain Omega-3 supplements	Stroke	Mixed	12	62,040	1,563	RR	1.03	0.94	1.12
Druesne-Pecollo et al. 2010 (146)	β-carotene supplements	Breast cancer	Mixed	4	79,378	913	RR	0.96	0.85	1.10
Druesne-Pecollo et al. 2010 (146)	β-carotene supplements	Cancer	Mixed	8	180,702	10,600	RR	1.01	0.98	1.04
Hanson et al. 2020 (147)	Long-chain Omega-3 supplements + intake	Breast cancer	Mixed	12	44,295	661	RR	1.03	0.89	1.20

Hanson et al. 2020 (147)	Long-chain Omega-3 supplements + intake	Prostate cancer	Mixed	7	38,525	1,021	RR	1.10	0.97	1.24
Hanson et al. 2020 (147)	Omega-6 supplements + intake	Breast cancer	General	1	200	4	RR	1.00	0.14	6.96
Hanson et al. 2020 (147)	Polyunsaturated fatty acid supplements + intake	Breast cancer	Mixed	2	5,198	79	RR	1.11	0.71	1.73
Hanson et al. 2020 (147)	α-Linolenic acid supplements + intake	Prostate cancer	Mixed	2	4,010	46	RR	1.30	0.72	2.32
Hooper et al. 2018 (148)	Omega-6 supplements + intake	All-cause mortality	Mixed	10	4,506	979	RR	1.00	0.88	1.12
Hooper et al. 2018 (148)	Omega-6 supplements + intake	Combined cardiovascular events	Mixed	7	4,962	1,404	RR	0.97	0.81	1.15
Hooper et al. 2018 (148)	Omega-6 supplements + intake	Cardiovascular mortality	Mixed	7	4,019	472	RR	1.09	0.76	1.55
Jenkins et al. 2018 (149)	Vitamin C supplements	Cardiovascular disease	Mixed	2	15,497	1,459	RR	0.99	0.90	1.10
Jenkins et al. 2018 (149)	Vitamin C supplements	Cardiovascular mortality	Mixed	2	15,497	646	RR	1.07	0.92	1.25
Jenkins et al. 2018 (149)	Vitamin C supplements	Stroke	Mixed	2	15,497	525	RR	0.92	0.78	1.09
Jenkins et al. 2018 (149)	Vitamin E supplements	Cardiovascular disease	Mixed	10	100,475	7,936	RR	0.96	0.89	1.03
Jenkins et al. 2018 (149)	Vitamin E supplements	Cardiovascular mortality	Mixed	11	102,533	2,887	RR	0.95	0.89	1.02
Jenkins et al. 2018 (149)	Vitamin E supplements	Stroke	Mixed	11	100,575	1,956	RR	0.98	0.88	1.08
Jenkins et al. 2018 (149)	Iron supplements	Cardiovascular mortality	Mixed	2	760	31	RR	0.80	0.40	1.58
Jenkins et al. 2018 (149)	Iron supplements	Myocardial infarction	Mixed	1	459	5	RR	0.34	0.06	2.01
Jenkins et al. 2018 (149)	β-carotene supplements	Cardiovascular disease	Mixed	3	70,118	2,912	RR	1.03	0.96	1.10
Jenkins et al. 2018 (149)	β-carotene supplements	Coronary heart disease	Mixed	2	21,841	2,081	RR	1.02	0.94	1.10
Jenkins et al. 2018 (149)	β-carotene supplements	Stroke	Mixed	3	58,761	2,104	RR	1.06	0.95	1.19
Khan et al. 2019 (150)	Long-chain Omega-3 supplements	All-cause mortality	Mixed	41	134,034	10,707	RR	0.98	0.93	1.02
Moazzen et al. 2018 (151)	Folate supplements	Colorectal cancer	NA	NA	NA	NA	RR	1.07	0.86	1.43
Park et al. 2017 (152)	Vitamin A supplements	Bladder cancer	Mixed	5	19,285	442	RR	0.86	0.65	1.13
Rees et al. 2013 (153)	Selenium supplements	All-cause mortality	Mixed	2	18,452	1,336	RR	0.97	0.88	1.08
Rutjes et al. 2018 (154)	B-Vitamins supplements	Dementia / MCI	Mixed	1	1,803	99	RR	1.01	0.69	1.48

Schwingshackl et al. 2017 (155)	Vitamin C supplements	Cancer	NA	3	NA	NA	RR	0.99	0.91	1.06
Schwingshackl et al. 2017 (155)	Vitamin E supplements	Cancer	NA	7	NA	NA	RR	1.02	0.99	1.06
van Die et al. 2014 (156)	Soy / Isoflavonoes supplements + intake	Prostate cancer	Mixed	2	122	32	RR	0.49	0.26	0.95
Vinceti et al. 2018 (157)	Selenium supplements	Cancer mortality	Mixed	2	18,698	359	RR	0.81	0.49	1.32
Vinceti et al. 2018 (157)	Selenium supplements	Lung cancer	Mixed	3	20,259	299	RR	1.03	0.78	1.37
Vinceti et al. 2018 (157)	Selenium supplements	Prostate cancer	Mixed	5	19,869	1,084	RR	0.91	0.75	1.12
Vollset et al. 2013 (158)	Folate supplements	Prostate cancer	Mixed	12	44,177	656	RR	1.15	0.99	1.34
Zhao et al. 2017 (159)	Iron supplements	Gestational diabetes	General	2	3,858	439	RR	0.88	0.72	1.07

[1] Mixed population: Population including people with various pre-existing conditions such as cancer, cardiovascular diseases / chronic heart diseases, cognitive symptoms, diseases of the digestive system / eye / genitourinary system / liver / nervous system, endocrine / nutritional / metabolic diseases, musculoskeletal diseases.

[2] General population: General healthy.

MCI: mild cognitive impairment; n: number; NA: not applicable/assessed; RR: risk ratio; 95% CI: 95% confidence interval.

Supplemental Table 3: Characteristics of included systematic reviews of cohort studies examining dietary intake

Reference	Exposure (as defined by the authors)	Comparison	Outcome (as defined by the authors)	Population: Mixed[1] or General[2]	Studies, n	Participants	Cases	Estimate	Effect	95% CI	
Aburto et al. 2013 (160)	Low sodium intake	Low vs. High	All-cause mortality	General	2	22,550	NA	RR	0.95	0.71	1.27
Aburto et al. 2013 (160)	Low sodium intake	Low vs. High	Cardiovascular disease	General	3	81,280	NA	RR	0.87	0.64	1.18
Aburto et al. 2013 (160)	Low sodium intake	Low vs. High	Cardiovascular mortality	General	3	81,280	NA	RR	0.87	0.64	1.18
Alexander et al. 2015 (161)	Long-chain Omega-3 intake + supplements	High vs. Low	Prostate cancer	General	12	255,643	NA	RR	1.00	0.93	1.09
Applegate et al. 2018 (162)	Soy intake	High vs. Low	Prostate cancer	General	7	NA	NA	RR	0.90	0.82	0.99
Aune et al. 2012 (163)	β-carotene intake	High vs. Low	Breast cancer	General	10	825,911	18,191	RR	0.93	0.88	0.98
Aune et al. 2018 (164)	Vitamin C intake	High vs. Low	All-cause mortality	General	16	315,214	38,079	RR	0.86	0.80	0.92
Aune et al. 2018 (164)	Vitamin C intake	High vs. Low	Cancer	General	7	181,318	7,068	RR	0.87	0.78	0.95
Aune et al. 2018 (164)	Vitamin C intake	High vs. Low	Cardiovascular disease	General	9	246,711	7,986	RR	0.84	0.77	0.91
Aune et al. 2018 (164)	Vitamin C intake	Per 100 mg/d	Cardiovascular mortality	General	9	NA	NA	RR	0.88	0.83	0.94
Aune et al. 2018 (164)	Vitamin C intake	High vs. Low	Stroke	General	13	298,066	7,294	RR	0.84	0.77	0.91
Aune et al. 2018 (164)	Vitamin E intake	High vs. Low	All-cause mortality	General	9	229,83	15,321	RR	0.98	0.93	1.04
Aune et al. 2018 (164)	Vitamin E intake	High vs. Low	Cancer	General	5	168,182	5,578	RR	1.01	0.92	1.10
Aune et al. 2018 (164)	Vitamin E intake	High vs. Low	Cardiovascular disease	General	8	NA	NA	RR	0.90	0.78	1.03
Aune et al. 2018 (164)	Vitamin E intake	Per 5 μg/d	Cardiovascular mortality	General	7	233,310	7,852	RR	1.00	0.98	1.02
Aune et al. 2018 (164)	Vitamin E intake	High vs. Low	Stroke	General	10	311,965	7,003	RR	0.89	0.78	1.02
Aune et al. 2018 (164)	β-carotene intake	High vs. Low	All-cause mortality	General	8	142,798	11,729	RR	0.82	0.78	0.87
Aune et al. 2018 (164)	β-carotene intake	High vs. Low	Cancer	General	4	46,280	2,627	RR	0.90	0.81	1.00

