

SYSTEMATIC REVIEW AND META-ANALYSIS

Relation of Different Fruit and Vegetable Sources With Incident Cardiovascular Outcomes: A Systematic Review and Meta-Analysis of Prospective Cohort Studies

Andreea Zurbau , PhD, RD; Fei Au-Yeung, MSc; Sonia Blanco Mejia , MD, MSc; Tauseef A. Khan, PhD; Vladimir Vuksan, PhD; Elena Jovanovski, PhD; Lawrence A. Leiter, MD; Cyril W. C. Kendall, PhD; David J. A. Jenkins, MD, PhD; John L. Sievenpiper , MD, PhD

BACKGROUND: Public health policies reflect concerns that certain fruit sources may not have the intended benefits and that vegetables should be preferred to fruit. We assessed the relation of fruit and vegetable sources with cardiovascular outcomes using a systematic review and meta-analysis of prospective cohort studies.

METHODS AND RESULTS: MEDLINE, EMBASE, and Cochrane were searched through June 3, 2019. Two independent reviewers extracted data and assessed study quality (Newcastle-Ottawa Scale). Data were pooled (fixed effects), and heterogeneity (Cochrane-Q and I^2) and certainty of the evidence (Grading of Recommendations Assessment, Development, and Evaluation) were assessed. Eighty-one cohorts involving 4 031 896 individuals and 125 112 cardiovascular events were included. Total fruit and vegetables, fruit, and vegetables were associated with decreased cardiovascular disease (risk ratio, 0.93 [95% CI, 0.89–0.96]; 0.91 [0.88–0.95]; and 0.94 [0.90–0.97], respectively), coronary heart disease (0.88 [0.83–0.92]; 0.88 [0.84–0.92]; and 0.92 [0.87–0.96], respectively), and stroke (0.82 [0.77–0.88], 0.82 [0.79–0.85]; and 0.88 [0.83–0.93], respectively) incidence. Total fruit and vegetables, fruit, and vegetables were associated with decreased cardiovascular disease (0.89 [0.85–0.93]; 0.88 [0.86–0.91]; and 0.87 [0.85–0.90], respectively), coronary heart disease (0.81 [0.72–0.92]; 0.86 [0.82–0.90]; and 0.86 [0.83–0.89], respectively), and stroke (0.73 [0.65–0.81]; 0.87 [0.84–0.91]; and 0.94 [0.90–0.99], respectively) mortality. There were greater benefits for citrus, 100% fruit juice, and pommes among fruit sources and allium, carrots, cruciferous, and green leafy among vegetable sources. No sources showed an adverse association. The certainty of the evidence was “very low” to “moderate,” with the highest for total fruit and/or vegetables, pommes fruit, and green leafy vegetables.

CONCLUSIONS: Fruits and vegetables are associated with cardiovascular benefit, with some sources associated with greater benefit and none showing an adverse association.

REGISTRATION: URL: <https://www.clinicaltrials.gov>; Unique identifier: NCT03394339.

Key Words: cardiovascular outcomes ■ cohort ■ fruit ■ nutrition ■ vegetables

Increased fruit and vegetable consumption is the cornerstone of dietary guidance for cardiovascular disease (CVD) prevention. Their benefit as part of heart healthy diets is balanced against an increasing concern of their contribution to an excess

intake of sugars.^{1,2} Some influential commentators have even questioned the value of the proverbial “apple a day.”³ Public health outlets are emphasizing vegetables before fruit intake and discouraging the intake of certain sources of fruit, such as fruit

Correspondence to: John L. Sievenpiper, MD, PhD, 6138-61 Queen St E, Toronto, Ontario, Canada M5C 2T2. E-mail: john.sievenpiper@utoronto.ca
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CLINICAL PERSPECTIVE

What Is New?

- Public health policies discourage the consumption of certain fruit sources (eg, 100% fruit juice, dried fruit, and tropical fruit) because of their sugar content and emphasize vegetable consumption before fruit.
- We examined the relation of fruit and vegetable sources with cardiovascular disease outcomes.

What Are the Clinical Implications?

- In this systematic review and meta-analysis of 81 unique cohorts, we identified that fruits and vegetables are associated with cardiovascular benefit and no fruit or vegetable sources are associated with cardiovascular harm.
- Certain fruit and vegetable sources showed greater associations with cardiovascular benefit, including citrus, 100% fruit juice, and pomes fruit and allium, carrots, and cruciferous and green leafy vegetables.

Nonstandard Abbreviations and Acronyms

GRADE Grading of Recommendations Assessment, Development, and Evaluation

NOS Newcastle-Ottawa Scale

juice and dried, tropical, and canned fruit, some of which have been reflected in health policies.⁴⁻⁸

Given the longstanding perceived value of fruit and vegetables in reducing global CVD morbidity and mortality⁹ and in light of developing efforts to limit dietary sugars, there is a need to reassess the role of different fruit and vegetable sources in CVD prevention. Whether different fruit and vegetable sources show comparable CVD risk reduction is unclear. Systematic reviews and meta-analyses of prospective cohort studies have shown evidence of a cardiovascular benefit of broad categories of fruits and vegetables,¹⁰⁻¹⁶ but the relative contributions of specific fruit and vegetable sources and the certainty of the estimates for these sources are underexplored. We, therefore, conducted a systematic review and meta-analysis of prospective cohort studies using Grading of Recommendations Assessment, Development, and Evaluation (GRADE) approach to assess the role of different fruit and vegetable sources in CVD risk reduction and to quantify the certainty of the evidence to inform public health policy.

METHODS

All supporting data are available within the article and its online supplementary files. We followed the *Cochrane Handbook for Systematic Reviews and Interventions*¹⁷ and reported results in accordance with Meta-Analysis of Observational Studies in Epidemiology¹⁶ and Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines.¹⁸ The protocol was registered at Clinicaltrials.gov (identifier, NCT03394339).

Search Strategy

We searched MEDLINE, EMBASE, and the Cochrane Library databases through June 3, 2019, using the search strategy presented in Table S1 and restrictions for prospective cohorts. We supplemented the search with manual searches of the references of included studies.

Study Selection

Prospective cohort studies that reported the association of fruit and/or vegetable intake with CVD, coronary heart disease (CHD), or stroke incidence and mortality with a minimum follow-up time of 1 year in individuals free of disease at baseline were included. Cohorts that presented data on exposures to fruits and vegetables within the context of a dietary index were not included unless fruits and/or vegetables were presented separately from the other components of the diet index.

Data Extraction

Two reviewers (A.Z., F.A.) independently extracted relevant information, including study design, sample size, subject characteristics, exposure, outcomes, assessment method, dose for each quantile, number of events, population, person-years of follow-up, duration of follow-up, covariates adjustments, and risk ratios (RRs; or odds ratios or hazard ratios) with 95% CIs for each quantile of exposure. We contacted authors for missing data. Data on CVD outcomes were extracted for exposures to total fruits and vegetables, fruits, vegetables, and their sources. Potatoes were not included in the present analysis as they are nutritionally classified as a starchy food and are largely omitted in quantifications of exposure to vegetables.

Outcomes

Outcomes were CVD, CHD, and stroke incidence and mortality.

Risk of Bias

Included studies were assessed for risk of bias with the Newcastle-Ottawa Scale (NOS),¹⁹ which awards

up to 9 points based on cohort selection (up to 4 points), outcome ascertainment (up to 3 points), and degree of covariate adjustments (up to 2 points with adjustment for age as the primary confounding variable awarded 1 point and adjustment for $\geq 7/9$ secondary confounding variables, including sex, family history, smoking, markers of adiposity, energy intake, physical activity, presence of diabetes mellitus, hypertension [or related medications], and dyslipidemia [or related medications]). Studies achieving ≥ 7 points were considered high quality. Disagreements in NOS score between the 2 reviewers were resolved by a third reviewer (J.L.S.).

Statistical Analysis

Review Manager version 5.3 (The Nordic Cochrane Centre, Denmark) and STATA version 13.0 (StataCorp, TX) were used to conduct all analyses. We prespecified in our analysis plan the use of the generic inverse variance method with DerSimonian and Laird random effects models to pool the natural log-transformed RRs of extreme quantiles, comparing the highest versus the lowest (reference) exposures.²⁰ On the basis of a deviation from our prespecified analysis plan requested by the statistical reviewer, we present the generic inverse variance with fixed effects models as the primary analysis and the DerSimonian and Laird random effects models as a secondary analysis in the Supplemental Material. Hazard ratios and odds ratios (as cumulative incidence $<10\%$) were considered equivalent to RR.²¹ Studies that provided RR on a continuous scale (ie, per dose increment) were scaled to the highest quantile reported for the exposure in the respective cohort as necessary. Test for differences between fruit and vegetable categories were conducted in RevMan, with a test for subgroup differences, with $P<0.05$ indicating a significant difference between fruit categories or vegetable categories on a given outcome. We also conducted a dose-response analysis. A random-effects linear dose-response was modeled using a generalized least square trend (*g/st*) for estimation of summarized dose-response data, as per Greenland and Longnecker²² and Orsini.²³ A 2-stage multivariate random-effects method was used to model a nonlinear association using restricted cubic splines with 3 knots.²³ A Wald test was used to evaluate linear and nonlinear dose-response trends. The median dose of each quantile was used, and when not provided we chose the midpoint of the upper and lower boundaries for each quantile as the assigned dose. For open-ended lower and upper quantiles, we defined lowest and highest boundary as the same as the adjacent category cutoff. Servings per day were calculated, with one serving defined as 80 g of fruits and/or vegetables and their categories, with the exception of citrus fruit (122 g), fruit juice (125 g), and green leafy vegetables (88 g), or unless otherwise specified.²⁴

Heterogeneity was assessed by the Cochran Q statistic and quantified by the I^2 statistic. An $I^2 \geq 50\%$ and $P_Q < 0.1$ was considered evidence of substantial heterogeneity.^{25,26} Sensitivity analyses and a priori subgroup analyses were used to explore sources of heterogeneity. We performed sensitivity analyses by systematically removing each study with recalculation of the summary estimates. A priori subgroup analyses were conducted for all comparisons with ≥ 10 observations. Subgroup analyses included age (less than median versus median or greater), sex (males, females, and mixed), follow-up years (less than median versus median or greater), number of covariates in extracted model (<8 versus ≥ 8 covariates), exposure assessment tool (validated Food Frequency Questionnaire [FFQ], unvalidated FFQ, and food record), risk of bias score (<6 versus ≥ 6), and country of data collection. Wald test in metaregression was used to assess differences within each subgroup. Because of the exploratory intent of our subgroup analyses, we did not prespecify adjustment for the false discovery rate in our prespecified analysis plan. On the basis of a deviation from our prespecified analysis plan requested by the statistical reviewer, we adjust for the false discovery rate in our subgroup analyses using the Holm-Bonferroni procedure. If ≥ 10 cohort comparisons were available, then publication bias was assessed by visual inspection of funnel plots for asymmetry and formal testing with the Begg and Egger tests. If publication bias was suspected ($P<0.10$), the Duval and Tweedie trim and fill method imputed missing study data in attempt to adjust for funnel plot asymmetry.²⁷

Grading the Evidence

The GRADE method was used to assess the certainty of the evidence for each comparison on a 4-point scale, ranging from “very low” to “high.”^{28–40} Because of their inherent limitations, observational studies start at a “low” certainty of evidence that can be downgraded or upgraded based on established criteria. Criteria to downgrade included risk of bias (weight of studies shows high risk of bias by NOS), inconsistency (substantial unexplained heterogeneity, $I^2 > 50\%$, and $P_Q < 0.10$), indirectness (presence of factors that limit generalizability based on populations, exposures, and outcomes), imprecision (95% CIs cross minimally important difference of 5% [RR, 0.95–1.05]), and publication bias (significant evidence of small study effects). Criteria to upgrade included a large risk estimate (RR < 0.5 or > 2 in the absence of plausible confounders), a dose-response gradient, and attenuation by plausible confounders.

RESULTS

Flow of the Literature

Figure 1 illustrates a flow of the literature. Of 4271 reports, we included a total of 117 publications^{41–156} of 81

unique prospective cohort studies of 4 031 896 individuals and 125 112 cardiovascular events.

Study Characteristics

The Table shows the characteristics of the included studies.⁴¹⁻¹⁵⁶ Participants were from 69 countries with cohorts distributed worldwide (36 from Europe, 23 from North America, 1 from South America, 17 from Asia, 4 from Australia, and 1 large global cohort including 18 countries worldwide). The median participant age at baseline was 55 (range, 7–90) years with a median follow-up of 11 (range, 2–37) years. Median (range) intakes in servings per day in the highest quantiles were 7.4 (2.6–10.4) fruits and vegetables, 2.6 (0.29–11.0) fruits, 2.85 (0.74–11.0) vegetables, 0.4 (0.3–0.5) bananas, 0.27 (0.13–0.7) berries, 0.71 (0.22–2.2) citrus fruit, 0.82 (0.4–2.28) fruit juice, 0.95 (0.29–2.0) pommes, 2.37 (2.1–2.65) watermelon,

0.54 (0.07–2) allium vegetables, 9.5 (5–14) carrots, 0.43 (0.1–3.0) cruciferous vegetables, 0.71 (0.25–1.5) green leafy vegetables, and 0.63 (0.29–2.0) tomatoes. Doses were not available for apricots and celery. Dietary intake was assessed by self-administered validated food frequency questionnaire (54%), interview administered validated FFQ (10%), unvalidated FFQ (19%), or 24-hour recalls/food records (17%).

Table S2 lists the variables that were statistically adjusted in the included studies. Age, the prespecified primary confounding variable, was adjusted for in 95% of included studies, of which 55% also adjusted for all 9 of the prespecified secondary confounding variables.

Study Quality

Table S3 summarizes the NOS assessment of included studies. There was a high risk of bias in associations

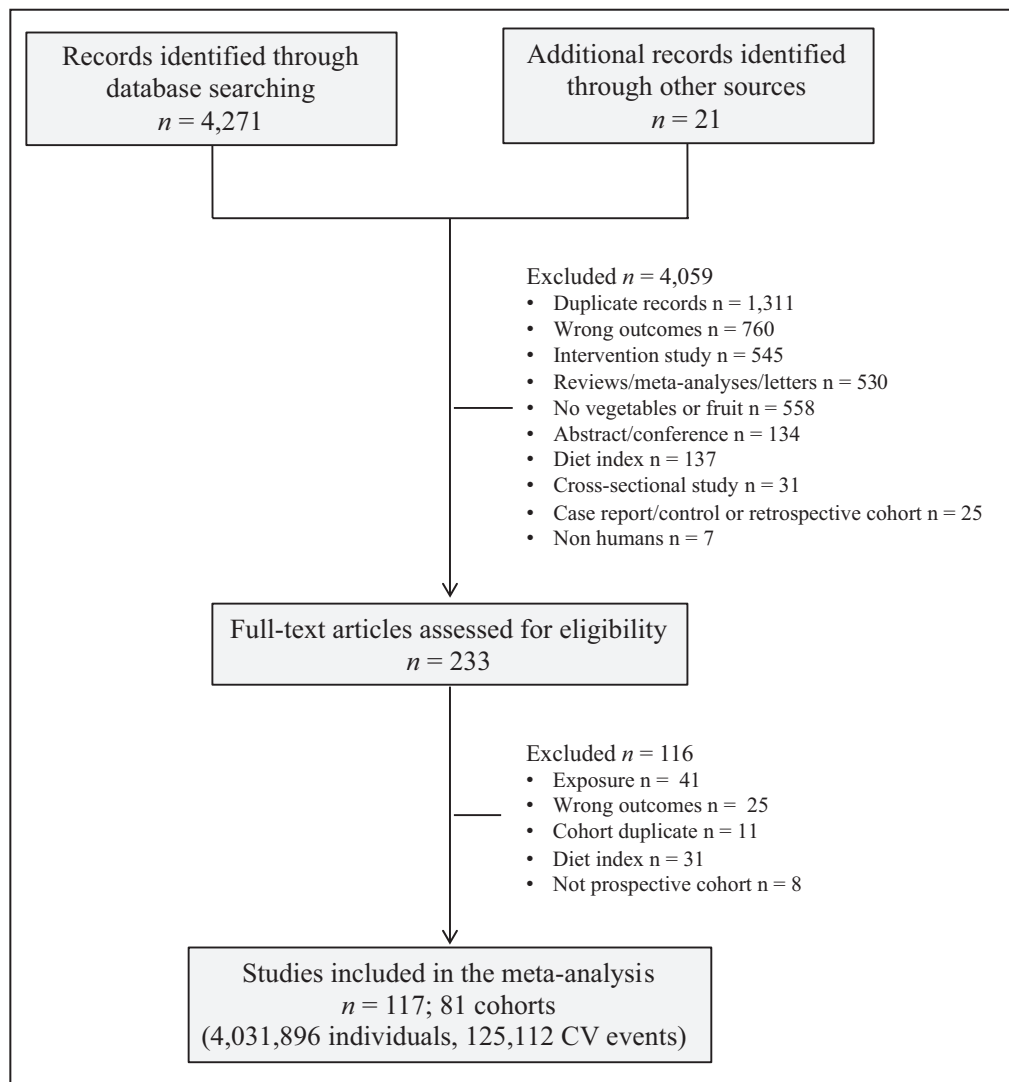


Figure 1. Summary of evidence search and selection.