Aune et al. 2018 (164)	β-carotene intake	High vs. Low	Cardiovascular disease	General	4	39,643	1,767	RR	0.98	0.84	1.15
Aune et al. 2018 (164)	β-carotene intake	High vs. Low	Coronary heart disease	General	4	99,345	2,104	RR	0.73	0.63	0.85
Aune et al. 2018 (164)	β-carotene intake	High vs. Low	Stroke	General	7	201,587	5,468	RR	0.84	0.75	0.94
Cao et al. 2016 (165)	Omega-6 intake	High vs. Low	Breast cancer	General	5	206,521	8,308	RR	1.10	0.88	1.38
Cao et al. 2016 (165)	Polyunsaturated fatty acid intake	High vs. Low	Breast cancer	General	16	1,012,099	33,209	RR	1.05	0.96	1.14
Chen et al. 2016 (166)	Omega-3 intake + supplements	High vs. Low	All-cause mortality	General	6	361,273	27,624	RR	0.91	0.84	0.98
Chowdhury et al. 2012 (145)	Long-chain Omega-3 intake	High vs. Low	Cerebrovascular disease	General	10	301,023	4,197	RR	0.90	0.80	1.01
Chowdhury et al. 2014 (167)	Long-chain Omega-3 intake	T3 vs. T1	Coronary heart disease	Mixed	16	422,786	9,089	RR	0.87	0.78	0.97
Chowdhury et al. 2014 (167)	Long-chain Omega-3 intake	T3 vs. T1	Coronary heart disease mortality	Mixed	NA	104,681	1,483	RR	0.90	0.70	1.14
Chowdhury et al. 2014 (167)	Omega-6 intake	High vs. Low	Coronary heart disease	Mixed	8	206,376	8,155	RR	0.98	0.90	1.06
Doets et al. 2013 (168)	Vitamin B12 intake	Per 1 μg/d	Dementia	General	3	5,254	431	RR	0.99	0.99	1.00
Fu et al. 2015 (169)	α-Linolenic acid intake	Per 0.5 g/d increase	Prostate cancer	General	5	430,090	7,781	RR	0.99	0.98	1.00
Hossain et al. 2019 (170)	Vitamin D supplements	Yes vs. No	Breast cancer	General	2	37,707	1,611 (1 study unclear)	RR	0.94	0.87	1.02
Hunnicutt et al. 2014 (171)	Iron intake	High vs. Low	Coronary heart disease mortality	General	2	103,548	694	RR	0.91	0.69	1.19
Hunnicutt et al. 2014 (171)	Iron intake	High vs. Low	Myocardial infarction	General	3	65,871	625	RR	0.86	0.66	1.13
Jayedi et al. 2018 (172)	Selenium intake	High vs. Low	All-cause mortality	General	3	141,404	10,285	RR	0.79	0.73	0.85
Li et al. 2020 (173)	Linoleic acid intake	High vs. Low	All-cause mortality	Mixed	11	708,379	170,076	RR	0.87	0.81	0.94
Li et al. 2020 (173)	Linoleic acid intake	High vs. Low	Cardiovascular mortality	Mixed	14	793,131	50,786	RR	0.87	0.82	0.92
Moazzen et al. 2018 (151)	Folate	High vs. Low	Colorectal cancer	NA	NA	NA	NA	RR	0.96	0.76	1.21
Pan et al. 2012 (174)	α-Linolenic acid intake	High vs. Low	Cardiovascular disease	General	11	328,888	9,161	RR	0.93	0.85	1.03

Touvier et al. 2011 (175)	Vitamin D intake	Per 100 IU/d	Colorectal cancer	General	10	NA	NA	RR	0.95	0.93	0.98
Vinceti et al. 2018 (157)	Selenium intake	High vs. Low	Cancer mortality	General	1	133,957	2,603	OR	0.93	0.83	1.04
Vinceti et al. 2018 (157)	Selenium intake	High vs. Low	Lung cancer	General	2	6,313	274	OR	1.32	0.95	1.84
Vinceti et al. 2018 (157)	Selenium intake + supplements	High vs. Low	Prostate cancer	Mixed	4	162,566	8,896	OR	0.99	0.85	1.15
Wang et al. 2014 (176)	Folate intake	High vs. Low	Prostate cancer	General	5	192,702	NA	RR	1.02	0.95	1.09
Wu et al. 2012 (177)	Docosahexaenoic acid + Eicosapentaenoic acid intake	High vs. Low	Type 2 diabetes	General	12	523,938	23,739	RR	1.04	0.94	1.16
Wu et al. 2012 (177)	α-Linolenic acid intake	High vs. Low	Type 2 diabetes	General	7	131,940	7,365	RR	0.92	0.80	1.05
Wu et al. 2020 (178)	Carotenoids intake	High vs. Low	Bladder cancer	General	4	353,321	NA	RR	1.09	0.93	1.27
Zhang et al. 2015 (179)	Vitamin D intake	High vs. Low	Lung cancer	Mixed	3	135,244	3,004	RR	0.89	0.74	1.06
Zhao et al. 2017 (159)	Iron supplements	Yes vs. No	Gestational diabetes	General	2	14,475	1,367	RR	1.75	0.56	5.47
Zheng et al. 2013 (180)	Marine Omega-3 intake	High vs. Low	Breast cancer	General	10	443,616	11,519	RR	0.85	0.76	0.96

[1] Mixed population: Population including people with various pre-existing conditions such as cancer, cardiovascular diseases / chronic heart diseases, cognitive symptoms, diseases of the digestive system / eye / genitourinary system / liver / nervous system, endocrine / nutritional / metabolic diseases, musculoskeletal diseases.

[2] General population: General healthy.

d: day; g: gram; IU: international unit; mg: milligram; µg: microgram; n: number; NA: not applicable/assessed; OR: odds ratio; RR: risk ratio; T: tertile; vs: versus; 95% CI: 95% confidence interval

Supplemental Table 4: Characteristics of included systematic reviews of cohort studies examining biomarkers