CV indicates cardiovascular.

Table. Table of Study Characteristics

Study	Cohort	Country	Participants (Men:Women)	Age, y	Follow-Up, y	Dietary Assessment	Exposure	Quantiles	Outcomes	Incidence (Men:Women)
Adriouch, 2018 ⁴¹	NutriNet-Sante	France	84 158 (17 931:66 227)	44.1±14.5	4.9±1.6	24-h recall	Fruit category	3	CVD incidence CHD incidence Stroke incidence	602 309 293
Appleby, 2002 ⁴²	Health Food Shoppers	United Kingdom	10 741 (4325:6416)	16–89	18–24	Unvalidated FFQ	Fruit	2	CVD mortality CHD mortality Stroke mortality	1202 (591:611) 605 (347:258) 356 (142:214)
Atkins, 2014 ⁴³	British Regional Heart	England	3328 (3328:0)	60–79	11.3	Validated FFQ	Fruit and/or vegetable	2	CVD incidence CVD mortality CHD incidence	582 327 307
Bahadoran, 2017 ⁴⁴	Theran Lipid and Glucose	Iran	2369 (1047:1322)	≥19	6	Validated FFQ	Vegetable categories	3	CVD risk	79
Bazzano, 2002 ⁴⁵	National Health and Nutrition Examination Survey Epidemiologic Follow-up Study	United States	9608	25–74	19	Unvalidated FFQ	Fruit and vegetable	4	CVD mortality CVD incidence IHD mortality IHD incidence Stroke mortality Stroke incidence	1145 N/A 639 1786 218 888
Belin, 2011 ⁴⁶	WHI-OS (Women's Health Initiative Observational Study)	United States	93 676 (0:93 676)	50–79	10	Self-administered validated FFQ	Fruit, vegetable	2	CVD incidence	6006
Bendinelli, 2011 ⁴⁷	EPIC	Italy	29 689 (0:29 689)	50.0±7.9	7.85	Validated FFQ	Fruit, vegetable, categories	4	CHD incidence	144
Berard, 2017 ⁴⁸	MONICA	France	1311	35–64	16–18	Food recall	Fruit, vegetable	5	CVD mortality	41
Bhupathiraju, 2013 ⁴⁹	NHS (Nurses' Health Study) and HPFS (Health Professionals Follow-Up Study)	United States	113 276 (42 135:71 141)	40–75 (men) 30–55 (women)	22 (men) 24 (women)	Validated FFQ	Fruit and/or vegetable, categories	5	CHD incidence	6189 (3607:2582)
Bingham, 2008 ⁵⁰	EPIC	United Kingdom	11 134	45–75	4	Validated FFQ	Fruit and vegetable	5	IHD risk	678
Blekenhorst, 2017 ⁵¹	PLSAW (Perth Longitudinal Study of Aging Women)	Australia	1226 (0:1226)	75.1±2.7	15	Validated FFQ	Vegetable, categories	Per 5–75 g/d	CVD mortality IHD mortality Stroke mortality	238 128 92
Bos, 2014 ⁵²	Rotterdam Study	The Netherlands	3570 (1405:2165)	69.4±6.3	12.9	Unvalidated FFQ	Fruit and vegetable	3	Stroke risk	545
Buijsse, 2008 ⁵³	Zutphen Elderly Study	The Netherlands	559 (559:0)	65–84	15	Unvalidated FFQ	Vegetable category	Per 1-SD increase	CVD mortality	197

(Continued)

Table. Continued

Study	Cohort	Country	Participants (Men:Women)	Age, y	Follow-Up, y	Dietary Assessment	Exposure	Quantiles	Outcomes	Incidence (Men:Women)
Buil-Cosiales, 2016 ⁵⁵	PREDIMED (Prevención con Dieta Mediterránea)	Spain	7216	55–80	6	Validated FFQ	Fruit, vegetable, categories	5	CVD composite score CVD mortality MI incidence Stroke incidence	342 104 118 169
Buil-Cosiales, 2017 ⁵⁴	SUN (Seguimiento University of Navarra)	Spain	17 007 (6633:10 374)	38	10.3	Validated FFQ	Fruit, vegetable, categories	5	CVD incidence	112
Cassidy, 2012 ⁵⁶	NHS	United States	69 622 (0:69 622)	30–55	14	Validated FFQ	Fruit, vegetable	5	Stroke incidence	1803
Collin, 2019 ⁵⁷	REGARDS (Reasons for Geographic and Racial Differences in Stroke)	United States	13 440 (7972:5469)	≥45	6±1.8	Validated FFQ	Fruit category	12 oz/d	CHD mortality	168
Conrad, 2018 ⁵⁸	NHANES	United States	29 133 (13 926:15 207)	46.3 (95% CI, 45.8–46.7)	6.5	24-h recall	Vegetable	3	CVD mortality CHD mortality	726 556
Dauchet, 2004 ⁵⁹	PRIME	France, North Ireland	8087 (8087:0)	50–59	5	Interview	Fruit category	3	CHD event	133
Dauchet, 2010 ⁶⁰	PRIME	France, North Ireland	8060 (8060:0)	50–59	10	Interview-validated FFQ	Fruit and/or vegetable	3	CVD risk Acute coronary syndrome	612 367
Du, 2016 ⁶¹	China Kadoorie Biobank	China	451 665 (186 086:265 579)	50.5±10.4	N/A, ≈7.14 y	Interview unvalidated FFQ	Fruit	5	Acute coronary event Hemorrhagic stroke event Other CVD events Ischemic stroke	2551 14 579 11 054 3523
Du, 2017 ⁶²	China Kadoorie Biobank	China	462 342 (189 560:272 782)	51±10.5	≈7	Interview unvalidated FFQ	Fruit	4	CVD mortality IHD mortality Ischemic stroke mortality Hemorrhagic stroke mortality	6166 2038 585 2351
Elwood, 2013 ⁶³	Carphilly Cohort Study	United Kingdom	2235 (2235:0)	45–59	30	Unvalidated FFQ	Fruit and vegetable	2	CVD incidence	N/A
Eriksen, 2015 ⁶⁴	SABRE (Southall and Brent Revised)	United Kingdom	2096	40–69	21	Validated FFQ	Fruit, vegetable	2	CVD incidence CHD incidence	571 520
Fitzgerald, 2012 ⁶⁵	Women's Health Study	United States	34 827 (0:34 827)	55 (46–68) (mean [95% CI])	14.6	Validated FFQ	Fruit, vegetable	5	CVD risk	1094

(Continued)

Table. Continued

Study	Cohort	Country	Participants (Men:Women)	Age, y	Follow-Up, y	Dietary Assessment	Exposure	Quantiles	Outcomes	Incidence (Men:Women)
Fraser, 1992 ⁶⁶	Adventist Health Study	United States	26 473 (10 003:16 740)	Men: 51.3±16.0 Women: 53.2±16.6 (mean±SD)	6	Validated FFQ	Fruit	3	CHD mortality CHD event	463 134
Gardener, 2011 ⁶⁷	NOMAS (Northern Manhattan Study)	United States	2568 (924:1644)	69±10 (Mean±SD)	9	Interview validated FFQ	Fruit, vegetable	Continuous	CVD mortality CVD incidence MI incidence Ischemic stroke incidence	314 518 133 171
Gaziano, 1995 ⁶⁸	Massachusetts Health Care Panel Study	United States	1299 (494:805)	≥66	4.75	Unvalidated FFQ	Fruit and vegetable categories	2	CVD mortality	161
Genkinger, 2004 ⁶⁹	Odyssey	United States	6151 (2276:3875)	30–93	13	Validated FFQ	Fruit, vegetable categories	5	CVD mortality	378
Gillman, 1995 ⁷⁰	Framingham Study	United States	832 (832:0)	45–65	18–22	24-h recall	Fruit and vegetable	5	Stroke mortality Stroke incidence	14 97
Goetz, 2016 ⁷¹	REGARDS	United States	16 678	≥45	6.0±1.9	Validated FFQ	Fruit categories	5	CHD events	589
Goetz, 2016 ⁷²	REGARDS	United States	20 024 (9011:11 013)	≥45	6.5	Validated FFQ	Fruit, vegetable	5	Stroke incidence	524
Gunge, 2017 ⁷³	Danish Diet, Cancer and Health Cohort	Denmark	57 053 (25 759:28 809)	50–64	13.6	Validated FFQ	Fruit and vegetable categories	2	MI incidence	2322 (1669:653)
Gunnell, 2013 ⁷⁴	Health and Wellbeing Surveillance System	Australia	14 890 (6114:8776)	45–97	6	Validated FFQ	Fruit and vegetable	2	IHD hospitalization	538
Hansen, 2010 ⁷⁶	Danish Diet, Cancer and Health	Denmark	53 383 (25 065:28 318)	50–64	7.7	Validated FFQ	Fruit, vegetable categories	4	Acute coronary syndrome	1075 (820:255)
Hansen, 2017 ⁷⁵	Danish Diet, Cancer and Health	Denmark	55 338	50–64	13.5	Validated FFQ	Fruit and vegetable categories	2	Stroke incidence	2283
Harriss, 2007 ⁷⁷	Melbourne Collaborative	Australia	40 653 16 673:23 980	40–69	10.4	Validated FFQ	Fruit, vegetable	4	CVD mortality IHD mortality	697 407
Hertog, 1997 ⁷⁸	Caerphilly Prospective Study	South Wales	1900 (1900:0)	45–59	14.6	Validated FFQ	Vegetable categories	4	IHD mortality	131
Hirvonen, 2000 ⁸⁰	Finnish Male Smokers in the ATBC Study	Finland	26 497 (26 497:0)	50–69	6.1	Validated FFQ	Fruit category	4	Cerebral infarction Subarachnoid hemorrhage Intracerebral hemorrhage	736 83 95

(Continued)

Table. Continued

Study	Cohort	Country	Participants (Men:Women)	Age, y	Follow-Up, y	Dietary Assessment	Exposure	Quantiles	Outcomes	Incidence (Men:Women)
Hirvonen, 2001 ⁷⁹	Finnish Male Smokers in the ATBC Study	Finland	25, 373 (25, 373:0)	50–69	6.1	Validated FFQ	Fruit, vegetable, categories	5	CHD mortality MI event	815 1122
Hjartaker, 2015 ⁸¹	Migrant Study	Norway	9766 (9766:0)	42–73	20.3	Unvalidated FFQ	Fruit and/or vegetable, categories	4	CVD mortality CHD mortality Stroke mortality	4595 2386 1034
Hodgson, 2016 ⁸²	Australian Women aged 70–85 y	Australia	1456 0:1456	>70	15	Validated FFQ	Fruit category	3	CVD mortality	235
Holmberg, 2009 ⁸³	Swedish National Farm Register	Sweden	1738 (1738:0)	50±6.0	12	Unvalidated FFQ	Fruit and vegetable	2	CHD incidence	138
Iso, 2007 ⁸⁴	Japan Collaborative Cohort	Japan	N/A	40–79	N/A	Validated FFQ	Fruit or vegetable categories	3	IHD mortality CaVD mortality	N/A N/A
Jacques, 2015 ⁸⁵	Framingham Offspring	United States	2880 (1302:1578)	28–62 (mean=54)	14.9	Validated FFQ	Fruit categories	3	CVD incidence CHD incidence	518 261
Johnsen, 2003 ⁸⁶	Danish Diet, Cancer and Health	Denmark	54 506	50–64	3.09	Validated FFQ	Fruit and/or vegetable	5	Stroke incidence	266
Joshi, 1999 ⁸⁷	NHS and HPFS cohorts	United States	114 279 (38 683:75 596)	30–55 (men) 40–75 (women)	8 (men) 14 (women)	Validated FFQ	Fruit and/or vegetable, categories	5	Ischemic stroke incidence	570 (366:204)
Joshi, 2009 ⁸⁸	NHS and HPFS cohorts	United States	109 788 (38 918:70 870)	30–55 (men) 40–75 (women)	14–16	Validated FFQ	Fruit and/or vegetable, categories	5	CVD incidence	3892
Keli, 1996 ⁸⁹	Zutphen Elderly	The Netherlands	552 (552:0)	50–69	15	Interview	Fruit, vegetable categories	3	Stroke risk	42
Kim, 2013 ⁹⁰	British Women's Heart and Health Study	United Kingdom	3080 (0:3080)	60–79	7	Unvalidated FFQ	Fruit	2	CVD incidence	329
Knekt, 1994 ⁹³	Finnish Mobile Clinic Health	Finland	5133 (2748:2385)	30–69	14	Interview unvalidated FFQ	Fruit, vegetable	3	CHD mortality	244 (186:58)
Knekt, 1996 ⁹²	Finnish Mobile Clinic Health	Finland	5133 (2748:2385)	30–69	26	Interview unvalidated FFQ	Fruit or vegetable categories	4	CHD death	473 (324:149)
Knekt, 2000 ⁹¹	Finnish Mobile Clinic Health	Finland	9208	≥15	28	Interview unvalidated FFQ	Fruit or vegetable categories	5	CaVD incidence	824
Kobylecki, 2015 ⁹⁴	Copenhagen City Heart	Denmark	78 527	20–100	10	Self-reported unvalidated FFQ	Fruit and vegetable	3	IHD incidence	2823
Kondo, 2019 ⁹⁵	NIPPON DATA80	Japan	9115 (4002:5113)	30–79	29	3-d food record	Fruit or vegetable	3	CVD mortality	1070
Kvaavik, 2010 ⁹⁶	Health and Lifestyle Survey	United Kingdom	4866 (2509:2377)	43.7±16.3	20	Interview Unvalidated FFQ	Fruit and vegetable	2	CVD mortality	431

(Continued)

Table. Continued

Study	Cohort	Country	Participants (Men:Women)	Age, y	Follow-Up, y	Dietary Assessment	Exposure	Quantiles	Outcomes	Incidence (Men:Women)
Lai, 2015 ⁹⁷	UK Women's Cohort	United Kingdom	30 458 (0:30 458)	35–69	16.7	Validated FFQ	Fruit, categories	5–6	CVD mortality CHD mortality Stroke mortality	286 138 148
Larsson, 2009 ⁹⁸	Finnish Male Smokers in the ATBC Study	Finland	26 556 (26 556:0)	50–69	13.6	Validated FFQ	Fruit, vegetable	5	Stroke incidence	2702
Larsson, 2013 ⁹⁹	Swedish Mammography and Swedish Men Cohorts	Sweden	74 961 40 291:34 670	45–83	10.2	Validated FFQ	Fruit and/or vegetable, categories	5	Stroke incidence	4089
Leenders, 2013 ¹⁰¹	EPIC	Europe (10 countries)*	451 151 129 882:321 269	25–70	12.8 (median)	Validated FFQ and 7-d food record	Fruit and/or vegetable	4	CVD mortality	5125
Leenders, 2014 ¹⁰⁰	EPIC	Europe (10 countries)*	451 151 (129 882:321 269)	25–70	13	Validated FFQ and 7-d food record	Fruit and/or vegetable	4	CHD mortality Stroke mortality	2139 1291
Lin, 2007 ¹⁰²	NHS	United States	66 360 (0:66 360)	30–55	12	Validated FFQ	Fruit, vegetable, categories	5	CHD mortality MI event	324 938
Lin, 2017 ¹⁰³	Survey of Health & Living Status of the Elderly	Taiwan	4176	≥50	11	Interview FFQ	Fruit and vegetable	2	CVD mortality	N/A
Liu, 2000 ¹⁰⁵	Women's Health Study	United States	39 127 (0:39 127)	45–89	5	Validated FFQ	Fruit and/or vegetable	5	CVD incidence MI event	418 126
Liu, 2001 ¹⁰⁴	The Physician's Health Study	United States	15 520 (15 520:0)	40–84	6	Validated FFQ	Vegetable	5	CHD incidence	1148
Mann, 1997 ¹⁰⁶	The Oxford Vegetarian Study	United Kingdom	10 802 (4102:6700)	16–79	13.3	Validated FFQ	Fruit, vegetable, categories	3	IHD mortality	64
Manuel, 2015 ¹⁰⁷	Canadian Community Health Survey	Canada	82 259 (37 483:44 746)	20–83 (men: 48.2; women: 49.4)	8.6	Interview FFQ	Fruit and vegetable	3	Stroke incidence	1551
Miller, 2017 ¹⁰⁸	PURE (Prospective Urban and Rural Epidemiology)	18 Countries†	135 335	35–70	7.4 (Median)	Validated FFQ	Fruit and/or vegetable	4	CVD events MI Stroke Cardiovascular mortality	4784 N/A N/A N/A
Mink, 2007 ¹⁰⁹	Iowa Women's Health	United States	34 492 (0:34 492)	55–69	16	Validated FFQ	Fruit or vegetable categories	3	CVD mortality CHD mortality Stroke mortality	2316 1329 469

(Continued)

Table. Continued

Study	Cohort	Country	Participants (Men:Women)	Age, y	Follow-Up, y	Dietary Assessment	Exposure	Quantiles	Outcomes	Incidence (Men:Women)
Mizrahi, 2009 ¹⁰	Finnish Mobile Clinic Health Examination Survey	Finland	3932	40–74	24	Interview	Fruit, vegetable, categories	4	Stroke risk	625
Mori, 2018 ¹¹	Japan Public Health Center Based Prospective Study	Japan	88 184 (40 622:47 562)	45–74	16.9	Validated FFQ	Vegetable categories	5	CHD mortality Stroke mortality	1968 (1192:776) 1470 (856:614)
Mytton, 2018 ¹²	EPIC-Norfolk	England	22 992 (10 002:12 990)	40–79	16.4	7-d food record	Fruit and vegetable	5	CVD incidence	4965
Nagura, 2009 ¹³	Japan Collaborative	Japan	59 485 (25 206:34 279)	40–79	12.7	Validated FFQ	Fruit, vegetable	4	CVD mortality CHD mortality Stroke mortality	2243 (1207:1036) 452 (258:194) 1053 (559:494)
Nakamura, 2008 ¹⁴	Takayama	Japan	29 079 (13 355:15 724)	≥35 (men: 54.0; women: 55.1)	7.33	Validated FFQ	Fruit, vegetable	4	CVD mortality	384 (200:184)
Nechuta, 2010 ¹⁵	Shanghai Women's Health	China	71 243 (0:71 243)	40–70	9	Interview Validated FFQ	Fruit and vegetable	Daily	CVD mortality	775
Neelakantan, 2018 ¹⁶	Singapore Chinese Health Study	China	57 078	45–74	17	Validated FFQ	Fruit or vegetable	1 Serving/d	CVD mortality	4871
Ness, 2005 ¹⁷	Boyd Orr Cohort	United Kingdom (England and Scotland)	4028 (1995:2033)	3.5–11.2	37	Household survey	Fruit, vegetable	4	CHD mortality Stroke mortality	298 83
Nothlings, 2008 ¹⁸	EPIC	Europe (10 countries) [†]	10 262	35–70	9	Validated FFQ	Fruit or vegetable	80 g/d	CVD mortality	517
Okuda, 2015 ¹⁹	NIPPON DATA80	Japan	9112 (4000:5112)	30–79	24	Household survey	Fruit and/or vegetable	4	CVD mortality CHD mortality Stroke mortality	823 165 385
Oude Griep, 2010 ²⁰	MORGEN	The Netherlands	19 819	20–59	10.5	Validated FFQ	Fruit, vegetable	4	CHD incidences	245
Oude Griep, 2011 ²²	MORGEN	The Netherlands	20 069 (8988:11 081)	20–68	10.3	Validated FFQ	Fruit and vegetable	4	Stroke incidence	233
Oude Griep, 2011 ²¹	MORGEN	The Netherlands	20 069 (8989:11 081)	42±11	10.5	Validated FFQ	Fruit or vegetable categories	3–4	CHD incidence	245
Oyebode, 2014 ²³	HSE (Health Survey for England)	England	65 226 (28 960:36 266)	56.6±14.3	7.7	24-h recall	Fruit and/or vegetable	4	CVD mortality	1554
Pham, 2007 ²⁴	Miyako Study	Japan	9651 (4254:5397)	Men: 56.5±10.63; women: 57.4±10.89 (mean±SD)	13.8	Questionnaire	Fruit, vegetable	2	Stroke mortality	226
Rebello, 2014 ²⁵	Singapore Chinese Health Study	China	53 469 (23 501:29 968)	45–7	15	Interview validated FFQ	Fruit and vegetable	5	IHD mortality	1660 (1022:638)

(Continued)

Table. Continued

Study	Cohort	Country	Participants (Men:Women)	Age, y	Follow-Up, y	Dietary Assessment	Exposure	Quantiles	Outcomes	Incidence (Men:Women)
Rissanen, 2003 ¹²⁶	Kuopio Ischaemic Heart Disease Risk Factor	Finland	1950 (1950:0)	42–60	12.8	4-d food record	Fruit and vegetable	5	CVD mortality	115
Saglimbene, 2017 ¹²⁷	DIET-HD	Europe and South America	9757	N/A	1.5	Validated FFQ	Fruit, categories	2	CVD mortality	N/A
Sahyoun, 1996 ¹²⁸	Nutrition Status Study	United States	680	60–101	9–12	3-d food record	Fruit, vegetable, categories	3	CHD mortality	101
Sauvaaget, 2003 ¹²⁹	Life Span Study	Japan	39 337 (14 966:23 471)	34–103	16	Validated FFQ	Fruit, vegetable, categories	3	Stroke mortality	1926 (692:1234)
Scheffers, 2019 ¹³⁰	EPIC Netherlands and MORGEN	The Netherlands	34 560 (25 574:39 886)	20–69	14.6	Validated FFQ	Fruit and categories	5	CVD incidence CHD incidence Stroke incidence	3801 2135 1135
Sesso, 2003 ¹³¹	WHS (Women's Health Study)	United States	38 445 (0:38 445)	45–89	6.9	Validated FFQ	Fruit or vegetable categories	4	CVD incidence	729
Sesso, 2003 ¹³³	WHS	United States	38 445 (0:38 445)	≥45	7.2	Validated FFQ	Vegetable categories	5	CVD incidence MI incidence Stroke incidence	729 201 247
Sesso, 2007 ¹³²	WHS	United States	38 176 (0:38 176)	54.5	10.1	Validated FFQ	Fruit category	4	CVD mortality CVD incidence MI incidence Stroke incidence	204 1004 289 339
Shah, 2018 ¹³⁴	Cooper Center Longitudinal Study	United States	11 376 (8577:2799)	47	18	3-d food record	Fruit or vegetable	Continuous	CVD mortality	249
Sharma, 2013 ¹³⁵	Multi Ethnic Cohort	United States	174 028 (78 410:95 618)	45–75	7.5	Validated FFQ	Fruit, vegetable	5	Stroke mortality	860 (434:426)
Sharma, 2014 ¹³⁶	Multi Ethnic Cohort	United States	164 617 (72 866:91 751)	45–75	5–8	Validated FFQ	Fruit, vegetable	5	IHD mortality	1951 (1140:811)
Simila, 2013 ¹³⁷	ATBC	Finland	21 955 (21 955:0)	50–69	19	Validated FFQ	Fruit, fruit juices	Daily	CHD risk	4379
Sonestedt, 2015 ¹³⁸	Malmö Diet and Cancer	Sweden	26 445 (10 048:16 397)	44–74	14	Validated FFQ	Fruit, vegetable	5	CVD incidence CHD incidence Stroke incidence	2921 N/A N/A
Sotomayor, 2018 ¹³⁹	Renal Transplant Recipients	The Netherlands	400 (217:183)	52±12	7.2	Unvalidated FFQ	Fruit	3	CVD mortality	49
Steffen, 2003 ¹⁴⁰	ARIC (Atherosclerosis Risk in Communities)	United States	11 940 (5271:6669)	45–64 (men: 54.4±5.7; women: 54.1±5.7)	11	Interview validated FFQ	Fruit and vegetable	5	CHD incidence Ischemic stroke incidence	535 214

(Continued)

Table. Continued

Study	Cohort	Country	Participants (Men:Women)	Age, y	Follow-Up, y	Dietary Assessment	Exposure	Quantiles	Outcomes	Incidence (Men:Women)
Stefler, 2016 ¹⁴¹	HAPIEE (Health, Alcohol and Psychosocial Factors in Eastern Europe)	Poland, Russia, Czech Republic	19 263	57	7.1	Validated FFQ	Fruit and/or vegetable	4	CVD mortality CHD mortality Stroke mortality	438 226 109
Strandhagen, 2000 ¹⁴²	Men Born in 1913	Sweden	730 (730:0)	54	26	Interview unvalidated FFQ	Fruit, vegetable	5	CVD mortality CVD incidence	226 209
Takachi, 2008 ¹⁴³	Japan Public Health Center Based Prospective Study	Japan	77 891 (35 909:41 982)	45–74	5.9	Validated FFQ	Fruit and/or vegetable, categories	4	CVD incidence	1386 (830:556)
Tanaka, 2013 ¹⁴⁴	Japan Diabetes Complications Study	Japan	1414	40–70	8.1 (Median)	Validated FFQ	Fruit and vegetable	4	CHD incidence Stroke incidence	96 68
Tognon, 2014 ¹⁴⁵	MONICA	Denmark	1849 (901:948)	30–59	11	Food record	Fruit, vegetable	2	CVD mortality CVD incidence MI mortality MI incidence Stroke mortality Stroke incidence	223 755 64 161 40 167
Tucker, 2005 ¹⁴⁶	Baltimore Longitudinal Study of Aging	United States	501 (501:0)	34–80	18	7-d food record	Fruit and/or vegetable	2	CHD mortality	71
Von Ruesten, 2013 ¹⁴⁷	EPIC	Germany	23 531 (9098:14 433)	35–65	8	Validated FFQ	Fruit, vegetable, categories	Daily	CVD incidence	363
Vormund, 2015 ¹⁴⁸	MONICA	Switzerland	17 861 (8663:9198)	16–92	21.4 (Mean)	24-h recall	Fruit, vegetable	Daily	CVD mortality	1385
Wang, 2016 ¹⁴⁹	Linxian Nutrition Intervention Trials	China	2455 (1105:1340)	40–69	19–26	Unvalidated FFQ	Fruit and/or vegetable, categories	2	CHD mortality Stroke mortality	355 (men) 452 (women)
Watkins, 2000 ¹⁵⁰	CPS-11 (Cancer Prevention Study 11)	United States	1 063 023 (453 962:609 061)	≥30	7	Unvalidated FFQ	Vegetable		CHD mortality	13 761 (9156:4605)
Whiteman, 1999 ¹⁵¹	OXCHECK	United Kingdom	10 522 (4929:5593)	35–64	9	Unvalidated FFQ	Fruit, green vegetables	2–3	IHD mortality	144
Yamada, 2011 ¹⁵²	Jidhi Medical School Cohort	Japan	10 623 (4147:6476)	N/A	10.7	Validated FFQ	Fruit category	5	CVD event MI event Stroke event	758 (270:488) 565 (383:182) 99 (76:23)
Yokoyama, 2000 ¹⁵³	Shibata Study	Japan	2121 (880:1241)	≥40	20	Unvalidated FFQ	Fruit, vegetable	3	Stroke incidence	196 (91:105)

(Continued)

Table. Continued

Study	Cohort	Country	Participants (Men:Women)	Age, y	Follow-Up, y	Dietary Assessment	Exposure	Quantiles	Outcomes	Incidence (Men:Women)
Yoshizaki, 2019 ¹⁶⁴	Japan Public Health Centre Based Prospective Study	Japan	16 498 (7726:8772)	45–74	14	Validated FFQ	Fruit and/or vegetable	3	CHD incidence Stroke incidence	839 197
Yu, 2014 ¹⁵⁵	Shanghai Men and Women's Health Study	China	122 635 (55 424:67 211)	40–74	5.4–9.8	Interview validated FFQ	Fruit and/or vegetable, categories	4	CHD incidence	365 (217:148)
Zhang, 2011 ¹⁵⁶	Shanghai Men and Women's Health Study	China	134 796 (61 436:73 360)	40–74 40–70	4.5 10.2	Interview validated FFQ	Fruit, vegetable, and categories	5	CVD mortality	5393 (1951:3442)
Zhang, 2011 ¹⁵⁷	MONICA	Finland	36 686 (17 287:19 399)	25–74	13.7	24-h recall	Fruit, veg	4	Stroke incidence	1478

ATBC, alpha-tocopherol, beta-carotene cancer prevention; CeVD indicates cerebrovascular disease; CHD, coronary heart disease; CVD, cardiovascular disease; DIET-HD, dietary intake, death and hospitalization in adult with early stage kidney disease treated with hemodialysis; EPIC, European Prospective Investigation into Cancer and Nutrition; FFQ, Food Frequency Questionnaire; IHD, ischemic heart disease; MI, myocardial infarction; MONICA, monitoring of trends and determinants in cardiovascular disease; MORGENT, monitoring project on risk factors for chronic diseases; N/A, Not Available; NHANES, National Health and Nutrition Examination Survey; NIPPON DATA80, National Integrated Project for Prospective Observation of non-communicable disease and its trends in aged; and OXCHECK, Oxford and Collaborators health check.

*The EPIC cohort represented the following countries: France, Germany, Greece, Italy, the Netherlands, Spain, United Kingdom, Sweden, Denmark, and Norway.

†The PURE cohort represented the following countries: high income: Canada, Sweden, United Arab Emirates; middle income: Argentina, Brazil, Chile, China, Colombia, Iran, Malaysia, Poland, South Africa, Turkey, Occupied Palestinian Territory; low income: Bangladesh, India, Pakistan, Zimbabwe.

between fruit juice, cruciferous, green leafy, and tomato vegetables, and CHD and stroke mortality and citrus and stroke mortality as >35% of the pooled risk estimate was derived from Iso et al,⁸⁴ which was scored 5 on the NOS. The association between apricots and CVD mortality was derived from one study, Saglimbene et al,¹⁵⁸ which was scored 1 on the NOS. Although most studies had scores reduced because of self-administered ascertainment of exposure, 88% of studies received a total score ≥ 6 , which was considered high quality.

Cardiovascular Disease CVD Incidence

Figure 2 and Figures S1 through S11 show the relation of total and specific fruit and vegetables with CVD incidence. We found a lower risk associated with the highest versus the lowest intakes of fruits and vegetables (RR, 0.93 [95% CI, 0.89–0.96], no significant heterogeneity), fruits (RR, 0.91 [95% CI, 0.88–0.95], no significant heterogeneity), and vegetables (RR, 0.94 [95% CI, 0.90–0.97], no significant heterogeneity). Figures S12 and S13 summarize the relation of sources of fruit or vegetables with CVD incidence. A significant interaction by fruit source was observed ($P<0.001$), with significant associations with lower risk limited to citrus (RR, 0.88 [95% CI, 0.80–0.86], no significant heterogeneity) and pommes (RR, 0.76 [95% CI, 0.66–0.88], no significant heterogeneity). We found no significant associations from the highest versus lowest intakes of berries (RR, 1.27 [95% CI, 0.95–1.71], heterogeneity not applicable) and juice (RR, 1.00 [95% CI, 0.93–1.07], no significant heterogeneity) fruit. No interaction by vegetable source was observed ($P=0.227$).

CVD Mortality

Figure 3 and Figures S14 through S30 show the relation of total and specific fruit and vegetables with CVD mortality. We found a lower risk associated with the highest versus the lowest intakes of fruits and vegetables (RR, 0.89 [95% CI, 0.85–0.93], substantial heterogeneity [$I^2=68\%$, $P<0.001$]), fruits (RR, 0.88 [95% CI, 0.86–0.91], substantial heterogeneity [$I^2=79\%$, $P<0.001$]), and vegetables (RR, 0.87 [95% CI, 0.85–0.90], substantial heterogeneity [$I^2=59\%$, $P<0.001$]). Figures S31 and S32 summarize the association of sources of fruits or vegetables with CVD mortality. A significant interaction by fruit ($P=0.001$) and vegetable sources ($P<0.001$) was observed with significant associations with lower risk limited to pommes fruit (RR, 0.86 [95% CI, 0.80–0.92], no significant heterogeneity) and to allium (RR, 0.33 [95% CI, 0.22–0.49], heterogeneity not applicable), cruciferous (RR, 0.85 [95% CI, 0.82–0.89], no significant heterogeneity), and green leafy (RR, 0.87 [95% CI, 0.81–0.94], substantial heterogeneity [$I^2=88\%$, $P<0.001$]) vegetables. There was

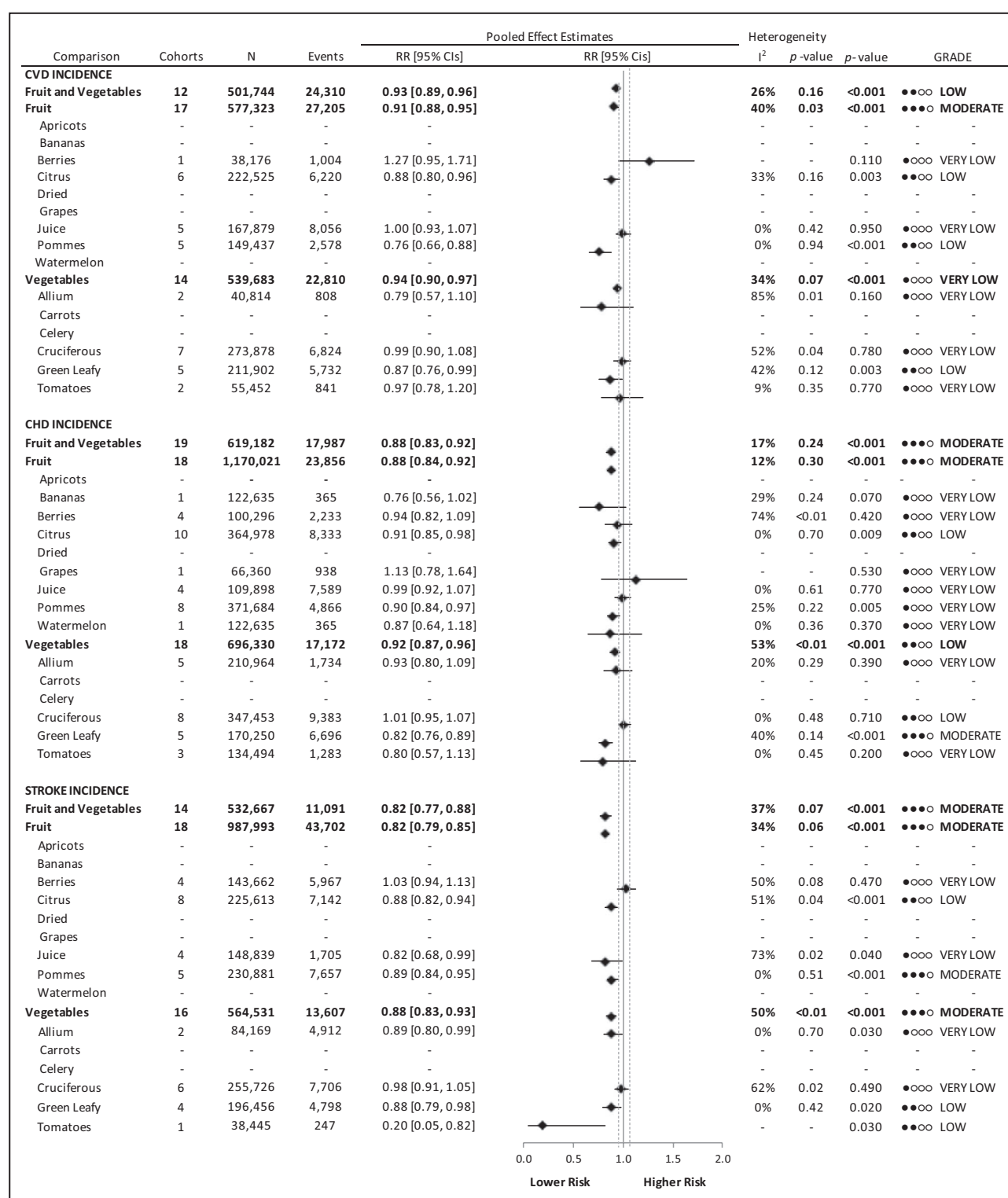


Figure 2. Relation between intake of fruits and vegetables and total incident cardiovascular disease (CVD) (highest vs lowest level of intake).