Reference	Exposure (as defined by the authors)	Comparison	Outcome (as defined by the authors)	Population: Mixed[1] or General[2]	Studies, n	Participants	Cases	Estimate	Effect	95% CI	
Aburto et al. 2013 (160)	Low urinary sodium excretion	Low vs. High	All-cause mortality	Mixed	5	34,494	NA	RR	0.94	0.82	1.09
Aburto et al. 2013 (160)	Low urinary sodium excretion	Low vs. High	Cardiovascular disease	Mixed	6	37,431	NA	RR	0.91	0.71	1.15
Aburto et al. 2013 (160)	Low urinary sodium excretion	Low vs. High	Cardiovascular mortality	Mixed	4	32,079	NA	RR	0.98	0.73	1.32
Alexander et al. 2015 (161)	Omega-3 biomarkers	High vs. Low	Prostate cancer	General	9	14,807	5,750	RR	1.07	0.94	1.20
Applegate et al. 2018 (162)	Genistein (serum + plasma)	High vs. Low	Prostate cancer	General	6	NA	NA	RR	0.97	0.83	1.13
Aune et al. 2012 (163)	β-carotene biomarkers	High vs. Low	Breast cancer	General	13	14,212 (NA in 1 study)	3,987 (NA in 1 study)	RR	0.82	0.64	1.04
Aune et al. 2018 (164)	Vitamin C biomarkers	High vs. Low	All-cause mortality	General	8	47,238	7,528	RR	0.68	0.60	0.77
Aune et al. 2018 (164)	Vitamin C biomarkers	High vs. Low	Cancer	General	5	47,678	1,831	RR	0.68	0.57	0.80
Aune et al. 2018 (164)	Vitamin C biomarkers	High vs. Low	Cardiovascular disease	General	5	45,273	2,792	RR	0.61	0.45	0.83
Aune et al. 2018 (164)	Vitamin C biomarkers	Per 50 µmol/L	Cardiovascular mortality	General	5	NA	NA	RR	0.75	0.64	0.88
Aune et al. 2018 (164)	Vitamin C biomarkers	High vs. Low	Stroke	General	5	27,843	957	RR	0.60	0.49	0.73
Aune et al. 2018 (164)	Vitamin E biomarkers	High vs. Low	All-cause mortality	General	6	47,853	18,316	RR	0.89	0.72	1.08
Aune et al. 2018 (164)	Vitamin E biomarkers	High vs. Low	Cancer	General	10	56,258	7,201	RR	0.80	0.74	0.87
Aune et al. 2018 (164)	Vitamin E biomarkers	High vs. Low	Cardiovascular disease	General	6	47,012	8,053	RR	0.79	0.56	1.10
Aune et al. 2018 (164)	Vitamin E biomarkers	Per 500 µg/dl	Cardiovascular mortality	General	6	NA	NA	RR	0.98	0.89	1.06
Aune et al. 2018 (164)	Vitamin E biomarkers	High vs. Low	Stroke	General	5	69,569	1,966	RR	0.71	0.58	0.85
Aune et al. 2018 (164)	β-carotene biomarkers	High vs. Low	All-cause mortality	General	7	23,141	5,659	RR	0.68	0.55	0.83

Aune et al. 2018 (164)	β-carotene biomarkers	High vs. Low	Cancer	General	6	36,812	2,654	RR	0.76	0.65	0.89
Aune et al. 2018 (164)	β-carotene biomarkers	High vs. Low	Cardiovascular disease	General	7	34,090	3,232	RR	0.71	0.57	0.88
Aune et al. 2018 (164)	β-carotene biomarkers	High vs. Low	Coronary heart disease	General	4	3,179	1,128	RR	0.73	0.57	0.94
Aune et al. 2018 (164)	β-carotene biomarkers	High vs. Low	Stroke	General	3	30,144	1,548	RR	0.85	0.71	1.01
Cao et al. 2016 (165)	Serum Omega-6	High vs. Low	Breast cancer	General	7	3,511	1,334	RR	0.84	0.60	1.18
Cao et al. 2016 (165)	Serum PUFA	High vs. Low	Breast cancer	General	4	1,475	645	RR	0.59	0.27	1.30
Chen et al. 2016 (166)	Eicosapentaenoic acid biomarkers	High vs. Low	All-cause mortality	General	3	6,410	3,205	RR	0.74	0.60	0.90
Chowdhury et al. 2012 (145)	Long-chain Omega-3 biomarkers	High vs. Low	Stroke	General	4	4,096	1,177	RR	1.04	0.90	1.20
Chowdhury et al. 2014 (167)	Docosahexaenoic acid + Eicosapentaenoic acid biomarkers	T3 vs. T1	Coronary heart disease mortality	Mixed	NA	2,441	223	RR	0.70	0.53	0.91
Chowdhury et al. 2014 (167)	Long-chain Omega-3 biomarkers	T3 vs. T1	Coronary heart disease	General	4	10,558	2,753	RR	0.84	0.63	1.11
Chowdhury et al. 2014 (167)	Omega-6 biomarkers	T3 vs. T1	Coronary heart disease	General	2	7,432	1,877	RR	0.94	0.84	1.06
Doets et al. 2013 (168)	Vitamin B12 (serum + plasma)	Per 50 pmol/L	Dementia	General	4	2,630	263	RR	1.00	0.98	1.02
Fu et al. 2015 (169)	α-Linolenic acid biomarkers	Per 0.1% increase	Prostate cancer	General	9	563,233 (NA in 1 study)	5,750	RR	1.00	0.98	1.03
Hossain et al. 2019 (170)	Plasma Vitamin D	Not deficient vs. deficient	Breast cancer	General	1	1,414	707	OR	1.02	0.68	1.54
Hunnicutt et al. 2014 (171)	Serum ferritin	High vs. Low	Coronary heart disease mortality	General	2	6,039	1,503	RR	1.00	0.76	1.31
Hunnicutt et al. 2014 (171)	Serum ferritin	High vs. Low	Myocardial infarction	General	1	1,931	51	RR	2.20	1.20	4.02
Jayedi et al. 2018 (172)	Selenium (serum + plasma)	High vs. Low	All-cause mortality	General	7	23,516	6,623	RR	0.62	0.45	0.79
Li et al. 2020 (173)	Linoleic acid (serum + plasma)	High vs. Low	All-cause mortality	Mixed	3	4,813	1,712	RR	0.86	0.76	0.97
Li et al. 2020 (173)	Linoleic acid (serum + plasma)	High vs. Low	Cardiovascular mortality	Mixed	4	8,348	1,093	RR	0.78	0.67	0.91

Moazzen et al. 2018 (151)	Folate biomarkers	High vs. Low	Colorectal cancer	NA	NA	NA	NA	RR	0.71	0.59	0.86
Pan et al. 2012 (174)	α-Linolenic acid biomarkers	High vs. Low	Cardiovascular disease	General	14	25,108	8,001	RR	0.88	0.74	1.05
Touvier et al. 2011 (175)	Vitamin D biomarkers	Per 100 IU/L	Colorectal cancer	General	6	NA	NA	RR	0.96	0.94	0.97
Vinceti et al. 2018 (157)	Selenium biomarkers	High vs. Low	Cancer mortality	Mixed	6	45,864	1,343	OR	0.63	0.39	1.02
Vinceti et al. 2018 (157)	Selenium (serum + plasma)	High vs. Low	Lung cancer	Mixed	9	185,472	1,225	OR	0.91	0.70	1.18
Vinceti et al. 2018 (157)	Selenium (serum + plasma)	High vs. Low	Prostate	Mixed	13	335,237	4,990	OR	0.86	0.75	0.99
Wang et al. 2014 (176)	Serum folate	High vs. Low	Prostate cancer	General	5	9,810	NA	RR	1.21	1.05	1.39
Wu et al. 2012 (177)	Docosahexaenoic acid + Eicosapentaenoic acid biomarkers	High vs. Low	Type 2 diabetes	General	5	10,382	1,581	RR	0.94	0.82	1.09
Wu et al. 2012 (177)	α-Linolenic acid biomarkers	High vs. Low	Type 2 diabetes	General	6	13,291	1,833	RR	0.87	0.74	1.01
Wu et al. 2020 (178)	Carotenoids (serum + plasma)	High vs. Low	Bladder cancer	General	2	1,757	NA	RR	0.65	0.42	1.02
Zhang et al. 2015 (179)	Serum Vitamin D	High vs. Low	Lung cancer	General	9	153,534	2,404	RR	0.83	0.77	0.90
Zhao et al. 2017 (159)	Serum ferritin	High vs. Low	Gestational diabetes	General	4	5,399	507	RR	1.62	1.14	2.30
Zheng et al. 2013 (180)	Omega-3 biomarkers	High vs. Low	Breast cancer	General	7	4,529	1,485	RR	0.86	0.71	1.03

[1] Mixed population: Population including people with various pre-existing conditions such as cancer, cardiovascular diseases / chronic heart diseases, cognitive symptoms, diseases of the digestive system / eye / genitourinary system / liver / nervous system, endocrine / nutritional / metabolic diseases, musculoskeletal diseases.

[2] General population: General healthy.

dl: deciliter; IU: international unit; L: liter; µg: microgram; mL: milliliter; µmol: micromole; n: number; NA: not applicable/assessed; ng: nanogram; OR: odds ratio; pmol: picomole; RR: risk ratio; T: tertile; vs: versus; CI: 95% confidence interval

Supplemental Table 5: Methodological quality assessment of the included systematic reviews.