Pooled risk estimates are represented by the black diamond, with principal exposures highlighted in bold. Principal exposures (fruits and vegetables, fruits, and vegetables) represent the pooled data of the risk estimates reported for these exposures and were not tabulated by pooling fruit and vegetable varieties. Values of $I^2 \geq 50\%$ indicate substantial heterogeneity, with significance at $P > 0.10$. The mean important difference of 5% change in relative risk, indicating a clinically relevant association with lower or higher risk, is indicated by the dashed gray lines. CHD indicates coronary heart disease; GRADE, Grading of Recommendations Assessment, Development, and Evaluation; and RR, risk ratio.

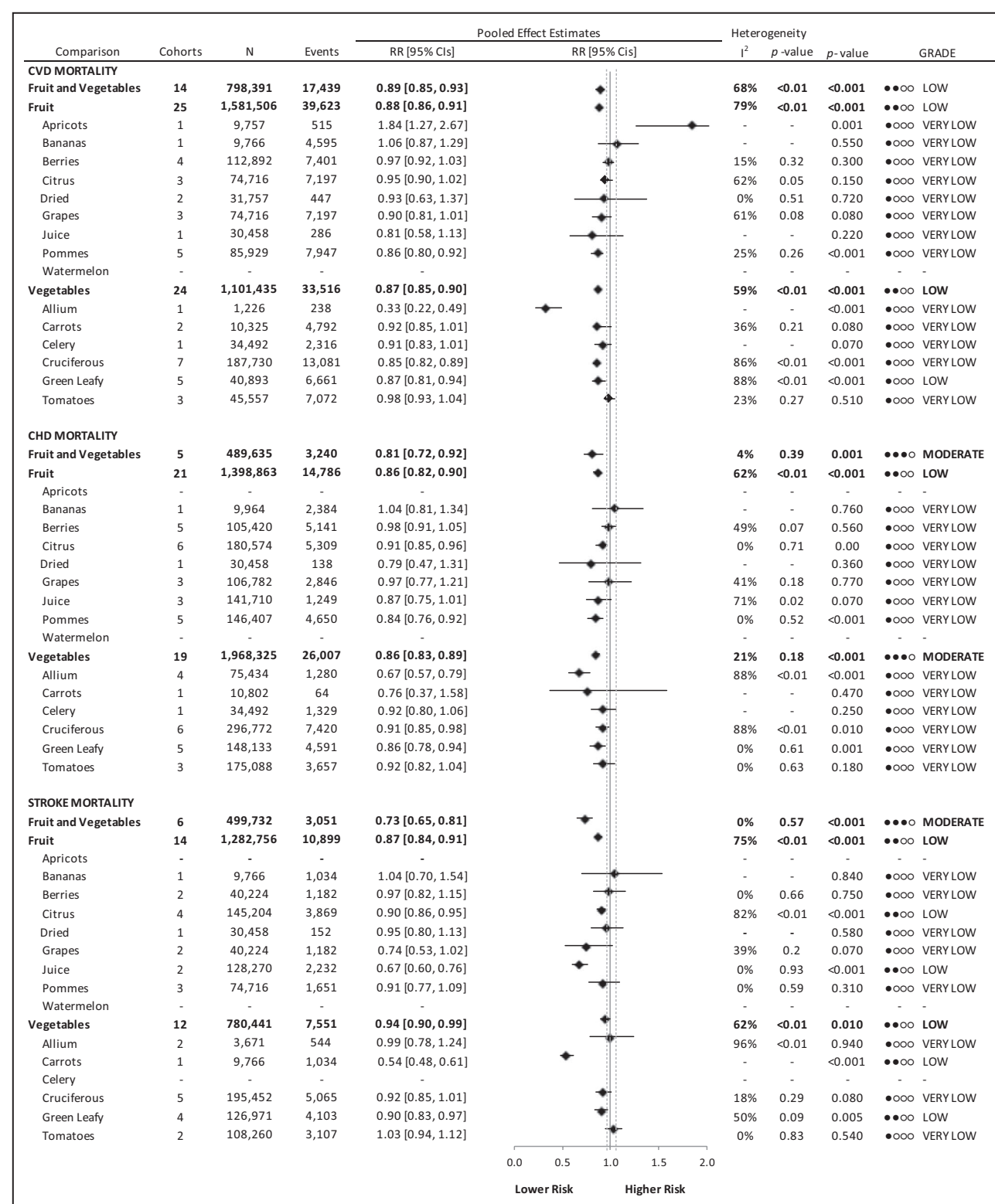


Figure 3. Relation between intake of fruits and vegetables and cardiovascular mortality (highest vs lowest level of intake). Pooled risk estimates are represented by the black diamond, with principal exposures highlighted in bold. Principal exposures (fruits and vegetables, fruits, and vegetables) represent the pooled data of the risk estimates reported for these exposures and were not tabulated by pooling fruit and vegetable varieties. Values of $I^2 \geq 50\%$ indicate substantial heterogeneity, with significance at $P > 0.10$. The mean important difference of 5% change in relative risk, indicating a clinically relevant association with lower or higher risk, is indicated by the dashed gray lines. CHD indicates coronary heart disease; CVD, cardiovascular disease; GRADE, Grading of Recommendations Assessment, Development, and Evaluation; and RR, risk ratio.

a significant increased risk with CVD mortality from the highest versus lowest intake of apricots (RR, 1.84 [95% CI, 1.27–2.67], heterogeneity not applicable). We found no significant associations from the highest versus lowest intakes of bananas (RR, 1.06 [95% CI, 0.87–1.29], heterogeneity not applicable), berries (RR, 0.97 [95% CI, 0.92–1.03], no significant heterogeneity), citrus (RR, 0.95 [95% CI, 0.90–1.02], substantial heterogeneity [$I^2=62\%$, $P=0.049$]), juice (RR, 0.81 [95% CI, 0.58–1.13], heterogeneity not applicable), and grapes (RR, 0.90 [95% CI, 0.81–1.01], substantial heterogeneity [$I^2=61\%$, $P=0.077$]) fruit and carrots (RR, 0.92 [95% CI, 0.85–1.01], no significant heterogeneity), celery (RR, 0.91 [95% CI, 0.83–1.01], heterogeneity not applicable), and tomato (RR, 0.98 [95% CI, 0.93–1.04], no significant heterogeneity) vegetables.

Figures S33 through S55 show the dose-response analyses for total and specific fruit and vegetables and CVD incidence and mortality. A nonlinear model best fit the data for citrus fruit and incident CVD ($P=0.033$), with a plateau at 0.5 servings/day, total fruits and vegetables with CVD mortality ($P<0.001$), with a plateau at 4 daily servings, and fruits and CVD mortality ($P=0.003$), with a plateau in risk reduction after 2 daily servings. An inverse dose-response gradient was found for the following associations: total fruits and vegetables (RR, 0.97 [95% CI, 0.96–0.99] per serving/day), fruits (RR, 0.97 [95% CI, 0.95–0.99] per serving/day), pomes (RR, 0.87 [95% CI, 0.75–0.99] per serving/day), and green leafy vegetables (RR, 0.72 [95% CI, 0.56–0.93]) with CVD incidence and total fruits and vegetables (RR, 0.72 [95% CI, 0.56–0.93] per serving/day), fruits (RR, 0.92 [95% CI, 0.89–0.96] per serving/day), and vegetables (RR, 0.94 [95% CI, 0.92–0.97] per serving/day) with CVD mortality.

Coronary Heart Disease

CHD Incidence

Figure 2 and Figures S56 through S69 show the relation of total and specific fruit and vegetables with CHD incidence. We found a lower risk associated with the highest versus the lowest intakes of fruits and vegetables (RR, 0.88 [95% CI, 0.83–0.92], no significant heterogeneity), fruits (RR, 0.88 [95% CI, 0.84–0.92], no significant heterogeneity), and vegetables (RR, 0.92 [95% CI, 0.87–0.96], substantial heterogeneity [$I^2=53\%$, $P=0.002$]). Figures S70 and S71 summarize the relation of sources of fruits or vegetables with CHD incidence. No interaction by fruit source was observed ($P=0.375$). A significant interaction by vegetable sources was seen ($P<0.001$) with significant associations with lower risk limited to green leafy vegetables (RR, 0.82 [95% CI, 0.76–0.89], no significant heterogeneity). We found no significant associations from the highest versus lowest intakes

of allium (RR, 0.93 [95% CI, 0.80–1.09], no significant heterogeneity), cruciferous (RR, 1.01 [95% CI, 0.95–1.07], no significant heterogeneity), and tomato (RR, 0.80 [95% CI, 0.57–1.13], no significant heterogeneity) vegetables.

CHD Mortality

Figure 3 and Figures S72 through S87 show the relation of total and specific fruit and vegetables with CHD mortality. We found a lower risk associated with the highest versus the lowest intakes of fruits and vegetables (RR, 0.81 [95% CI, 0.72–0.92], no significant heterogeneity), fruits (RR, 0.86 [95% CI, 0.82–0.90], substantial heterogeneity [$I^2=62\%$, $P<0.001$]), and vegetables (RR, 0.86 [95% CI, 0.83–0.89], no significant heterogeneity). Figures S88 and S89 summarize the relation of sources of fruits or vegetables with CHD mortality. No significant interaction was found by fruit sources ($P=0.144$). A significant interaction by vegetable source was seen ($P=0.023$), with significant associations with lower risk limited to allium (RR, 0.67 [95% CI, 0.57–0.79], substantial heterogeneity [$I^2=88\%$, $P<0.001$]), cruciferous (RR, 0.91 [95% CI, 0.85–0.98], substantial heterogeneity [$I^2=88\%$, $P<0.001$]), and green leafy (RR, 0.86 [95% CI, 0.78–0.94], no significant heterogeneity) vegetables. We found no significant associations from the highest versus lowest intakes of carrots (RR, 0.76 [95% CI, 0.37–1.58], heterogeneity not applicable), celery (RR, 0.92 [95% CI, 0.80–1.06], heterogeneity not applicable), and tomato (RR, 0.92 [95% CI, 0.82–1.04], no significant heterogeneity) vegetables.

Figures S90 through S116 show the dose-response analyses for fruit and vegetables and CHD incidence and mortality. A nonlinear model best fit the data for citrus fruit ($P=0.005$) and green leafy vegetables ($P=0.004$) and incident CHD and total fruits and vegetables and CHD mortality ($P=0.044$), with plateaus in risk reductions following 0.5, 0.5, and 3 daily servings, respectively. An inverse dose-response was found in the associations between total fruits and vegetables (RR, 0.97 [95% CI, 0.96–0.98] per serving/day), fruits (RR, 0.96 [95% CI, 0.93–0.99] per serving/day), vegetables (RR, 0.98 [95% CI, 0.95–0.99] per serving/day), and green leafy vegetables (RR, 0.85 [95% CI, 0.76–0.94] per serving/day) with CHD incidence and fruits (RR, 0.94 [95% CI, 0.90–0.97] per serving/day) and vegetables (RR, 0.89 [95% CI, 0.83–0.96] per serving/day) with CHD mortality.

Stroke

Stroke Incidence

Figure 2 and Figures S117 through S127 show the relation of total and specific fruit and vegetables with

stroke incidence. We found a lower risk associated with the highest versus the lowest intakes of fruits and vegetables (RR, 0.82 [95% CI, 0.77–0.88], no significant heterogeneity), fruits (RR, 0.82 [95% CI, 0.79–0.85], no significant heterogeneity), and vegetables (RR, 0.88 [95% CI, 0.83–0.93], substantial heterogeneity [$I^2=50\%$, $P=0.006$]). Figures S128 and S129 summarize the relation of sources of fruits or vegetables with stroke incidence. A significant interaction by fruit ($P=0.017$) and vegetable sources ($P=0.044$) was observed with significant associations with lower risk limited to citrus (RR, 0.88 [95% CI, 0.82–0.94], substantial heterogeneity [$I^2=51\%$, $P=0.04$]), juice (RR, 0.82 [95% CI, 0.68–0.99], substantial heterogeneity [$I^2=73\%$, $P=0.02$]), and pommes (RR, 0.89 [95% CI, 0.84–0.95], no significant heterogeneity) fruit and to allium (RR, 0.89 [95% CI, 0.80–0.99], no significant heterogeneity), green leafy (RR, 0.88 [95% CI, 0.79–0.98], no significant heterogeneity), and tomato (RR, 0.20 [95% CI, 0.05–0.82], heterogeneity not applicable) vegetables. We found no significant associations from the highest versus lowest intakes of berries (RR, 1.03 [95% CI, 0.94–1.13], substantial heterogeneity [$I^2=50\%$, $P=0.078$]) fruit and cruciferous (RR, 0.98 [95% CI, 0.91–1.05], substantial heterogeneity [$I^2=62\%$, $P=0.022$]) vegetables.

Stroke Mortality

Figure 3 and Figures S130 through S144 show the relation of total and specific fruits and vegetables with stroke mortality. We found a lower risk associated with the highest versus the lowest intakes of fruits and vegetables (RR, 0.73 [95% CI, 0.65–0.81], no significant heterogeneity), fruits (RR, 0.87 [95% CI, 0.84–0.91], substantial heterogeneity [$I^2=75\%$, $P<0.001$]), and vegetables (RR, 0.94 [95% CI, 0.90–0.99], substantial heterogeneity [$I^2=62\%$, $P=0.001$]). Figures S145 and S146 summarize the relation of sources of fruit or vegetables with stroke mortality. A significant interaction by fruit ($P<0.001$) and vegetable sources ($P<0.001$) was observed with significant associations, with lower risk limited to citrus (RR, 0.90 [95% CI, 0.86–0.95], substantial heterogeneity [$I^2=82\%$, $P<0.001$]) and juice (RR, 0.67 [95% CI, 0.60–0.76], no significant heterogeneity) fruit and carrots (RR, 0.54 [95% CI, 0.48–0.61], heterogeneity not applicable) and green leafy (RR, 0.90 [95% CI, 0.83–0.97], substantial heterogeneity [$I^2=50\%$, $P=0.09$]) vegetables. We found no significant associations from the highest versus lowest intakes of bananas (RR, 1.04 [95% CI, 0.70–1.54], heterogeneity not applicable), berries (RR, 0.97 [95% CI, 0.82–1.15], no significant heterogeneity), grapes (RR, 0.74 [95% CI, 0.53–1.02], no significant heterogeneity), and pommes (RR, 0.91 [95% CI, 0.77–1.09],

no significant heterogeneity) fruit and allium (RR, 0.99 [95% CI, 0.79–1.24], substantial heterogeneity [$I^2=96\%$, $P<0.001$]), cruciferous (RR, 0.92 [95% CI, 0.85–1.01], no significant heterogeneity), and tomato (RR, 1.03 [95% CI, 0.94–1.12], no significant heterogeneity) vegetables.

Figures S147 through S171 show the dose-response analyses for fruit and vegetables and stroke mortality and incidence. A nonlinear model best fit the data for citrus fruit ($P=0.039$) and vegetables ($P=0.012$) and stroke incidence and fruit ($P<0.001$) and green leafy ($P=0.043$) vegetables and stroke mortality, with plateaus in risk reductions following 0.5, 1, 2, and >0.7 daily servings, respectively. An inverse dose-response gradient was found in the associations between total fruits and vegetables (RR, 0.95 [95% CI, 0.92–0.98] per serving/day), fruits (RR, 0.92 [95% CI, 0.88–0.96] per serving/day), citrus fruit (RR, 0.83 [95% CI, 0.69–0.98] per serving/day), pommes (RR, 0.87 [95% CI, 0.79–0.96] per serving/day), green leafy vegetables (RR, 0.88 [95% CI, 0.79–0.97] per serving/day), and tomatoes (RR, 0.67 [95% CI, 0.52–0.87] per serving/day) with stroke incidence and fruits and vegetables (RR, 0.93 [95% CI, 0.88–0.98] per serving/day), fruits (RR, 0.85 [95% CI, 0.78–0.92] per serving/day), vegetables (RR, 0.93 [95% CI, 0.87–0.99] per serving/day), citrus fruit (RR, 0.67 [95% CI, 0.57–0.80] per serving/day), fruit juice (RR, 0.54 [95% CI, 0.36–0.89] per serving/day), carrots (RR, 0.44 [95% CI, 0.28–0.69] per serving/day), and green leafy vegetables (RR, 0.85 [95% CI, 0.73–0.98] per serving/day) with stroke mortality.

Sensitivity Analyses

The systematic removal of each study did not modify the direction or significance of the association estimates or the evidence for heterogeneity (data not shown).

Subgroup Analyses

Figures S172 through S188 illustrate a priori categorical subgroup analyses. There were no statistically significant subgroup differences. Inverse associations were predominately limited to studies with statistical adjustments of ≥ 8 potential confounders. Confining analyses to studies using validated exposure assessment techniques did not alter the associations. No effect modification was seen by sex, age, follow-up duration, NOS, or study location.

Publication Bias

Figures S189 through S205 illustrate publication bias analyses for comparisons with at least 10 observations. Visual inspection and formal analysis with the Begg and Egger test did not show evidence of

publication bias in any comparison, except for vegetable intake with CVD ($P_{\text{Begg}}=0.015$, $P_{\text{Egger}}=0.004$), CHD ($P_{\text{Begg}}=0.018$, $P_{\text{Egger}}=0.004$), and stroke ($P_{\text{Begg}}=0.545$, $P_{\text{Egger}}=0.018$) mortality and fruit intake with stroke mortality ($P_{\text{Begg}}=0.820$, $P_{\text{Egger}}=0.031$), which were subsequently unsupported by the trim and fill test.

GRADING OF RECOMMENDATIONS ASSESSMENT, DEVELOPMENT, AND EVALUATION

Figures 2 and 3 and Tables S4 through S9 summarize the GRADE assessments. The certainty of the evidence was rated as “moderate” for 11, “low” for 21, and “very low” for 52 of the exposure-outcome relationships. Our certainty in the evidence was strongest for the associations of total fruits and vegetables with lower risks of CHD incidence and CHD and stroke mortality; fruits with lower risks of CVD, CHD, and stroke incidence; vegetables with lower risks of CHD mortality and stroke incidence; pomes fruit with lower risks of stroke incidence; and green leafy vegetables with lower risks of CHD incidence. The evidence was rated as “moderate” in each case, because of an upgrade for dose-response gradient in the absence of any downgrades. The associations for specific types of fruits and vegetables were rated largely as “very low,” because of downgrades for imprecision, risk of bias, indirectness, and/or inconsistency. The fixed effects model improved our certainty in the evidence for fruit and CVD incidence by improving precision of the pooled risk estimate. There were no other marked differences between the random effects and fixed effects models.

DISCUSSION

We conducted a systematic review and meta-analysis of 81 unique prospective cohorts involving 4 031 896 individuals and 125 112 cardiovascular events to assess the relation of total and specific fruit and vegetable consumption on CVD incidence and mortality outcomes. Pooled analyses of highest versus lowest consumption illustrate a lower risk in CVD, CHD, and stroke incidence or mortality by 7% to 27% from total fruit and vegetable intake, 9% to 18% from fruit intake, and 5% to 14% from vegetable intake. Of the specific fruit sources, highest versus lowest intakes of citrus and pomes fruit showed significant risk reductions in most CVD outcomes, from 9% to 12% and from 10% to 24%, respectively, and fruit juice showed a significant risk reduction in stroke incidence and mortality by 18% and 33%, respectively. Most notably of the vegetable categories, one daily serving of green leafy vegetables was associated

with 12% to 18% risk reduction in CVD, CHD, and stroke incidence and CHD mortality. There was a consistent linear dose-response between fruits and vegetables and CHD, with a maximum daily intake of 7 fruit and 7 vegetable servings showing a risk reduction of $\sim 20\%$ and $\sim 30\%$ in CHD incidence and mortality, respectively.

Findings in the Context of Existing Literature

Our findings are consistent with those of previous systematic review and meta-analyses, which also detected inverse associations between fruits and/or vegetables and CVD mortality and incident outcomes.^{10,14,159} Our analyses were in line with those reported most recently by Aune et al, who observed the lowest risk on CVD, CHD, and stroke from maximum intakes of total fruits and vegetables.¹⁰ This is despite our division of CVD outcomes differing significantly, with the present study distinguishing between mortality and incidence data. Our findings on individual fruits and vegetables were also relatively consistent, highlighting a high versus low intake of citrus and pomes fruit, fruit juice, and green leafy vegetables as protective on CVD outcomes, suggesting they may independently play a valuable role in the diet. Nonetheless, the current study benefited from the inclusion of updated and novel large prospective cohorts, namely, the SUN (Seguimiento University of Navarra)¹⁶⁰ and PURE (Prospective Urban and Rural Epidemiology)¹⁶¹ cohorts, which combined contributed an additional 152 342 individuals and 4896 events to our analyses.

Numerous mechanisms have been proposed to explain the benefits of fruit and vegetable consumption on the cardiovascular system. Perhaps the most supported hypothesis is through their essential contribution to total dietary fiber, an established modifier of CVD risk factors.^{162,163}

Fruits with highlighted benefits in the present review tend to be of low glycemic index, a characteristic with demonstrated CVD risk factor reductions.¹⁶⁴ Their consumption has also been associated with improved weight management¹⁶⁵ and decreased prevalence of obesity,¹⁶⁶ a risk factor attributed to 7% to 44% of CVD incidence,¹⁶⁷ likely because of their low energy density and displacement of high calorie foods in the diet. The relationships between the extensive list of micronutrients offered by fruits and vegetables and CVD risk reduction has also been widely explored. They are a key source of antioxidants in the diet, necessary for eradicating free radicals, and may defend against damaging lipid oxidation.¹⁶⁸ Individual sources may offer distinct benefits, such as green leafy vegetables, which are dense in dietary nitrates, a compound linked to reductions in early prognostic

markers of CVD.¹⁶⁹⁻¹⁷¹ Interestingly, however, we did not observe a benefit from high consumption of berries as the most concentrated fruit source of antioxidants. Several vasoactive minerals, such as potassium, magnesium, and calcium, are also obtained from fruits and vegetables in the diet.¹⁷²⁻¹⁷⁴ Although each mechanism may be individually biologically plausible, the complexity of the nutrient combinations cannot be underestimated. A whole food approach is necessary to evaluate their efficacy in CVD risk reduction as it can account for additive and multiplicative mechanisms.

Strengths and Limitations

Our systematic review and meta-analysis has several strengths. It provides a comprehensive synthesis of the available knowledge on consumption of fruits, vegetables, and their varieties and CVD outcomes of importance to public health and clinical practice. We included a systematic search strategy to ensure all published prospective cohort data were identified and used a priori established approaches to explore the pooled risk estimates, including dose-response analyses. Finally, the certainty of the evidence was assessed using the GRADE approach with the evidence upgraded in several cases for the presence of a protective inverse dose-response gradient for the association of total fruits and vegetables, fruits, vegetables, and green leafy vegetables with CVD outcomes.

There are also several limitations of our systematic review and meta-analysis. Although ≈90% of the included prospective cohort studies were of high quality, residual confounding (measured and unmeasured) cannot be ruled out in observational studies. This issue is addressed in the GRADE assessment, which starts observational studies as “low” certainty. We downgraded the certainty of evidence because of imprecision in 55 of the 84 associations as the upper 95% CI crossed the minimal clinically important difference of a 5% reduction in relative risk, from which evidence of harm could not be excluded in 30 associations. Because of limited number of observations, indirectness was also present in several cases and the lack of reported exposures for different tropical fruit limited our exploration of this fruit category. Another source of uncertainty leading to downgrades in the evidence was the presence of high risk of bias in several of the studies that presented data on specific sources of fruits and vegetables. Last, the evidence was downgraded for inconsistency based on the presence of substantial unexplained heterogeneity in 19 of the 84 associations.

Balancing the strengths and limitations, the certainty of the evidence was rated as “very low” to “low” for most of the exposure-outcome relationships for the association of fruits and vegetables with cardiovascular

outcomes. The highest (“moderate”) rated evidence was for the cardiovascular benefit of total fruits and vegetables, fruits, vegetables, pommes fruit, and green leafy vegetables. The least certainty was for other specific fruit and vegetable sources.

Implications

Addressing the low prevalence of adequate fruit and vegetable consumption remains an important global health target.¹⁷⁵ With average intakes of 1 and 1.7 servings of fruit and vegetables per day, respectively, in developed countries, such as the United States,¹⁵⁰ there is an opportunity to increase intakes to meet the established minimum recommendations of 5 daily servings and realize the cardiovascular benefits.¹⁷⁶ We observed a linear dose relationship between fruits and vegetables and CHD and stroke risk, suggesting an increased cardiovascular benefit with additional servings and that targets beyond “5 a day” should also be considered. Successful strategies for increasing fruit and vegetable intake, nevertheless, are lacking and may benefit from emphasizing a larger variety of sources. Our synthesis highlighted that different sources of fruit, including 100% fruit juice, are associated with comparable CVD risk reduction as that of vegetables. Public health guidance to limit the intake of certain fruit sources because of concerns related to their contribution to sugars may have unintended harm in preventing people from meeting fruit and vegetable targets for CVD risk reduction.

CONCLUSIONS

Current evidence supports the role of a variety of fruits and vegetables for CVD prevention. Higher intakes of fruits and/or vegetables are associated with improvements in all CVD outcomes, with fruit associated with the largest risk reductions. Greater benefits may be seen for some fruits, including citrus, pommes, and 100% fruit juice, and vegetables, including allium, cruciferous, and green leafy vegetables, supporting recommendations for emphasizing specific fruit and vegetable sources in dietary guidelines. No fruit and vegetable sources were adversely associated with CVD, including fruit sources of concern, such as 100% fruit juice and dried fruit. Our certainty in the evidence ranges from “very low” to “moderate,” with the least certainty for specific sources of fruits and vegetables and the highest certainty for broad categories. More research of specific food sources of fruits and vegetables is needed to improve our estimates.

ARTICLE INFORMATION

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Affiliations

From the Department of Nutritional Sciences, Faculty of Medicine, University of Toronto, Ontario, Canada (A.Z., F.A.-Y., S.B.M., T.A.K., V.V., E.J., L.A.L., C.W.K., D.J.J., J.L.S.); Clinical Nutrition and Risk Factor Modification Center, St. Michael's Hospital, Toronto, Ontario, Canada (A.Z., F.A.-Y., S.B.M., V.V., E.J., L.A.L., C.W.K., D.J.J., J.L.S.); Toronto 3D Knowledge Synthesis and Clinical Trial Unit, Toronto, Ontario, Canada (A.Z., F.A.-Y., S.B.M., T.A.K., L.A.L., C.W.K., D.J.J., J.L.S.); Li Ka Shing Knowledge Institute (V.V., L.A.L., D.J.J., J.L.S.) and Division of Endocrinology and Metabolism (V.V., L.A.L., D.J.J., J.L.S.), St. Michael's Hospital, Toronto, Ontario, Canada; Department of Medicine, Faculty of Medicine, University of Toronto, Ontario, Canada (V.V., L.A.L., D.J.J., J.L.S.); and College of Pharmacy and Nutrition, University of Saskatchewan, Saskatoon, Saskatchewan, Canada (C.W.K.).

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Zurbau is a part-time employee at INQUIS Clinical Research Ltd., a contract research organization. Khan reports he has received research support from the Canadian Institutes of Health Research (CIHR), the International Life Science Institute (ILSI), and National Honey Board. He has been an invited speaker at the Calorie Control Council Annual meeting for which he has received an honorarium. Vuksan has a Canadian (2410556) and American (7326.404) patent on the medical use of viscous fiber blend for reducing blood glucose for treatment of diabetes mellitus, increasing insulin sensitivity, and reduction in systolic blood pressure and blood lipids issued. Kendall has received grants or research support from the Advanced Food Materials Network, Agriculture and Agri-Foods Canada, Almond Board of California, American Peanut Council, Barilla, CIHR, Canola Council of Canada, International Nut and Dried Fruit Council, International Tree Nut Council Research and Education Foundation, Loblaw Brands Ltd, Pulse Canada, and Unilever. He has received in-kind research support from the Almond Board of California, American Peanut Council, Barilla, California Walnut Commission, Kellogg Canada, Loblaw Companies, Quaker (Pepsico), Primo, Unico, Unilever, and White Wave Foods/Danone. He has received travel support and/or honoraria from the American Peanut Council, Barilla, California Walnut Commission, Canola Council of Canada, General Mills, International Nut and Dried Fruit Council, International Pasta Organization, Loblaw Brands Ltd, Nutrition Foundation of Italy, Oldways Preservation Trust, Paramount Farms, Peanut Institute, Pulse Canada, Sun-Maid, Tate & Lyle, Unilever, and White Wave Foods. He has served on the scientific advisory board for the International Tree Nut Council, International Pasta Organization, McCormick Science Institute, and Oldways Preservation Trust. He is a member of the International Carbohydrate Quality Consortium, Executive Board Member of the Diabetes and Nutrition Study Group of the European Association for the Study of Diabetes (EASD), is on the Clinical Practice Guidelines Expert Committee for Nutrition Therapy of the EASD, and is a Director of the Toronto 3D Knowledge Synthesis and Clinical Trials foundation. Jenkins has received research grants from Saskatchewan Pulse Growers, the Agricultural Bioproducts Innovation Program through the Pulse Research Network, the Advanced Foods and Material Network, Loblaw Companies Ltd, Unilever, Barilla, the Almond Board of California, Agriculture and Agri-food Canada, Pulse Canada, Kellogg's Company, Canada, Quaker Oats, Canada, Procter & Gamble Technical Centre Ltd, Bayer Consumer Care, Springfield, NJ, Pepsi/Quaker, International Nut & Dried Fruit (INC), Soy Foods Association of North America, the Coca-Cola Company (investigator-initiated, unrestricted grant), Solae, Haine Celestial, the Sanitarium Company, Orafit, the International Tree Nut Council Nutrition Research and Education Foundation, the Peanut Institute, Soy Nutrition Institute, the Canola and Flax Councils of Canada, the Calorie Control

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He has been on the speaker's panel, served on the scientific advisory board, and/or received travel support and/or honoraria from the Almond Board of California, Canadian Agriculture Policy Institute, Loblaw Companies Ltd, the Griffin Hospital (for the development of the NuVal scoring system), the Coca-Cola Company, EPICURE, Danone, Diet Quality Photo Navigation, Better Therapeutics (FareWell), Verywell, True Health Initiative, Institute of Food Technologists, Soy Nutrition Institute, Herbalife Nutrition Institute, Saskatchewan Pulse Growers, Sanitarium Company, Orafit, the Almond Board of California, the American Peanut Council, the International Tree Nut Council Nutrition Research and Education Foundation, the Peanut Institute, Herbalife International, Pacific Health Laboratories, Nutritional Fundamentals for Health, Barilla, Metagenics, Bayer Consumer Care, Unilever Canada and Netherlands, Solae, Kellogg, Quaker Oats, Procter & Gamble, the Coca-Cola Company, the Griffin Hospital, Abbott Laboratories, the Canola Council of Canada, Dean Foods, the California Strawberry Commission, Haine Celestial, PepsiCo, the Alpro Foundation, Pioneer Hi-Bred International, DuPont Nutrition and Health, Spherix Consulting and White Wave Foods, the Advanced Foods and Material Network, the Canola and Flax Councils of Canada, the Nutritional Fundamentals for Health, Agri-Culture and Agri-Food Canada, the Canadian Agri-Food Policy Institute, Pulse Canada, the Saskatchewan Pulse Growers, the Soy Foods Association of North America, the Nutrition Foundation of Italy, Nutra-Source Diagnostics, the McDougall Program, the Toronto Knowledge Translation Group (St. Michael's Hospital), the Canadian College of Naturopathic Medicine, The Hospital for Sick Children, the Canadian Nutrition Society, the American Society of Nutrition, Arizona State University, Paolo Sorbini Foundation, and the Institute of Nutrition, Metabolism and Diabetes. He received an honorarium from the US Department of Agriculture to present the 2013 W.O. Atwater Memorial Lecture. He received the 2013 Award for Excellence in Research from the International Nut and Dried Fruit Council. He received funding and travel support from the Canadian Society of Endocrinology and Metabolism to produce mini cases for the Canadian Diabetes Association. He is a member of the International Carbohydrate Quality Consortium. His wife, Alexandra L Jenkins, is a director and partner of INQUIS Clinical Research for the Food Industry, his 2 daughters, Wendy Jenkins and Amy Jenkins, have published a vegetarian book that promotes the use of the low glycemic index plant foods advocated here, The Portfolio Diet for Cardiovascular Risk Reduction (Academic Press/Elsevier 2020 ISBN:978-0-12-810510-8) and and his sister, Caroline Brydson, received funding through a grant from the St. Michael's Hospital Foundation to develop a cookbook for one of his studies. 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He is a member of the European Fruit Juice Association Scientific Expert Panel and Soy

Nutrition Institute (SNI) Scientific Advisory Committee. He is on the Clinical Practice Guidelines Expert Committees of Diabetes Canada, European Association for the study of Diabetes (EASD), Canadian Cardiovascular Society (CCS), and Obesity Canada. He serves or has served as an unpaid scientific advisor for the Food, Nutrition, and Safety Program (FNSP) and the Technical Committee on Carbohydrates of ILSI North America. He is a member of the International Carbohydrate Quality Consortium (ICQC), Executive Board Member of the Diabetes and Nutrition Study Group (DNSG) of the EASD, and Director of the Toronto 3D Knowledge Synthesis and Clinical Trials foundation. His wife is an employee of AB InBev. The remaining authors have no disclosures to report.