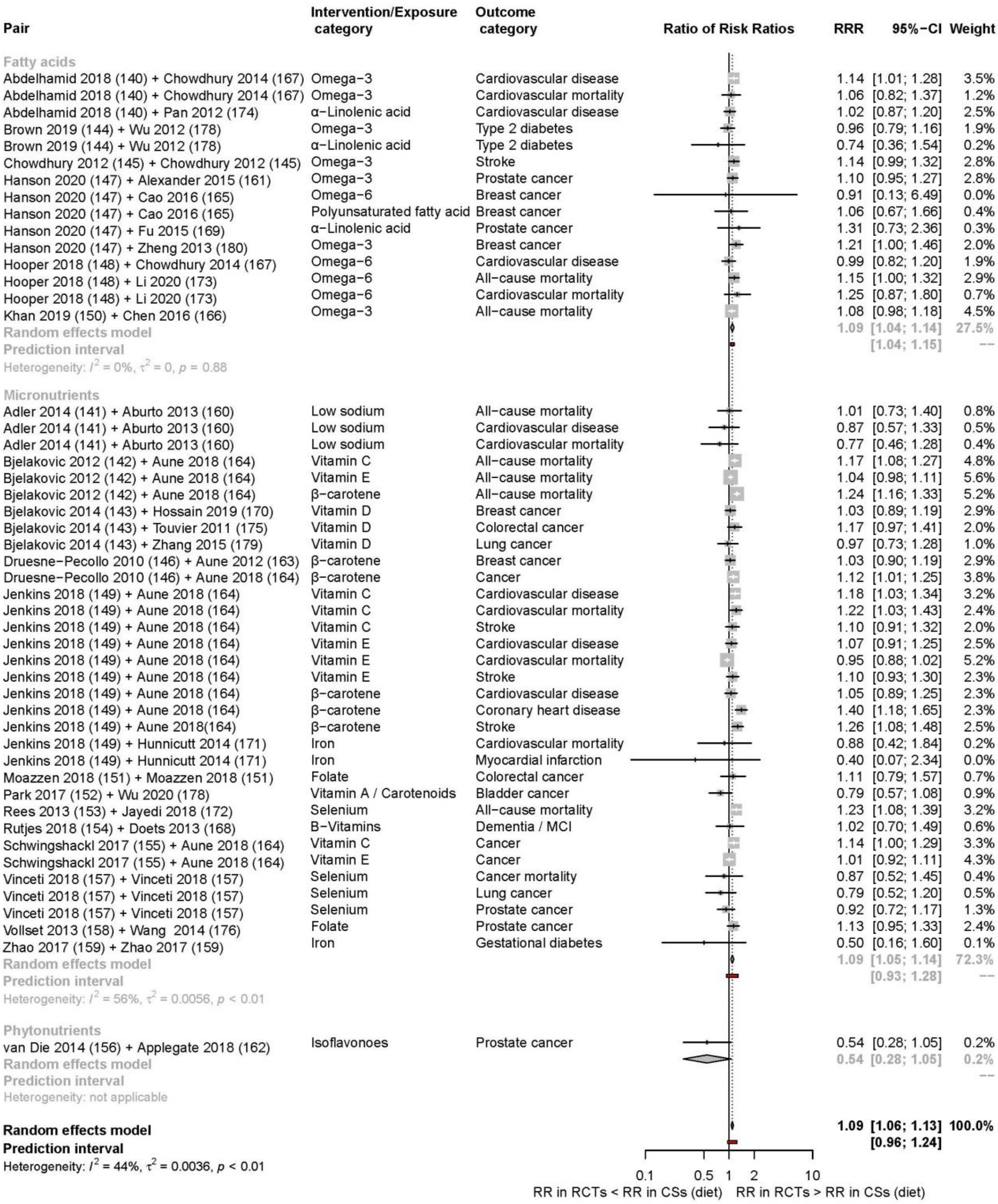
Reference	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	Overall confidence	Search period
Abdelhamid et al. 2018 (140)	Yes	Yes	Yes	Yes	Yes	Yes	Partial Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	High	1946-04/2017
Aburto et al. 2013 (160)	Yes	Partial Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes	Low	Until 08/2011
Adler et al. 2014 (141)	Yes	Yes	Yes	Partial Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	No	Low	1806-05/2013
Alexander et al. 2015 (161)	Yes	No	Yes	No	No	No	No	Partial Yes	No	No	Yes	No	No	No	Yes	No	Critically low	Until 2013
Applegate et al. 2018 (162)	Yes	No	Yes	No	Yes	No	No	Yes	Yes	No	Yes	Yes	Yes	No	Yes	Yes	Critically low	Until 05/2017
Aune et al. 2012 (163)	No	Yes	Yes	No	Yes	Yes	No	Yes	No	No	Yes	No	No	No	No	Yes	Critically low	Until 08/2011
Aune et al. 2018 (164)	Yes	No	Yes	Partial Yes	No	No	Yes	Yes	Yes	No	Yes	Yes	No	No	Yes	Yes	Critically low	Until 02/2018
Bjelakovic et al. 2012 (142)	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	High	1945-02/2011
Bjelakovic et al. 2014 (143)	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	High	Until 02/2014
Brown et al. 2019 (144)	Yes	Yes	No	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Low	Until 12/2018
Cao et al. 2016 (165)	No	No	No	No	Yes	No	No	Partial Yes	Yes	No	No	Yes	Yes	No	Yes	Yes	Critically low	Until 09/2015
Chen et al. 2016 (166)	Yes	No	Yes	Partial Yes	Yes	Yes	Partial Yes	Partial Yes	Yes	No	Yes	No	No	No	Yes	Yes	Critically low	01/1966-11/2015
Chowdhury et al. 2012 (145)	Yes	No	Yes	Partial Yes	Yes	Yes	No	Yes	No	No	Yes	No	No	No	Yes	Yes	Critically low	Until 09/2012
Chowdhury et al. 2014 (167)	Yes	Partial Yes	Yes	Yes	No	Yes	No	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	No	Low	Until 07/2013
Doets et al. 2013 (168)	Yes	No	Yes	No	No	No	No	Yes	No	No	No	No	No	No	No	Yes	Critically low	Until 02/2009
Druesne-Pecollo et al. 2010 (146)	Yes	No	Yes	No	Yes	Yes	No	Yes	No	No	Yes	No	No	No	No	No	Critically low	Until 04/2009
Fu et al. 2015 (169)	Yes	No	No	No	Yes	Yes	No	Yes	Yes	No	Yes	No	No	Yes	Yes	Yes	Critically low	Until 02/2014
Hanson et al. 2020 (147)	Yes	Yes	No	Yes	Yes	Yes	No	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes	Low	Until 12/2018
Hooper et al. 2018 (148)	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	High	1946-05/2017