Supplementary Materials

Tables S1–S9

Figures S1–S205

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Supplemental Material

Table S1. Search Strategy.

Search #	Medline 1946 to June 03, 2019	Embase 1946 to June 03, 2019	Cochrane Through to June 03, 2019
1	Vegetables/	exp vegetable/	Vegetables/
2	vegetable*.tw,kf.	vegetable*.tw,kw.	vegetable*.ti,ab,hw.
3	Vegetable Products/	1 or 2	1 or 2
4	or/1-3	fruit.mp.	fruit.mp.
5	fruit.mp.	exp Fruit/	Fruit/
6	exp Fruit/	4 or 5	4 or 5
7	5 or 6	3 or 6	3 or 6
8	4 or 7	cardiovascular disease/	cardiovascular diseases/
9	cardiovascular disease/	cardiovascular.tw,kw.	exp myocardial ischemia/
10	exp myocardial ischemia/	exp heart muscle ischemia/	cardiovascular.ti,ab,hw.
11	cardiovascular.tw,kf.	isch?em*.tw,kw.	isch?em*.ti,ab,hw.
12	isch?em*.tw,kf.	coronary.tw,kw.	coronary.ti,ab,hw.
13	coronary.tw,kf.	myocard*.tw,kw.	myocard*.ti,ab,hw.
14	myocard*.tw,kf.	angina.tw,kw.	angina.ti,ab,hw.
15	angina.tw,kf.	exp cerebrovascular disease/	exp cerebrovascular disorders/
16	exp cerebrovascular disorders/	stroke.tw,kw.	stroke*.ti,ab,hw.
17	stroke*.tw,kf.	cerebral vascular.tw,kw.	cerebral vascular.ti,ab,hw.
18	cerebral vascular.tw,kf.	cerebrovascular.tw,kw.	cerebrovascular.ti,ab,hw.
19	cerebrovascular.tw,kf.	Or / 8-18	Or / 8-
20	Or / 9-19	exp cohort analysis/	
21	exp cohort studies/	exp longitudinal study/	
22	cohort*.tw.	exp prospective study/	
23	controlled clinical trial.pt.	exp follow up/	
24	Epidemiologic methods/	cohort\$.tw.	
25	limit 24 to yr=1971-1988	Or / 20-24	
26	Or / 21- 25	7 and 19	
27	8 and 20	25 and 26	
28	26 and 27		

Table S2. Confounding Variables Among 117 Studies of Fruit and Vegetables and Cardiovascular Disease Outcomes.

Study	Adriouch, 2018 ⁴²	Appleby, 2002 ⁴³	Atkins, 2014 ⁴⁴	Bahadoran, 2017 ⁴⁵	Bazzano, 2002 ⁴⁶	Belin, 2011 ⁴⁷	Bendinelli, 2011 ⁴⁸	Berard, 2017 ⁴⁹	Bhupathiraju, 2013 ⁵⁰	Bingham, 2008 ⁵¹	Blekkhorst, 2017 ⁵²
No. of variables fully adjusted model	13	3	8	2	10	10	12	5	13	9	10
No. of multivariable models presented	1	1	2	2	2	1	2	1	2	1	8
Timing of measurement of confounding variables	BL	BL	BL	BL	BL, 1982-84, 86, 87, 92	BL	BL	BL	1984-86, q2y	BL	BL
Pre-specified primary confounding variables											
Age	✓	✓	✓		✓	✓	✓	✓	✓	✓	✓
Pre-specified secondary confounding variables											
Sex		✓	✓		✓		✓	✓		✓	N/A
Smoking	✓	✓	✓		✓	✓	✓		✓	✓	✓
BMI	✓		✓			✓			✓		✓
Physical activity	✓		✓		✓	✓	✓		✓	✓	✓
Alcohol	✓				✓		✓		✓	✓	✓
Blood pressure	✓					✓	✓			✓	
Energy	✓		✓		✓	✓	✓	✓	✓	✓	
Diabetes					✓	✓	✓				✓
Cholesterol						✓	✓			✓	✓
Other Confounding variables											
Education	✓				✓	✓	✓	✓			
Socioeconomic status			✓								✓
Menopause and/or hormone Use	✓						✓		✓		
Region/location											
Randomization treatment											✓
Ethnicity/nationality	✓				✓	✓					
Marital status											
Study center								✓			
Survey season	✓										
Employment status											
Follow-up duration											
Dietary Intake											
Vitamin/supplement					✓				✓		
Fruit and/or vegetable	✓										
Saturated fat											
Whole grains											
Fish/shellfish									✓		
Meat							✓				
Red meat									✓		
Dietary pattern score			✓	✓							
Processed meat											
Coffee											
Fibre											
Folate											
Sodium											
Vitamin E											
Disease History											
MI or family history of MI									✓		
CHD or family history of CHD											
CVD or family history of CVD				✓							
Medications											
ASA											✓
Other confounding variables not listed:	Sleep, WC								Cereal fibre, Trans fat	Weight	GFR

Table S2. Page 2/11

Study	Bos, 2014 ⁵³	Buijsse, 2008 ⁵⁴	BuilCosiales, 2016 ⁵⁶	BuilCosiales, 2017 ⁵⁵	Cassidy, 2012 ⁵⁷	Collin, 2019 ⁵⁸	Conrad, 2018 ⁵⁹	Dauchet, 2004 ⁶⁰	Dauchet, 2010 ⁶¹	Du, 2016 ⁶²
No. of variables fully adjusted model	7	15	17	14	13	12	10	10	12	13
No. of multivariable models presented	1	4	1	3	1	4	1	1	1	2
Timing of measurement of confounding variables	BL	BL	BL	1999, q2y	1976, q2y	BL	BL	BL	BL	BL
Pre-specified primary confounding variables										
Age	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
Pre-specified secondary confounding variables										
Sex	✓	✓	✓	✓	✓	✓	✓			✓
Smoking	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
BMI	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
Physical activity		✓	✓	✓	✓	✓		✓	✓	✓
Alcohol		✓	✓	✓	✓	✓				✓
Blood pressure	✓		✓	✓	✓			✓	✓	
Energy		✓	✓	✓	✓	✓				
Diabetes	✓		✓		✓			✓	✓	
Cholesterol					✓			✓	✓	
Other Confounding variables										
Education			✓	✓		✓	✓	✓	✓	✓
Socioeconomic status		✓				✓	✓			✓
Menopause and/or hormone Use					✓					
Region/location						✓				✓
Randomization treatment			✓							
Ethnicity/nationality							✓			
Marital status				✓						
Study center			✓					✓	✓	
Survey season										✓
Employment status								✓	✓	
Follow-up duration										
Dietary Intake										
Vitamin/supplement					✓				✓	
Fruit and/or vegetable			✓							
Saturated fat		✓				✓				
Whole grains			✓	✓						
Fish/shellfish										
Meat										✓
Red meat										
Dietary pattern score										
Processed meat										
Coffee										
Fibre		✓				✓				
Folate		✓								
Sodium										
Vitamin E										
Disease History										
MI or family history of MI										
CHD or family history of CHD	✓		✓	✓						
CVD or family history of CVD										
Medications										
ASA					✓					
Other confounding variables not listed:		Vitamin C, trans/PUFA, α -tocopherol	Olive oil, Statins	Dyslipidemia, Legumes, Olive oil			Cardiometabolic meds, added sugar, SFA:M/PUFA		Dyslipidemi	Dairy, Preserved vegetables

Table S2. Page 3/11

Study	Du, 2017 ⁶³	Elwood, 2013 ⁶⁴	Eriksen, 2015 ⁶⁵	Fitzgerald, 2012 ⁶⁶	Fraser, 1992 ⁶⁷	Gardener, 2011 ⁶⁸	Gaziano, 1995 ⁶⁹	Genkinger, 2004 ⁷⁰	Gillman, 1995 ⁷¹	Goetz, 2016 ⁷²	Goetz, 2016 ⁷³
No. of variables fully adjusted model	12	3	9	10	6	7	6	6	7	12	10
No. of multivariable models presented	14	1	1	1	1	1	1	2	1	1	1
Timing of measurement of confounding variables	BL	1979, q5y	BL	BL	BL	qy.	1976, qy	BL	BL	BL	BL
Pre-specified primary confounding variables											
Age	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
Pre-specified secondary confounding variables											
Sex	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
Smoking	✓		✓	✓	✓	✓	✓	✓	✓	✓	✓
BMI	✓		✓					✓	✓		
Physical activity	✓			✓	✓	✓			✓	✓	✓
Alcohol	✓		✓	✓						✓	
Blood pressure			✓								
Energy				✓	✓	✓		✓		✓	✓
Diabetes				✓			✓		✓		
Cholesterol			✓				✓	✓	✓		
Other Confounding variables											
Education	✓			✓		✓				✓	✓
Socioeconomic status	✓	✓	✓							✓	✓
Menopause and/or hormone Use				✓							
Region/location	✓									✓	✓
Randomization treatment				✓							
Ethnicity/nationality						✓					✓
Marital status											
Study center											
Survey season	✓										
Employment status			✓								
Follow-up duration											
Dietary Intake											
Vitamin/supplement											
Fruit and/or vegetable											
Saturated fat											
Whole grains											
Fish/shellfish											
Meat	✓										
Red meat											
Dietary pattern score											✓
Processed meat											
Coffee											
Fibre											
Folate											
Sodium											
Vitamin E											
Disease History											
MI or family history of MI											
CHD or family history of CHD											
CVD or family history of CVD											
Medications											
ASA											
Other confounding variables not listed:	Preserved vegetables				Weight		Functional status			Trans FA MUFA:SFA, %E sweets	

Table S2. Page 4/11

Study	Gunge, 2017 ⁷⁴	Gunnell, 2013 ⁷⁵	Hansen, 2010 ⁷⁷	Hansen, 2017 ⁷⁶	Harriss, 2007 ⁷⁸	Hertog, 1997 ⁷⁹	Hirvonen, 2000 ⁸¹	Hirvonen, 2001 ⁸⁰	Hjartaker, 2015 ⁸²	Hodgson, 2016 ⁸³	Holmberg, 2009 ⁸⁴
No. of variables fully adjusted model	18	10	11	13	15	13	10	11	9	15	0
No. of multivariable models presented	4	1	2	2	2	1	1	1	1	2	0
Timing of measurement of confounding variables	BL	BL	BL	BL	BL	BL, q5y	BL	BL	BL	BL	BL
Pre-specified primary confounding variables											
Age	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	
Pre-specified secondary confounding variables											
Sex	✓	✓	✓	✓	✓				✓	✓	
Smoking	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	
BMI	✓	✓	✓		✓	✓	✓	✓	✓	✓	
Physical activity	✓	✓	✓	✓	✓		✓	✓	✓	✓	
Alcohol	✓		✓	✓		✓			✓	✓	
Blood pressure	✓	✓	✓	✓	✓	✓	✓	✓		✓	
Energy	✓			✓	✓	✓				✓	
Diabetes				✓	✓		✓	✓		✓	
Cholesterol	✓	✓	✓	✓		✓	✓	✓		✓	
Other Confounding variables											
Education	✓		✓	✓	✓		✓	✓			
Socioeconomic status						✓			✓	✓	
Menopause and/or hormone Use	✓										
Region/location					✓						
Randomization treatment							✓	✓		✓	
Ethnicity/nationality					✓						
Marital status								✓			
Study center											
Survey season		✓		✓							
Employment status											
Follow-up duration	✓										
Dietary Intake											
Vitamin/supplement									✓		
Fruit and/or vegetable	✓				✓						
Saturated fat			✓								
Whole grains	✓		✓								
Fish/shellfish	✓										
Meat					✓						
Red meat	✓										
Dietary pattern score					✓						
Processed meat	✓										
Coffee									✓		
Fibre											
Folate											
Sodium											
Vitamin E						✓					
Disease History											
MI or family history of MI											
CHD or family history of CHD				✓		✓	✓	✓			
CVD or family history of CVD					✓					✓	
Medications											
ASA										✓	
Other confounding variables not listed:	WC	Charlson index, DM hospitalization		Weight		Vitamin C, B-carotene, Dietary fat				Cancer	

Table S2. Page 5/11

Study	Iso, 2007 ⁸⁵	Jacques, 2015 ⁸⁶	Johnsen, 2003 ⁸⁷	Joshiyura, 1999 ⁸⁸	Joshiyura, 2009 ⁸⁹	Keli, 1996 ⁹⁰	Kim, 2013 ⁹¹	Knekt, 1994 ⁹⁴	Knekt, 1996 ⁹³	Knekt, 2000 ⁹²	Kobylecki, 2015 ⁹⁵
No. of variables fully adjusted model	3	5	13	12	14	7	0	5	6	17	12
No. of multivariable models presented	1	2	2	1	198-86, q2y	1	0	2	1	1	3
Timing of measurement of confounding variables	BL	1991, q3-4y	BL	1980-6, q2y	1980-6, q2y	1960-73, 77, 85	BL	BL	BL	BL	BL
Pre-specified primary confounding variables											
Age	✓	✓	✓	✓	✓	✓		✓	✓	✓	✓
Pre-specified secondary confounding variables											
Sex	✓	✓	✓	✓					✓		✓
Smoking		✓	✓	✓	✓	✓		✓	✓	✓	✓
BMI		✓	✓	✓	✓				✓	✓	✓
Physical activity			✓	✓	✓						✓
Alcohol			✓	✓	✓	✓					✓
Blood pressure			✓	✓	✓	✓		✓	✓	✓	✓
Energy		✓	✓	✓	✓	✓		✓		✓	
Diabetes			✓	✓	✓					✓	
Cholesterol			✓	✓	✓	✓		✓	✓	✓	✓
Other Confounding variables											
Education			✓								
Socioeconomic status											✓
Menopause and/or hormone Use				✓	✓						
Region/location	✓									✓	
Randomization treatment											
Ethnicity/nationality											
Marital status											
Study center											
Survey season											
Employment status											
Follow-up duration											
Dietary Intake											
Vitamin/supplement				✓	✓						✓
Fruit and/or vegetable											
Saturated fat										✓	
Whole grains					✓						
Fish/shellfish						✓					
Meat											
Red meat			✓								
Dietary pattern score											
Processed meat											
Coffee											
Fibre										✓	
Folate											
Sodium											
Vitamin E										✓	
Disease History											
MI or family history of MI				✓							
CHD or family history of CHD					✓						
CVD or family history of CVD											
Medications											
ASA					✓						
Other confounding variables not listed:			Ω-3-FA							Occupation, Vit C/E, Querc P/MUFA	Maximal oxygen intake, CRP

Table S2. Page 6/11

Study	Kondo, 2019 ⁹⁶	Kvaavik, 2010 ⁹⁷	Lai, 2015 ⁹⁸	Larsson, 2009 ⁹⁹	Larsson, 2013 ¹⁰⁰	Leenders, 2013 ¹⁰²	Leenders, 2014 ¹⁰¹	Lin, 2007 ¹⁰³	Lin, 2017 ¹⁰⁴	Liu, 2000 ¹⁰⁶
No. of variables fully adjusted model	7	8	8	14	16	11	11	13	6	8
No. of multivariable models presented	1	2	2	2	2	1	1	2	1	3
Timing of measurement of confounding variables	BL	BL	BL	BL	BL	BL	BL	1990, q2y	BL	BL
Pre-specified primary confounding variables										
Age	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
Pre-specified secondary confounding variables										
Sex	✓	✓	✓	✓	✓	✓	✓		✓	
Smoking	✓		✓	✓	✓	✓	✓	✓		
BMI		✓	✓	✓	✓	✓	✓	✓	✓	
Physical activity			✓	✓	✓	✓	✓	✓		✓
Alcohol	✓		✓	✓	✓	✓	✓	✓		✓
Blood pressure		✓		✓	✓			✓	✓	✓
Energy	✓			✓	✓			✓		
Diabetes		✓		✓	✓	✓	✓	✓	✓	✓
Cholesterol				✓				✓		✓
Other Confounding variables										
Education					✓	✓	✓		✓	
Socioeconomic status		✓	✓							
Menopause and/or hormone Use								✓		
Region/location										
Randomization treatment				✓						✓
Ethnicity/nationality										
Marital status										
Study center						✓	✓			
Survey season										
Employment status										
Follow-up duration										
Dietary Intake										
Vitamin/supplement								✓		✓
Fruit and/or vegetable	✓		✓		✓	✓	✓			
Saturated fat										
Whole grains										
Fish/shellfish	✓									
Meat										
Red meat					✓		✓			
Dietary pattern score										
Processed meat					✓					
Coffee					✓					
Fibre										
Folate				✓						
Sodium	✓									
Vitamin E								✓		
Disease History										
MI or family history of MI					✓					
CHD or family history of CHD		✓								
CVD or family history of CVD				✓					✓	
Medications										
ASA					✓			✓		
Other confounding variables not listed:		Respiratory diseases		Magnesium						