Hossain et al. 2019 (170)	Yes	No	No	No	Yes	No	No	Yes	No	No	No	No	No	No	Yes	Yes	Critically low	01/2000-03/2018
Hunnicutt et al. 2014 (171)	Yes	No	Yes	No	Yes	Yes	No	Yes	No	No	Yes	No	No	No	Yes	Yes	Critically low	Until 06/2013
Jayedi et al. 2018 (172)	Yes	No	Yes	No	Yes	Yes	No	Partial Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes	Critically low	1966-10/2017
Jenkins et al. 2018 (149)	Yes	No	No	No	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	Critically low	01/2012-10/2017
Khan et al. 2019 (150)	Yes	No	No	No	Yes	Yes	No	Yes	Yes	No	No	No	Yes	Yes	Yes	Yes	Critically low	Until 03/2019
Li et al. 2020 (173)	Yes	No	Yes	No	No	Yes	No	No	Yes	No	Yes	Yes	No	Yes	Yes	Yes	Critically low	Until 07/2019
Moazzen et al. 2018 (151)	No	No	Yes	No	No	No	No	Partial Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes	Critically low	01/2000-09/2016
Pan et al. 2012 (174)	Yes	No	Yes	No	Yes	Yes	No	Yes	Yes	No	Yes	Yes	No	No	Yes	Yes	Critically low	1947-01/2012
Park et al. 2017 (152)	Yes	No	No	Partial Yes	Yes	No	No	Yes	Yes	No	Yes	Yes	No	No	Yes	Yes	Critically low	Until 07/2016
Rees et al. 2013 (153)	Yes	Yes	No	Yes	Yes	Yes	Partial Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes	Moderate	1806-10/2012
Rutjes et al. 2018 (154)	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes	High	Until 01/2018
Schwingshackl et al. 2017 (155)	Yes	Yes	No	Partial Yes	Yes	No	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Low	1966-08/2016
Touvier et al. 2011 (175)	Yes	Partial Yes	Yes	No	No	No	No	Partial Yes	No	No	Yes	No	No	Yes	Yes	Yes	Critically low	Until 06/2010
van Die et al. 2014 (156)	Yes	No	No	Partial Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	No	Critically low	Until 02/2013
Vinceti et al. 2018 (157)	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes	Moderate	Until 02/2017
Vollset et al. 2013 (158)	Yes	No	No	No	No	No	No	Partial Yes	No	No	No	No	No	Yes	No	Yes	Critically low	Until 12/2010
Wang et al. 2014 (176)	Yes	No	No	Partial Yes	Yes	Yes	No	Partial Yes	Yes	No	Yes	No	No	Yes	Yes	Yes	Critically low	Until 01/2014
Wu et al. 2012 (177)	Yes	No	No	Partial Yes	No	Yes	Yes	Yes	Yes	No	Yes	No	No	Yes	Yes	Yes	Critically low	Until 06/2011
Wu et al. 2020 (178)	Yes	Yes	No	Partial Yes	No	Yes	No	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes	Low	Until 04/2019
Zhang et al. 2015 (179)	Yes	No	No	Partial Yes	Yes	Yes	Partial Yes	No	Yes	No	Yes	No	No	Yes	Yes	No	Critically low	Until 10/2014
Zhao et al. 2017 (159)	Yes	No	Yes	No	Yes	Yes	No	Partial Yes	Yes	No	Yes	Yes	No	Yes	Yes	Yes	Critically low	Until 05/2016

Zheng et al. 2013 (180)	Yes	No	Yes	No	Yes	Yes	No	Yes	Yes	No	Yes	Yes	No	No	Yes	Yes	Critically low	Until 12/2012

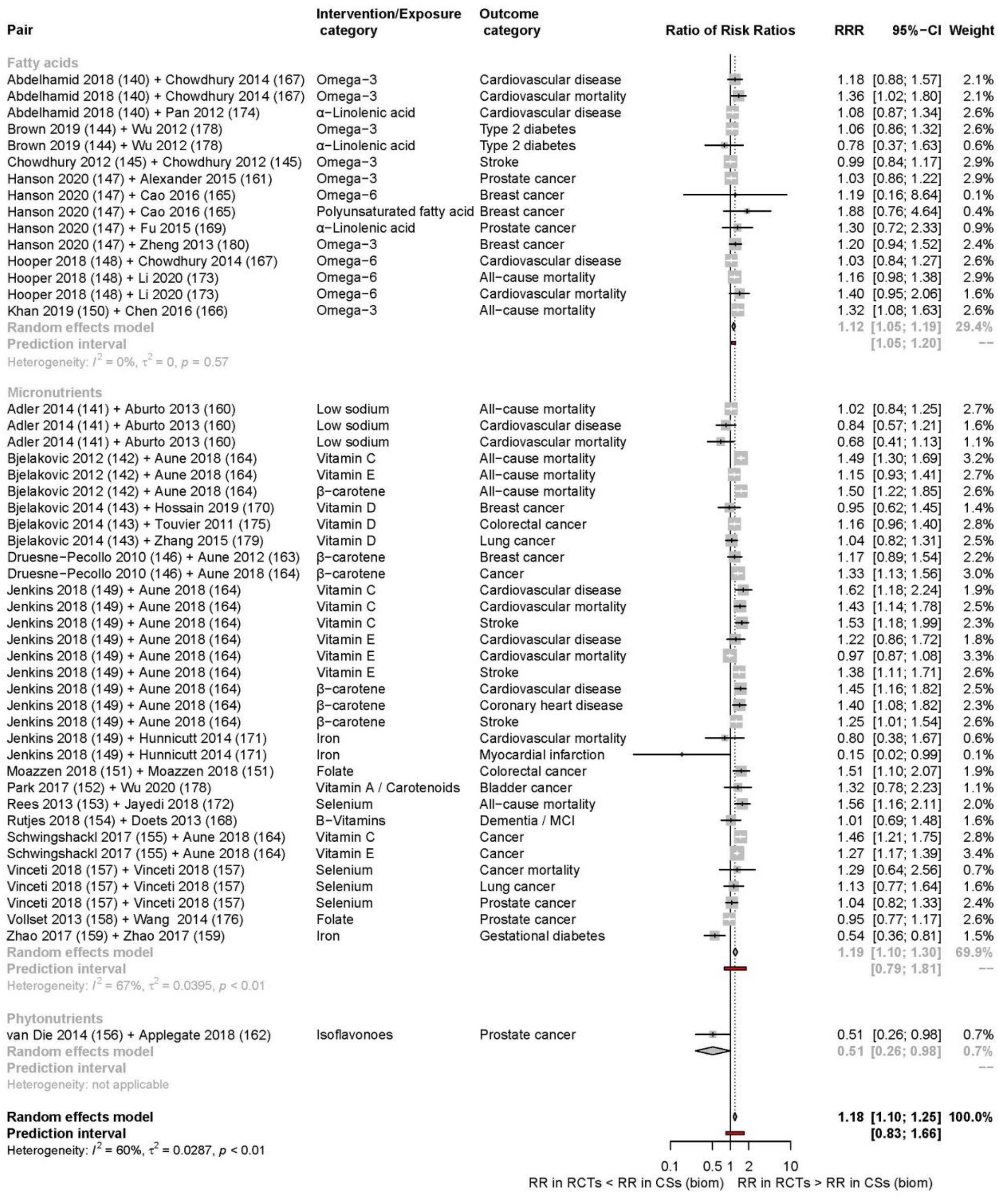
Items:

1. Did the research question and inclusion criteria for the review include the components of PICO?
2. Did the report of the review contain an explicit statement that the review methods were established prior to the conduct of the review and did the report justify any significant deviations from the protocol?
3. Did the review authors explain their selection of the study designs for inclusion in the review?
4. Did the review authors use a comprehensive literature search strategy?
5. Did the review authors perform study selection in duplicate?
6. Did the review authors perform data extraction in duplicate?
7. Did the review authors provide a list of excluded studies and justify the exclusions?
8. Did the review authors describe the included studies in adequate detail?
9. Did the review authors use a satisfactory technique for assessing the risk of bias (RoB) in individual studies that were included in the review?
10. Did the review authors report on the source of funding for the studies included in the review?
11. If meta-analysis was performed, did the review authors use appropriate methods for statistical combination of results?
12. If meta-analysis was performed, did the review authors assess the potential impact of RoB in individual studies on the results of the meta-analysis or other evidence synthesis?
13. Did the review authors account for RoB in individual studies when interpreting/discussing the results of the review?
14. Did the review authors provide a satisfactory explanation for, and discussion of, any heterogeneity observed in the results of the review?
15. If they performed quantitative synthesis, did the review authors carry out an adequate investigation of publication bias (small study bias) and discuss its likely impact on the results of the review?
16. Did the review authors report any potential sources of conflict of interest, including any funding they received for conducting the review?



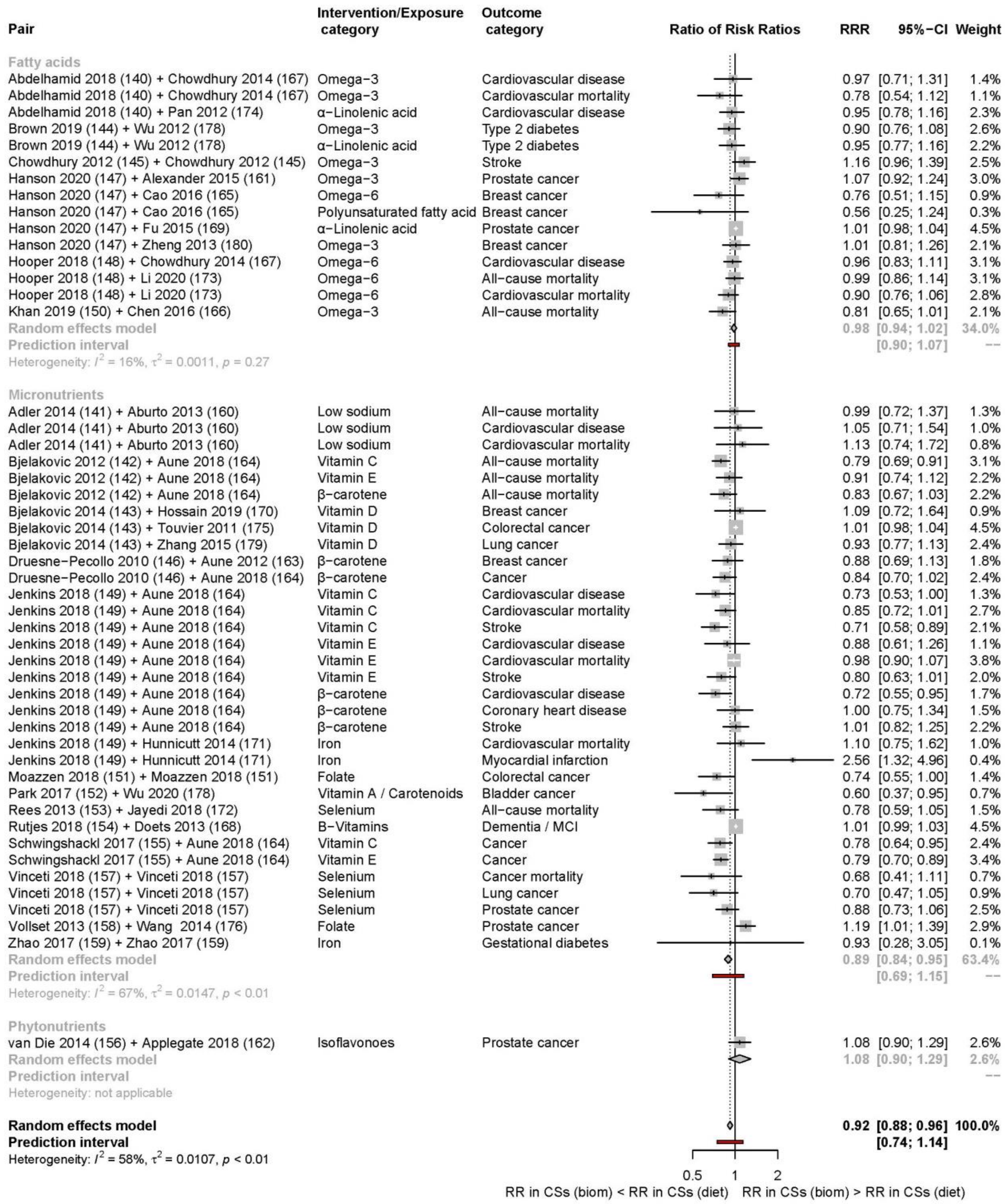
Supplemental Figure 3: Concordance analysis stratified by type of intervention/exposure (RCTs vs. CSs dietary intake).

CSs: cohort studies; MCI: mild cognitive impairment; RCTs: randomized controlled trials; RR: risk ratio; RRR: ratio of risk ratios; 95% CI: 95% confidence interval



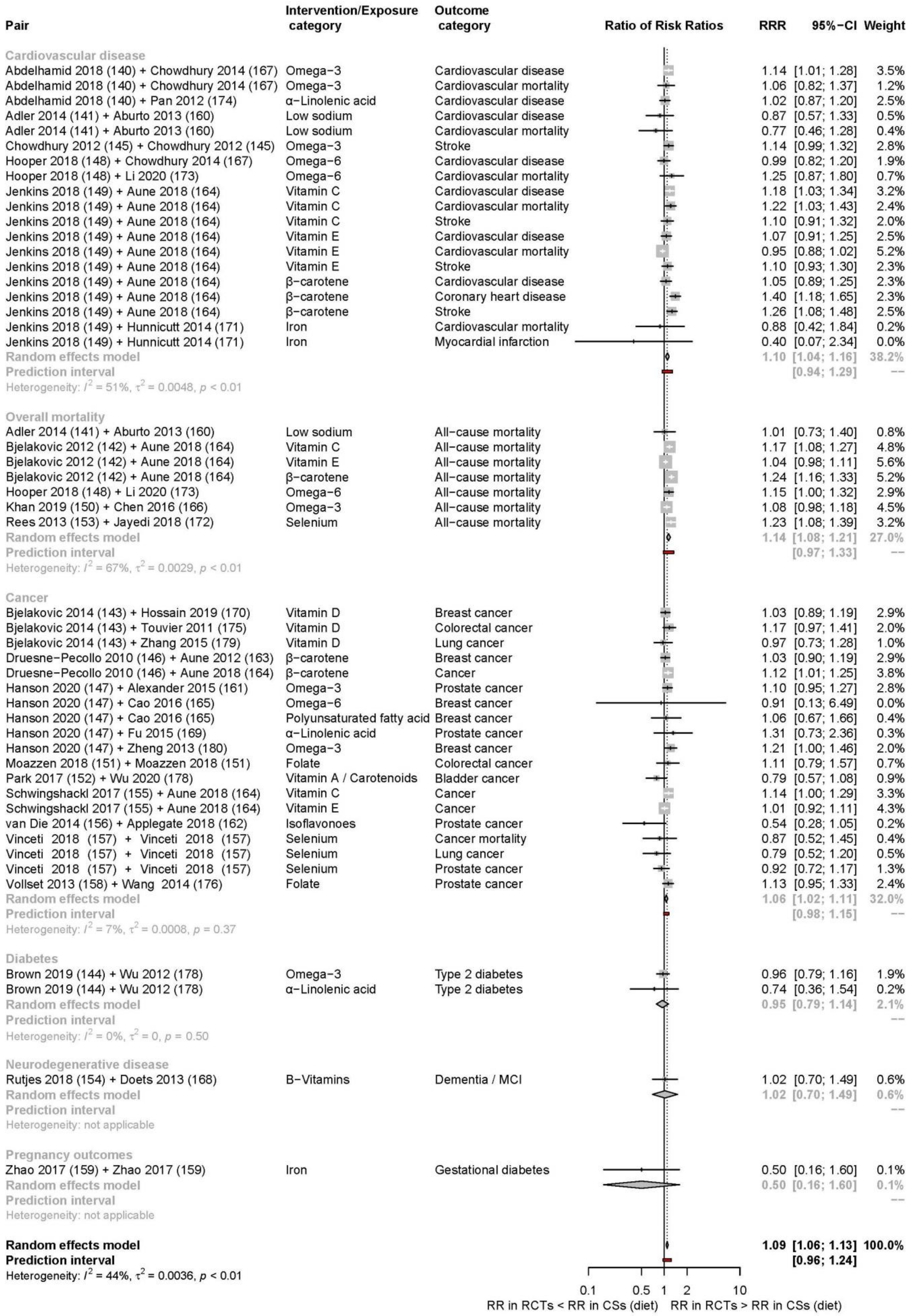
Supplemental Figure 4: Concordance analysis stratified by type of intervention/exposure (RCTs vs. CSs biomarkers of intake).