Table S2. Page 7/11

Study	Liu, 2001 ¹⁰⁵	Mann, 1997 ¹⁰⁷	Manuel, 2015 ¹⁰⁸	Miller, 2017 ¹⁰⁹	Mink, 2007 ¹¹⁰	Mizrahi, 2009 ¹¹¹	Mori, 2018 ¹¹²	Mytton, 2018 ¹¹³	Nagura, 2009 ¹¹⁴	Nakamura, 2008 ¹¹⁵
No. of variables fully adjusted model	11	5	1	17	11	8	16	16	16	15
No. of multivariable models presented	2	1	1	1	2	1	3	2	3	3
Timing of measurement of confounding variables	BL	BL	BL	BL	BL	BL	BL	BL	BL	BL
Pre-specified primary confounding variables										
Age	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
Pre-specified secondary confounding variables										
Sex	✓	✓		✓		✓	✓	✓	✓	✓
Smoking	✓	✓		✓	✓	✓	✓	✓	✓	✓
BMI	✓	✓			✓	✓	✓		✓	✓
Physical activity	✓			✓	✓	✓	✓	✓	✓	✓
Alcohol	✓						✓	✓	✓	✓
Blood pressure	✓			✓	✓	✓	✓	✓	✓	✓
Energy				✓	✓	✓	✓	✓		✓
Diabetes	✓			✓	✓		✓	✓	✓	✓
Cholesterol	✓			✓		✓		✓		
Other Confounding variables										
Education				✓	✓			✓	✓	✓
Socioeconomic status		✓								
Menopause and/or hormone Use					✓					✓
Region/location				✓						
Randomization treatment	✓									
Ethnicity/nationality										
Marital status					✓					✓
Study center				✓			✓			
Survey season										
Employment status							✓			
Follow-up duration										
Dietary Intake										
Vitamin/supplement	✓						✓			
Fruit and/or vegetable				✓			✓		✓	
Saturated fat									✓	✓
Whole grains										
Fish/shellfish										
Meat										
Red meat				✓						
Dietary pattern score										
Processed meat										
Coffee							✓			
Fibre				✓						
Folate										
Sodium							✓		✓	✓
Vitamin E										
Disease History										
MI or family history of MI								✓		
CHD or family history of CHD										
CVD or family history of CVD										
Medications										
ASA										
Other confounding variables not listed:				Waist:hip, bread, white meat	Waist:hip		Green tea	Family hx of diabetes/ stroke	Sleep, stress, Ω-3 FA, diet cholesterol	Dietary protein

Table S2. Page 8/11

Study	Nechuta, 2010 ¹¹⁶	Neelakantan, 2018 ¹¹⁷	Ness, 2005 ¹¹⁸	Nothlings, 2008 ¹¹⁹	Okuda, 2015 ¹²⁰	Oude Griep, 2010 ¹²¹	Oude Griep, 2011 ¹²³	Oude Griep, 2011 ¹²²	Oyebode, 2014 ¹²⁴	Pham, 2007 ¹²⁵
No. of variables fully adjusted model	7	12	8	11	11	12	15	15	8	9
No. of multivariable models presented	2	1	2	2	3	3	3	3	2	1
Timing of measurement of confounding variables	BL	BL	BL	BL	BL	BL	BL	BL	2001, qy	BL
Pre-specified primary confounding variables										
Age	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
Pre-specified secondary confounding variables										
Sex	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
Smoking		✓		✓	✓	✓	✓	✓	✓	✓
BMI	✓	✓			✓		✓	✓	✓	✓
Physical activity	✓	✓							✓	
Alcohol				✓	✓	✓	✓	✓	✓	✓
Blood pressure		✓		✓						✓
Energy		✓	✓	✓	✓	✓	✓	✓		
Diabetes		✓		✓			✓	✓		✓
Cholesterol							✓	✓		
Other Confounding variables										
Education	✓	✓				✓	✓	✓	✓	
Socioeconomic status	✓		✓						✓	
Menopause and/or hormone Use						✓	✓	✓		
Region/location			✓							
Randomization treatment										
Ethnicity/nationality		✓								
Marital status	✓									
Study center										
Survey season			✓							
Employment status										
Follow-up duration										
Dietary Intake										
Vitamin/supplement						✓	✓	✓		
Fruit and/or vegetable		✓								✓
Saturated fat										
Whole grains		✓				✓	✓	✓		
Fish/shellfish		✓			✓	✓	✓	✓		
Meat					✓					
Red meat										
Dietary pattern score										
Processed meat						✓	✓	✓		
Coffee										
Fibre										
Folate										
Sodium					✓					
Vitamin E										
Disease History										
MI or family history of MI				✓		✓	✓	✓		
CHD or family history of CHD										
CVD or family history of CVD										
Medications										
ASA										
Other confounding variables not listed:		Sleep, nuts, legumes, dairy	Child food expenditure, Townsend	Cancer hx, insulin tx, Waist:Hip	Dairy, soy					Blood transfusion

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Study	Rebello, 2014 ¹²⁶	Rissanen, 2003 ¹²⁷	Saglimbene, 2017 ¹²⁸	Sahyoun, 1996 ¹²⁹	Sauvaget, 2003 ¹³⁰	Scheffers, 2019 ¹³¹	Sesso, 2003 ¹³²	Sesso, 2003 ¹³⁴	Sesso, 2007 ¹³³	Shah, 2018 ¹³⁵	Sharma, 2013 ¹³⁶
No. of variables fully adjusted model	20	10	N/A	4	13	12	16	16	18	10	7
No. of multivariable models presented	3	4	N/A	3	4	4	2	2	4	2	1
Timing of measurement of confounding variables	BL	BL	N/A	BL	BL	BL	BL	BL	BL	BL	BL
Pre-specified primary confounding variables											
Age	✓	✓		✓	✓	✓	✓	✓	✓	✓	
Pre-specified secondary confounding variables											
Sex		✓		✓	✓	✓				✓	
Smoking	✓	✓			✓	✓	✓	✓	✓	✓	✓
BMI	✓	✓			✓	✓	✓	✓	✓	✓	
Physical activity	✓				✓	✓	✓	✓	✓	✓	✓
Alcohol	✓				✓	✓	✓	✓	✓	✓	✓
Blood pressure	✓	✓			✓	✓	✓	✓	✓	✓	
Energy	✓							✓	✓		✓
Diabetes		✓			✓		✓	✓	✓	✓	
Cholesterol		✓				✓	✓	✓	✓	✓	
Other Confounding variables											
Education	✓				✓	✓					✓
Socioeconomic status											
Menopause and/or hormone Use	✓						✓	✓	✓		
Region/location					✓			✓	✓		
Randomization treatment							✓	✓	✓		
Ethnicity/nationality	✓										✓
Marital status											
Study center											
Survey season	✓										
Employment status											
Follow-up duration		✓									✓
Dietary Intake											
Vitamin/supplement		✓									
Fruit and/or vegetable							✓	✓	✓		
Saturated fat	✓						✓	✓			
Whole grains											
Fish/shellfish											
Meat											
Red meat	✓										
Dietary pattern score						✓					
Processed meat											
Coffee											
Fibre							✓	✓	✓		
Folate							✓	✓	✓		
Sodium											
Vitamin E							✓				
Disease History											
MI or family history of MI					✓		✓	✓	✓		
CHD or family history of CHD											
CVD or family history of CVD										✓	
Medications											
ASA											
Other confounding variables not listed:	Sleep, bread, legumes, soy egg, PUFA	Maximal oxygen		Functional status, Health	Birth cohort, animal prod, radiation				Vitamin C, flavonoid, potassium		

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Study	Sharma, 2014 ¹³⁷	Simila, 2013 ¹³⁸	Sonestedt, 2015 ¹³⁹	Sotomayer, 2019 ¹⁴⁰	Steffen, 2003 ¹⁴¹	Stefler, 2016 ¹⁴²	Strandhagen, 2000 ¹⁴³	Takachi, 2008 ¹⁴⁴	Tanaka, 2013 ¹⁴⁵	Tucker, 2005 ¹⁴⁷	Tognon, 2014 ¹⁴⁶
No. of variables fully adjusted model	5	2	14	16	12	12	5	11	21	10	6
No. of multivariable models presented	1	1	3	4	3	1	2	2	3	3	1
Timing of measurement of confounding variables	BL	BL	BL	BL	BL	BL	BL	BL	BL	1961, biennially	BL
Pre-specified primary confounding variables											
Age		✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
Pre-specified secondary confounding variables											
Sex			✓	✓	✓	✓	✓	✓	✓	✓	✓
Smoking	✓		✓	✓	✓	✓	✓	✓	✓	✓	✓
BMI	✓		✓	✓	✓			✓	✓	✓	✓
Physical activity	✓		✓	✓	✓	✓		✓	✓	✓	✓
Alcohol	✓		✓	✓	✓	✓		✓	✓	✓	
Blood pressure				✓	✓		✓	✓	✓		
Energy			✓		✓	✓		✓	✓	✓	
Diabetes	✓			✓				✓	✓		
Cholesterol				✓	✓		✓		✓		
Other Confounding variables											
Education			✓	✓	✓	✓					✓
Socioeconomic status				✓							
Menopause and/or hormone Use											
Region/location											
Randomization treatment		✓									
Ethnicity/nationality					✓						
Marital status						✓					
Study center								✓			
Survey season			✓								
Employment status											
Follow-up duration				✓						✓	
Dietary Intake											
Vitamin/supplement						✓		✓		✓	
Fruit and/or vegetable			✓			✓				✓	
Saturated fat									✓	✓	
Whole grains			✓								
Fish/shellfish			✓								
Meat			✓								
Red meat											
Dietary pattern score					✓						
Processed meat											
Coffee			✓								
Fibre											
Folate											
Sodium									✓		
Vitamin E											
Disease History											
MI or family history of MI											
CHD or family history of CHD											
CVD or family history of CVD											
Medications											
ASA											
Other confounding variables not listed:			Fermented milk	eGFR, proteinuria, primary renal disease, hsCRP		Birth cohort, house score			†		

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Study	Von Ruesten, 2013 ¹⁴⁸	Vormund, 2015 ¹⁴⁹	Wang, 2016 ¹⁵⁰	Watkins, 2000 ¹⁵¹	Whiteman, 1999 ¹⁵²	Yamada, 2011 ¹⁵³	Yokoyama, 2000 ¹⁵⁴	Yoshizaki, 2019 ¹⁵⁵	Yu, 2014 ¹⁵⁶	Zhang, 2011 ¹⁵⁷	Zhang, 2011 ¹⁵⁸
No. of variables fully adjusted model	11	8	7	17	3	11	9	17	13	17	11
No. of multivariable models presented	2	3	1	1	1	2	1	3	2	1	1
Timing of measurement of confounding variables	BL, q2-3y	BL	BL	BL	BL	BL	BL	BL	BL	BL	BL
Pre-specified primary confounding variables											
Age	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
Pre-specified secondary confounding variables											
Sex	✓	✓	✓	✓	✓	✓	✓	✓		✓	✓
Smoking	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
BMI	✓	✓	✓	✓		✓	✓	✓	✓	✓	✓
Physical activity	✓			✓		✓	✓	✓	✓	✓	✓
Alcohol	✓		✓	✓		✓	✓	✓		✓	✓
Blood pressure	✓			✓		✓	✓	✓	✓	✓	✓
Energy								✓	✓	✓	
Diabetes				✓				✓	✓	✓	✓
Cholesterol	✓					✓	✓	✓	✓	✓	✓
Other Confounding variables											
Education	✓			✓		✓			✓	✓	
Socioeconomic status									✓	✓	
Menopause and/or hormone Use										✓	
Region/location		✓	✓			✓					
Randomization treatment											
Ethnicity/nationality		✓		✓							
Marital status		✓		✓		✓					
Study center							✓				
Survey season		✓	✓								
Employment status				✓			✓				
Follow-up duration											
Dietary Intake											
Vitamin/supplement	✓								✓	✓	
Fruit and/or vegetable	✓							✓			✓
Saturated fat										✓	
Whole grains											
Fish/shellfish								✓	✓		
Meat								✓			
Red meat				✓					✓		
Dietary pattern score											
Processed meat											
Coffee				✓							
Fibre											
Folate											
Sodium								✓			
Vitamin E											
Disease History											
MI or family history of MI											
CHD or family history of CHD							✓			✓	
CVD or family history of CVD											
Medications											
ASA				✓							
Other confounding variables not listed:				Stroke, Diuretics				Mental stress		Occupation, stroke	Stroke

ASA - acetylsalicylic acid; BL - baseline; CHD – coronary heart disease; CRP – C-reactive protein; CVD – cardiovascular disease; GFR – glomerular filtration rate; FA – fatty acid; MI – myocardial infarction; M/PUFA - mono/poly-unsaturated fatty acids; Querc – quercetin supplement; qXy - confounding variables measured once every X years; WC – waist circumference.

*Tanaka et al. (2013) adjusted for the following additional confounding variables: dyslipidemia, HbA1c, oral antihyperglycemic agents, insulin, retinopathy, dietary cholesterol, dietary fat and Ω -3 and Ω -6 FA.

Table S3: Newcastle-Ottawa Scale (NOS) for Assessing the Quality of Cohort Studies

Study	Selection [*]	Outcome [†]	Comparability [‡]	Total [§]
Adriouch, 2018 ⁴²	3	2	2	7
Appleby, 2002 ⁴³	1	1	1	3
Atkins, 2014 ⁴⁴	3	3	1	7
Bahadoran, 2017 ⁴⁵	2	1	0	3
Bazzano, 2002 ⁴⁶	2	3	1	6
Belin, 2011 ⁴⁷	3	3	2	8
Bendinelli, 2011 ⁴⁸	3	3	2	8
Berard, 2017 ⁴⁹	3	3	1	7
Bhupathiraju, 2013 ⁵⁰	2	2	1	5
Bingham, 2008 ⁵¹	2	0	2	4
Bleckenhorst, 2017 ⁵²	2	3	2	7
Bos, 2014 ⁵³	2	3	2	7
Buijsse, 2008 ⁵⁴	3	3	1	7
Buil-Cosiales, 2016 ⁵⁶	3	3	2	8
Buil-Cosiales, 2017 ⁵⁵	3	1	2	6
Cassidy, 2012 ⁵⁷	2	2	2	6
Collin, 2019 ⁵⁸	3	3	1	7
Conrad, 2018 ⁵⁹	3	3	1	7
Dauchet, 2004 ⁶⁰	3	3	2	8
Dauchet, 2010 ⁶¹	4	3	2	9
Du, 2016 ⁶²	4	3	1	8
Du, 2017 ⁶³	4	3	1	8
Elwood, 2013 ⁶⁴	3	3	1	7
Eriksen, 2015 ⁶⁵	3	3	2	8
Fitzgerald, 2012 ⁶⁶	2	2	1	5
Fraser, 1992 ⁶⁷	2	3	2	7
Gardener, 2011 ⁶⁸	4	2	1	7
Gaziano, 1995 ⁶⁹	2	3	1	6
Genkinger, 2004 ⁷⁰	3	3	1	7
Gillman, 1995 ⁷¹	3	3	2	8
Goetz, 2016 ⁷²	3	2	1	6
Goetz, 2016 ⁷³	3	3	1	7
Gunge, 2017 ⁷⁴	3	3	2	8

Study	Selection[*]	Outcome⁺	Comparability[‡]	Total[§]
Gunnell, 2013 ⁷⁵	3	1	2	6
Hansen, 2010 ⁷⁷	3	3	2	8
Hansen, 2017 ⁷⁶	2	3	2	7
Harriss, 2007 ⁷⁸	3	3	2	8
Hertog, 1997 ⁷⁹	2	3	2	7
Hirvonen, 2000 ⁸¹	2	3	2	7
Hirvonen, 2001 ⁸⁰	2	3	2	7
Hjartaker, 2015 ⁸²	2	3	1	6
Hodgson, 2016 ⁸³	2	3	2	7
Holmberg, 2009 ⁸⁴	2	3	0	5
Iso, 2007 ⁸⁵	2	2	1	5
Jacques, 2015 ⁸⁶	3	3	1	7
Johnsen, 2003 ⁸⁷	3	2	2	7
Joshi-pura, 1999 ⁸⁸	2	2	2	6
Joshi-pura, 2009 ⁸⁹	2	3	2	7
Keli, 1996 ⁹⁰	4	3	1	8
Kim, 2013 ⁹¹	1	3	0	4
Knekt, 1994 ⁹⁴	4	3	1	8
Knekt, 1996 ⁹³	2	3	2	7
Knekt, 2000 ⁹²	4	3	2	9
Kobylecki, 2015 ⁹⁵	3	3	2	8
Kondo, 2019 ⁹⁶	3	3	1	7
Kvaavik, 2010 ⁹⁷	4	3	1	8
Lai, 2015 ⁹⁸	3	3	1	7
Larsson, 2009 ⁹⁹	2	3	2	7
Larsson, 2013 ¹⁰⁰	3	3	2	8
Leenders, 2013 ¹⁰²	3	3	2	8
Leenders, 2014 ¹⁰¹	3	3	2	8
Lin, 2007 ¹⁰³	2	2	2	6
Lin, 2017 ¹⁰⁴	3	3	1	7
Liu, 2000 ¹⁰⁶	2	3	2	7
Liu, 2001 ¹⁰⁵	2	3	2	7
Mann, 1997 ¹⁰⁷	2	3	1	6
Manuel, 2015 ¹⁰⁸	4	3	1	8
Miller, 2017 ¹⁰⁹	3	3	2	8