CSs: cohort studies; MCI: mild cognitive impairment; RCTs: randomized controlled trials; RR: risk ratio; RRR: ratio of risk ratios; 95% CI: 95% confidence interval



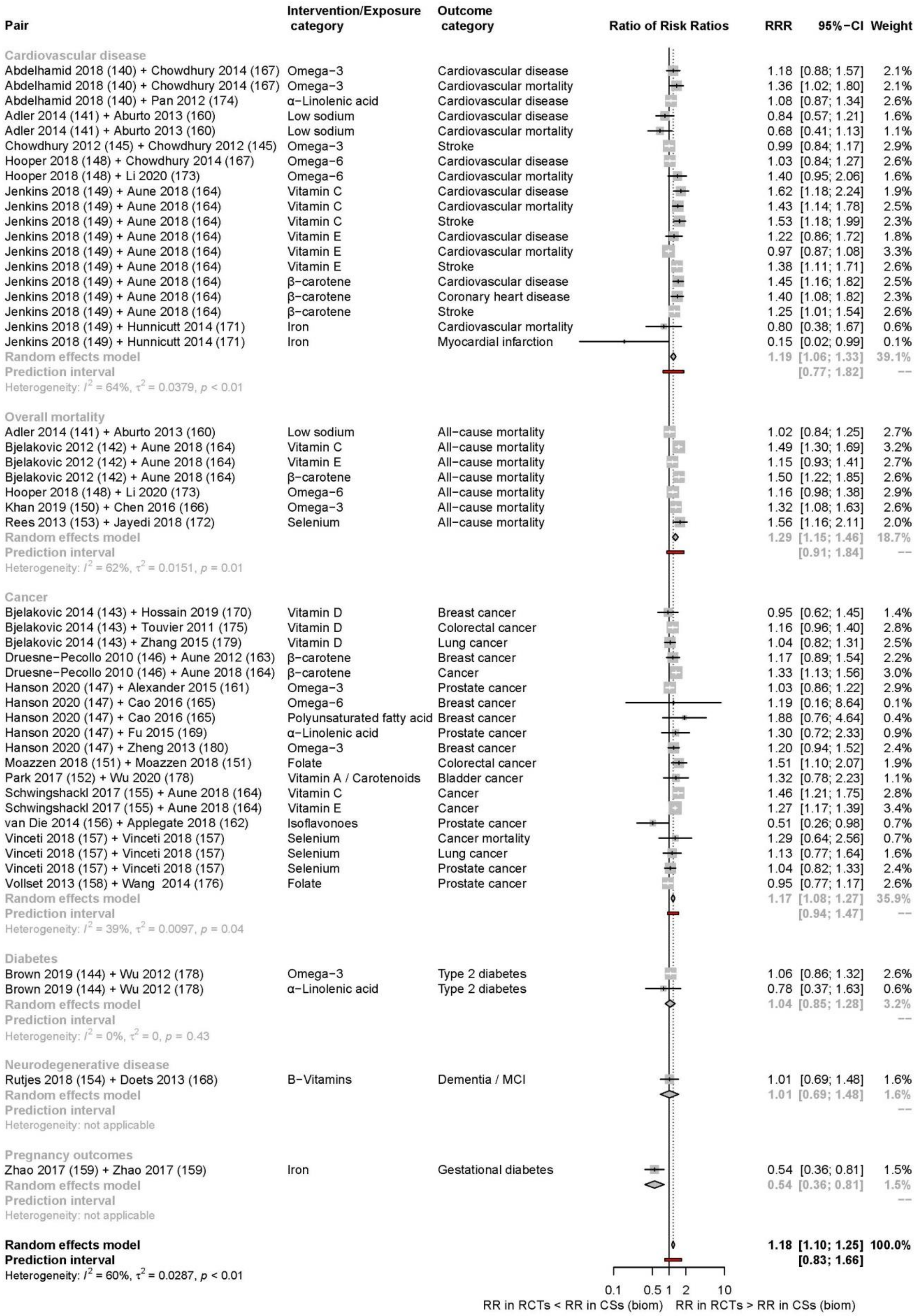
Supplemental Figure 5: Concordance analysis stratified by type of intervention/exposure (CSs dietary intake vs. CSs biomarkers of intake).

CSs: cohort studies; MCI: mild cognitive impairment; RCTs: randomized controlled trials; RR: risk ratio; RRR: ratio of risk ratios; 95% CI: 95% confidence interval



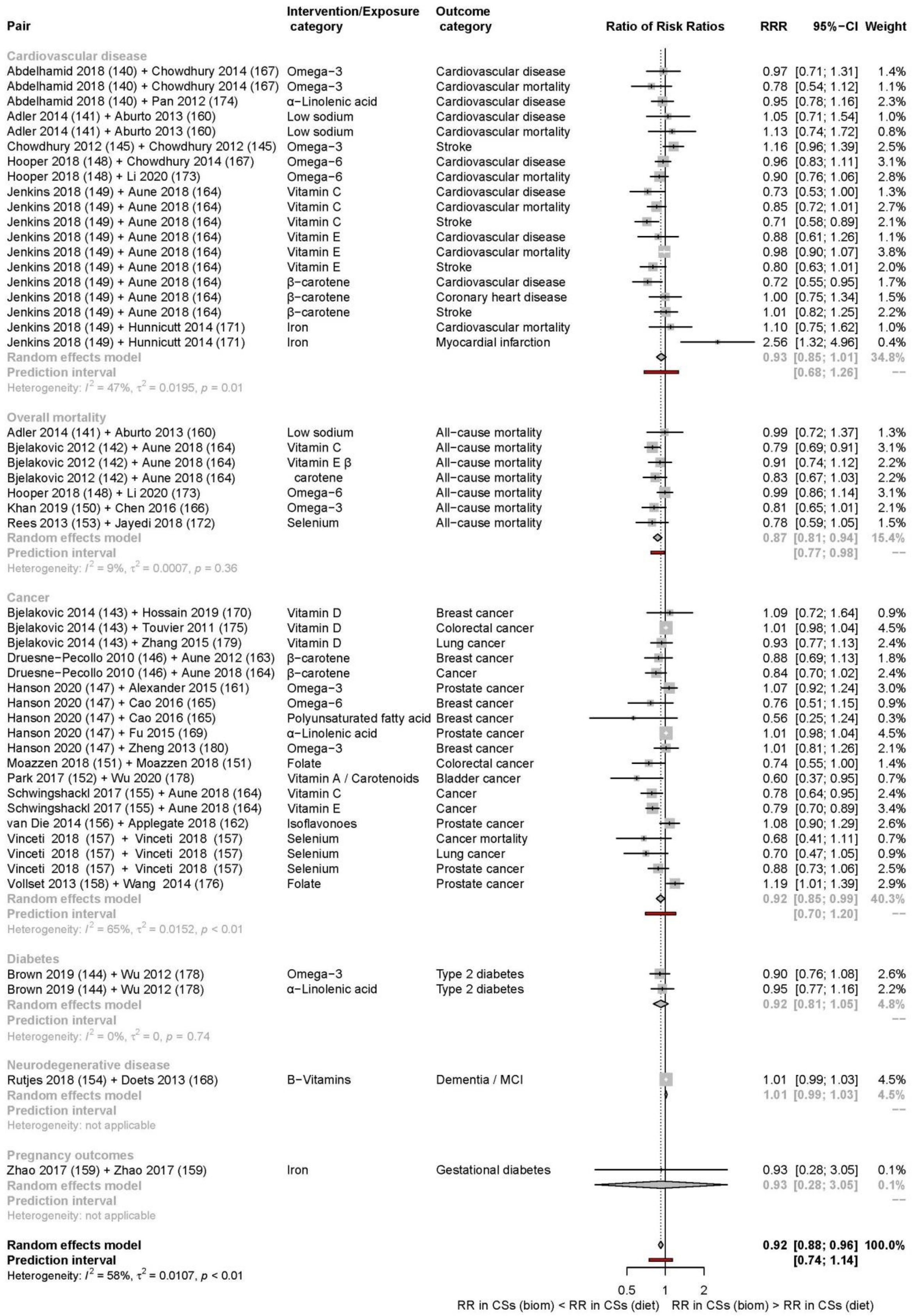
Supplemental Figure 6: Concordance analysis stratified by type of outcome (RCTs vs. CSs dietary intake).

CSs: cohort studies; MCI: mild cognitive impairment; RCTs: randomized controlled trials; RR: risk ratio; RRR: ratio of risk ratios; 95% CI: 95% confidence interval



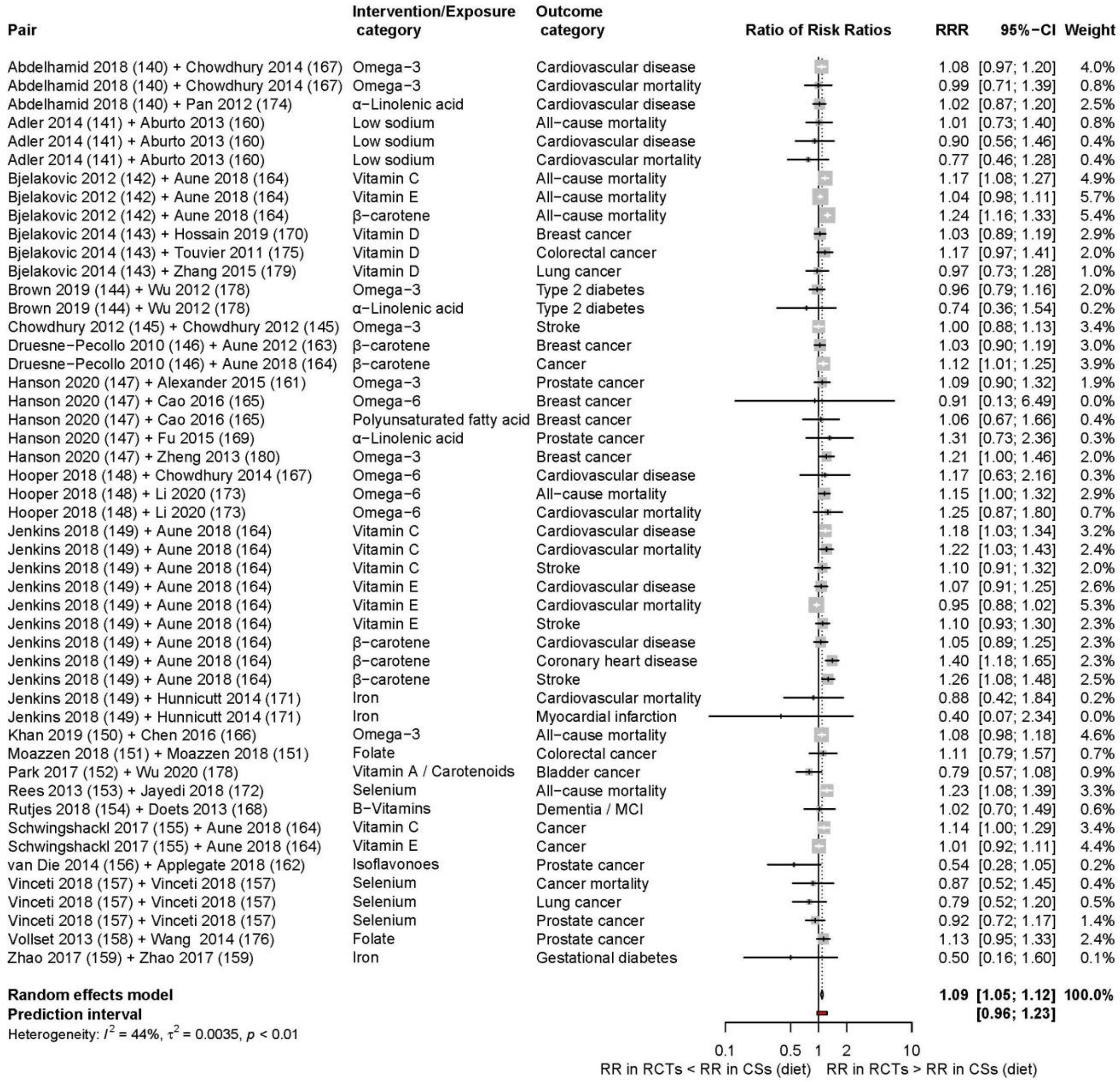
Supplemental Figure 7: Concordance analysis stratified by type of outcome (RCTs vs. CSs biomarkers of intake).

CSs: cohort studies; MCI: mild cognitive impairment; RCTs: randomized controlled trials; RR: risk ratio; RRR: ratio of risk ratios; 95% CI: 95% confidence interval



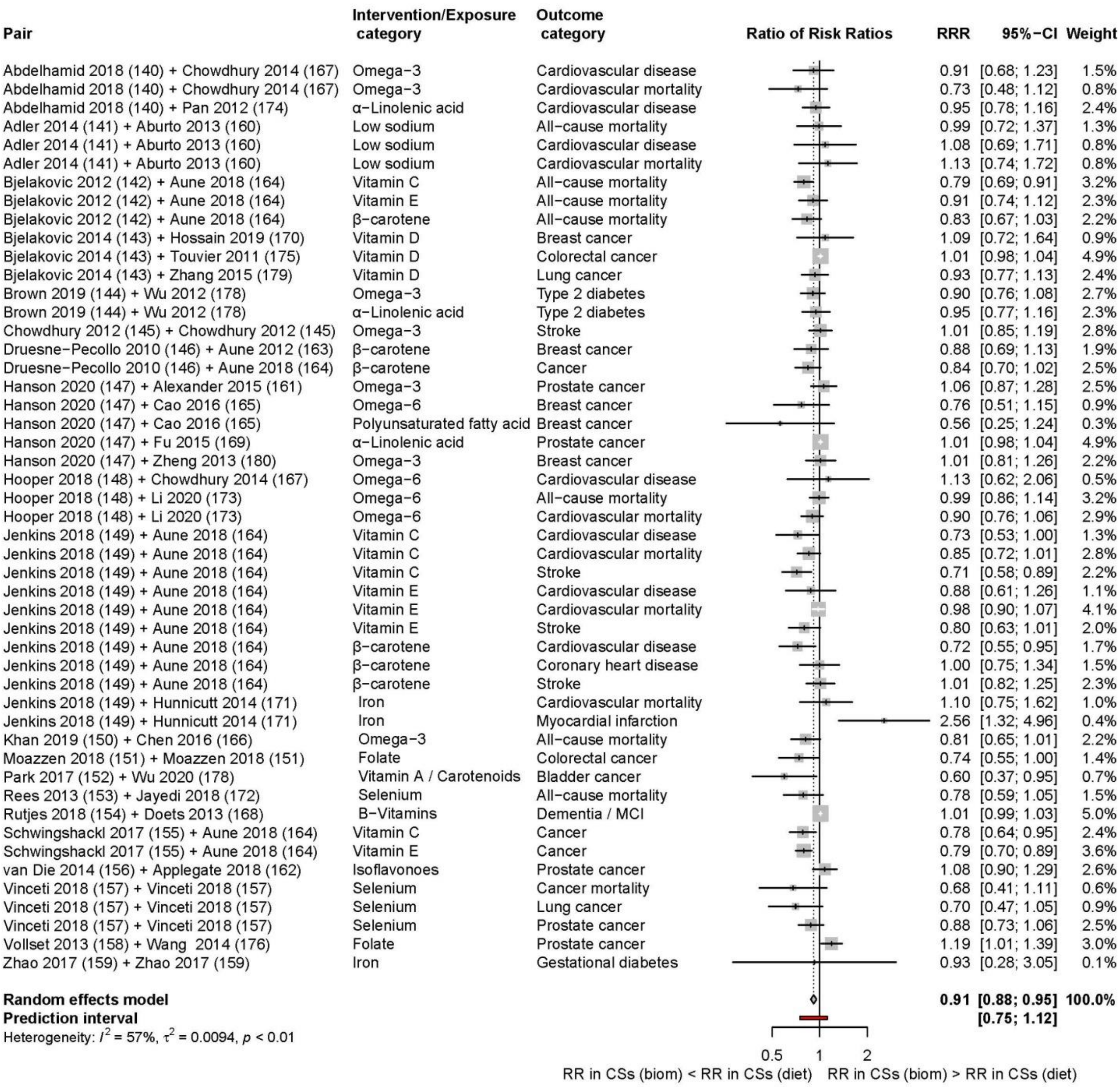
Supplemental Figure 8: Concordance analysis stratified by type of outcome (CSs dietary intake vs. CSs biomarkers of intake).

CSs: cohort studies; MCI: mild cognitive impairment; RCTs: randomized controlled trials; RR: risk ratio; RRR: ratio of risk ratios; 95% CI: 95% confidence interval



Supplemental Figure 9: Concordance sensitivity analysis using risk estimates for bodies of evidence from RCTs from systematic reviews of cohort studies that included also RCTs (RCTs vs. CSs dietary intake).

CSs: cohort studies; MCI: mild cognitive impairment; RCTs: randomized controlled trials; RR: risk ratio; RRR: ratio of risk ratios; 95% CI: 95% confidence interval



Supplemental Figure 10: Concordance sensitivity analysis using risk estimates for bodies of evidence from RCTs from systematic reviews of cohort studies that included also RCTs (RCTs vs. CSs biomarkers of intake).

CSs: cohort studies; MCI: mild cognitive impairment; RCTs: randomized controlled trials; RR: risk ratio; RRR: ratio of risk ratios; 95% CI: 95% confidence interval

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