Study	Selection[*]	Outcome⁺	Comparability[‡]	Total[§]
Mink, 2007 ¹¹⁰	3	3	2	8
Mizrahi, 2009 ¹¹¹	4	3	2	9
Mori, 2018 ¹¹²	3	3	2	8
Mytton, 2018 ¹¹³	3	3	2	8
Nagura, 2009 ¹¹⁴	3	3	2	8
Nakamura, 2008 ¹¹⁵	2	3	2	7
Nechuta, 2010 ¹¹⁶	3	3	1	7
Neelakantan, 2018 ¹¹⁷	3	3	2	8
Ness, 2005 ¹¹⁸	3	3	1	7
Nothlings, 2008 ¹¹⁹	2	3	1	6
Okuda, 2015 ¹²⁰	3	3	1	7
Oude Griep, 2010 ¹²¹	3	3	1	7
Oude Griep, 2011 ¹²³	2	3	2	7
Oude Griep, 2011 ¹²²	2	3	2	7
Oyebode, 2014 ¹²⁴	3	3	1	7
Pham, 2007 ¹²⁵	3	3	2	8
Rebello, 2014 ¹²⁶	3	3	1	7
Rissanen, 2003 ¹²⁷	2	3	2	7
Saglimbene, 2017 ¹²⁸	1	0	0	1
Sahyoun, 1996 ¹²⁹	1	3	1	5
Sauvaget, 2003 ¹³⁰	2	3	2	7
Scheffers, 2019 ¹³¹	3	3	2	8
Sesso, 2003 ¹³²	2	3	2	7
Sesso, 2003 ¹³⁴	2	3	2	7
Sesso, 2007 ¹³³	3	2	2	7
Shah, 2018 ¹³⁵	3	3	2	8
Sharma, 2013 ¹³⁶	3	2	0	5
Sharma, 2014 ¹³⁷	3	2	0	5
Simila, 2013 ¹³⁸	2	3	1	6
Sonestedt, 2015 ¹³⁹	4	3	2	9
Sotomayer, 2019 ¹⁴⁰	1	3	2	6
Steffen, 2003 ¹⁴¹	4	3	2	9
Stefler, 2016 ¹⁴²	2	3	1	6
Strandhagen, 2000 ¹⁴³	2	3	1	6
Takachi, 2008 ¹⁴⁴	3	3	2	8

Study	Selection*	Outcome†	Comparability‡	Total§
Tanaka, 2013 ¹⁴⁵	2	3	2	7
Tognon, 2014 ¹⁴⁶	3	3	1	7
Tucker, 2005 ¹⁴⁷	2	3	1	6
Von Ruesten, 2013 ¹⁴⁸	3	2	2	7
Vormund, 2015 ¹⁴⁹	3	3	1	7
Wang, 2016 ¹⁵⁰	1	3	1	5
Watkins, 2000 ¹⁵¹	3	3	2	8
Whiteman, 1999 ¹⁵²	3	3	1	7
Yamada, 2011 ¹⁵³	2	3	2	7
Yokoyama, 2000 ¹⁵⁴	2	3	2	7
Yoshizaki, 2019 ¹⁵⁵	3	3	2	8
Yu, 2014 ¹⁵⁶	3	3	2	8
Zhang, 2011 ¹⁵⁷	3	3	2	8
Zhang, 2011 ¹⁵⁸	3	2	2	7












*Maximum 4 points awarded for representativeness of exposed cohort, selection of non-exposed cohort, exposure assessment, and demonstration outcome not present at baseline.

†Maximum 3 points awarded for outcome assessment, follow-up length, and adequacy of follow-up.

‡Maximum 2 points awarded for adjusting for the pre-specified primary confounding variable (age) and 5 of the 7 pre-specified secondary confounding variables (sex, family history of CVD, smoking, body mass index, blood pressure (or hypertension/medications), cholesterol (or dyslipidemia/medications) and presence of diabetes mellitus).

§A maximum of 9 points could be awarded.

Table S4. GRADE Assessment for Fruits and Vegetables and Cardiovascular Disease Incidence

Quality Assessment								Study Event Rates (%)	Relative Risk (95% CI)	Certainty
No. of Cohorts	Design	Risk of Bias	Inconsistency	Indirectness	Imprecision	Publication Bias	Other			
Fruit and Vegetable Consumption on Cardiovascular Disease Incidence (follow-up median 10 years)										
12	observational	not serious	not serious	not serious	serious ¹	undetected	dose-response gradient ²	24,310/501,744 (4.9%)	0.93 (0.89, 0.96)	 LOW
Fruit Consumption on Cardiovascular Disease Incidence (follow-up median 10 years)										
16	observational	not serious	not serious	not serious	not serious	undetected	dose-response gradient ³	27,204/577,323 (4.7%)	0.91 (0.88, 0.95)	 LOW
Vegetable Consumption on Cardiovascular Disease Incidence (follow-up median 11 years)										
14	observational	not serious	not serious	not serious	serious ⁴	undetected	none	22,810/539,683 (4.2%)	0.94 (0.90, 0.97)	 VERY LOW
Berries Consumption on Cardiovascular Disease Incidence (follow-up median 10 years)										
1	observational	not serious	not serious ⁵	serious ⁶	serious ⁷	undetected ⁸	none	1,004/38,176 (2.6%)	1.27 (0.95, 1.71)	 VERY LOW
Citrus Fruit Consumption on Cardiovascular Disease Incidence (follow-up median 10 years)										
6	observational	not serious	not serious	not serious	serious ⁹	undetected ⁸	dose-response gradient ¹⁰	6,220/222,525 (2.8%)	0.88 (0.80, 0.96)	 LOW
Fruit Juice Consumption on Cardiovascular Disease Incidence (follow-up median 15 years)										
5	observational	not serious	not serious	not serious	serious ¹¹	undetected ⁸	none	8,056/167,879 (4.8%)	1.00 (0.93, 1.07)	 VERY LOW
Pommes Consumption on Cardiovascular Disease Incidence (follow-up median 8 years)										
5	observational	not serious	not serious	serious ¹²	not serious	undetected ⁸	dose-response gradient ¹³	2,578/149,437 (1.7%)	0.76 (0.66, 0.88)	 LOW
Allium Vegetables Consumption on Cardiovascular Disease Incidence (follow-up median 7 years)										
2	observational	not serious	serious ¹⁴	serious ¹⁵	serious ¹⁶	undetected ⁸	none	808/40,814 (2.0%)	0.79 (0.57, 1.10)	 VERY LOW
Cruciferous Vegetables Consumption on Cardiovascular Disease Incidence (follow-up median 9 years)										
7	observational	not serious	serious ¹⁷	not serious	serious ¹⁸	undetected ⁸	none	6,824/273,878 (2.5%)	0.99 (0.90, 1.08)	 VERY LOW
Green Leafy Vegetables Consumption on Cardiovascular Disease Incidence (follow-up median 7 years)										
5	observational	not serious	not serious	not serious	serious ¹⁹	undetected ⁸	dose-response gradient ²⁰	5,732/211,902 (2.7%)	0.87 (0.76, 0.99)	 LOW
Tomatoes Consumption on Cardiovascular Disease Incidence (follow-up median 9 years)										
2	observational	not serious	not serious	serious ²¹	serious ²²	undetected ⁸	none	841/55,452 (1.5%)	0.97 (0.78, 1.20)	 VERY LOW

¹ Downgrade for serious imprecision, as the lower bound of the 95% CI (RR, 0.89) includes the minimally important difference (MID) of 5% while the upper bound of the 95% CI (RR, 0.96) crosses the MID.

- ² Upgrade for a dose-response gradient, as the GLST analysis revealed a significant linear inverse relationship between total fruit and vegetable intake and incident CVD ($p<0.001$).
- ³ Upgrade for a dose-response gradient, as the GLST analysis revealed a significant linear inverse relationship between fruit intake and incident CVD ($p=0.004$).
- ⁴ Downgrade for serious imprecision, as the lower bound of the 95% CI (RR, 0.90) includes the MID of 5% while the upper bound of the 95% CI (RR, 0.97) crosses the MID.
- ⁵ No downgrade for inconsistency as analyses for inconsistency could not be performed due to <2 observations available.
- ⁶ Downgrade for serious indirectness as evidence is based on 1 cohort of female health-professionals residing in the USA and may not be generalizable to different populations.
- ⁷ Downgrade for serious imprecision, as the lower and upper bound of the 95% CIs (RR, 0.95 to 1.27) includes both clinically important benefit ($RR\leq 0.95$) and harm ($RR\geq 1.05$).
- ⁸ No downgrade for publication bias as publication bias could not be assessed due to lack of power for assessing funnel plot asymmetry and small study effects (i.e. <10 observations available).
- ⁹ Downgrade for serious imprecision, as the lower bound of the 95% CI (RR, 0.80) includes the MID of 5% while the upper bound of the 95% CI (RR, 0.96) crosses the MID.
- ¹⁰ Upgrade for a dose-response gradient, as the MKSPLINE analysis revealed a significant non-linear inverse relationship between citrus fruit intake and CVD incidence ($p=0.033$).
- ¹¹ Downgrade for serious imprecision, as the lower and upper bound of the 95% CIs (RR, 0.93 to 1.07) includes both clinically important benefit ($RR<0.95$) and harm ($RR\geq 1.05$).
- ¹² Downgrade for serious indirectness as evidence is based on a predominately ($>78\%$) female population and may not be generalizable to different populations.
- ¹³ Upgrade for a dose-response gradient, as the GLST analysis revealed a significant linear inverse relationship between pomes intake and incident CVD ($p=0.043$).
- ¹⁴ Downgrade for serious inconsistency given evidence of substantial inter-study heterogeneity ($I^2=85\%$, $p=0.01$), which could not be explored through sensitivity due to only 2 observations available.
- ¹⁵ Downgrade for serious indirectness as evidence is based on a predominately (97%) female populations of which most are health professionals, and may not be generalizable to different populations.
- ¹⁶ Downgrade for serious imprecision, as the lower bound of the 95% CI (RR, 0.57) includes the MID of 5% while the upper bound of the 95% CI (RR, 1.10) crosses the MID.
- ¹⁷ Downgrade for serious inconsistency as there was evidence of substantial inter-study heterogeneity ($I^2=52\%$, $p=0.04$). Although the removal of Buil-Cosiales et al. 2016 during sensitivity analysis did partially explain the heterogeneity ($I^2=27\%$, $p=0.22$), the presence of residual heterogeneity could not be excluded.
- ¹⁸ Downgrade for serious imprecision, as the lower and upper bound of the 95% CIs (RR, 0.90 to 1.08) includes both clinically important benefit ($RR\leq 0.95$) and harm ($RR\geq 1.05$).
- ¹⁹ Downgrade for serious imprecision, as the lower bound of the 95% CI (RR, 0.76) includes the minimally important difference (MID) of 5% while the upper bound of the 95% CI (RR, 0.99) crosses the MID.
- ²⁰ Upgrade for a dose-response gradient, as the MKSPLINE analysis revealed a significant non-linear inverse relationship between green leafy vegetables intake and CVD mortality ($p=0.01$).
- ²¹ Downgrade for serious indirectness as evidence is based on a predominately (88%) female population and may not be generalizable to different populations.
- ²² Downgrade for serious imprecision, as the lower and upper bound of the 95% CIs (RR, 0.78 to 1.20) includes both clinically important benefit ($RR\leq 0.95$) and harm ($RR\geq 1.05$).

Table S5. GRADE Assessment for Fruits and Vegetables and Cardiovascular Disease Mortality

Quality Assessment								Study Event Rates (%)	Relative Risk (95% CI)	Certainty
No. of Cohorts	Design	Risk of Bias	Inconsistency	Indirectness	Imprecision	Publication Bias	Other			
Fruit and Vegetable Consumption on Cardiovascular Disease Mortality (follow-up median 11 years)										
14	observational	not serious	serious ¹	not serious	not serious	undetected	dose-response gradient ²	17,439/798,391 (2.2%)	0.89 (0.85, 0.93)	⊕⊕○○ LOW
Fruit Consumption on Cardiovascular Disease Mortality (follow-up median 11 years)										
27	observational	not serious	serious ³	not serious	not serious	undetected	dose-response gradient ⁴	39,623/1,581,506 (2.5%)	0.88 (0.86, 0.91)	⊕⊕○○ LOW
Vegetable Consumption on Cardiovascular Disease Mortality (follow-up median 10 years)										
21	observational	not serious	serious ⁵	not serious	not serious	undetected	dose-response gradient ⁶	33,516/1,101,435 (3.0%)	0.87 (0.85, 0.90)	⊕⊕○○ LOW
Apricot Consumption on Cardiovascular Disease Mortality (follow-up median 1.5 years)										
1	observational	serious ⁷	not serious ⁸	serious ⁹	not serious	undetected ¹⁰	none	515/9,757 (5.3%)	1.84 (1.27, 2.67)	⊕○○○ VERY LOW
Bananas Consumption on Cardiovascular Disease Mortality 16(follow-up median 20.3 years)										
1	observational	not serious	not serious ⁸	serious ¹²	serious ¹³	undetected ¹⁰	none	4,595/9,766 (47.1%)	1.06 (0.87, 1.29)	⊕○○○ VERY LOW
Berries Consumption on Cardiovascular Disease Mortality (follow-up median 16 years)										
4	observational	not serious	not serious	serious ¹⁴	serious ¹⁵	undetected ¹⁰	none	7,401/112,892 (6.6%)	0.97 (0.92, 1.03)	⊕○○○ VERY LOW
Citrus Fruit Consumption on Cardiovascular Disease Mortality (follow-up median 17 years)										
3	observational	not serious	not serious ¹⁶	serious ¹⁷	serious ¹⁸	undetected ¹⁰	none	7,197/74,716 (9.6%)	0.95 (0.90, 1.02)	⊕○○○ VERY LOW
Dried Fruit Consumption on Cardiovascular Disease Mortality (follow-up median 17 years)										
2	observational	not serious	not serious	not serious	serious ¹⁹	undetected ¹⁰	none	447/31,757 (1.4%)	0.93 (0.63, 1.37)	⊕○○○ VERY LOW
Fruit Juice Consumption on Cardiovascular Disease Mortality (follow-up median 17 years)										
1	observational	not serious	not serious ⁸	serious ²⁰	serious ²¹	undetected ¹⁰	none	286/30,458 (0.9%)	0.81 (0.58, 1.13)	⊕○○○ VERY LOW
Grapes Consumption on Cardiovascular Disease Mortality (follow-up median 16.7 years)										
3	observational	not serious	not serious ²²	serious ²³	serious ²⁴	undetected ¹⁰	none	7,197/74,716 (9.6%)	0.90 (0.81, 1.01)	⊕○○○ VERY LOW
Pommes Consumption on Cardiovascular Disease Mortality (follow-up median 16 years)										
5	observational	not serious	not serious	serious ²⁵	not serious	undetected ¹⁰	none	7,947/85,929 (9.2%)	0.86 (0.80, 0.92)	⊕○○○ VERY LOW
Allium Vegetables Consumption on Cardiovascular Disease Mortality (follow-up median 15 years)										
1	observational	not serious	not serious ⁸	serious ²⁶	not serious	undetected ¹⁰	none	238/1,226 (19.4%)	0.33 (0.22, 0.49)	⊕○○○ VERY LOW
Carrots Consumption on Cardiovascular Disease Mortality (follow-up median 18 years)										

2	observational	not serious	not serious	serious ²⁷	serious ²⁸	undetected ¹⁰	none	4,792/10,325 (46.4%)	0.92 (0.85, 1.01)	⊕○○○ VERY LOW
Celery Consumption on Cardiovascular Disease Mortality (follow-up median 16 years)										
1	observational	not serious	not serious ⁸	serious ²⁹	serious ³⁰	undetected ¹⁰	none	2,316/34,492 (6.7%)	0.91 (0.83, 1.01)	⊕○○○ VERY LOW
Cruciferous Vegetables Consumption on Cardiovascular Disease Mortality (follow-up median 12 years)										
7	observational	not serious	serious ³¹	not serious	not serious	undetected ¹⁰	none	13,081/187,730 (7.0%)	0.85 (0.82, 0.89)	⊕○○○ VERY LOW
Green Leafy Vegetables Consumption on Cardiovascular Disease Mortality (follow-up median 21 years)										
5	observational	not serious	serious ³²	not serious	not serious	undetected ¹⁰	none	6,661/40,893 (16.3%)	0.87 (0.81, 0.94)	⊕⊕○○ LOW
Tomatoes Consumption on Cardiovascular Disease Mortality (follow-up median 16 years)										
3	observational	not serious	not serious	serious ³³	serious ³⁴	undetected ⁹	none	7,072/45,557 (15.5%)	0.98 (0.93, 1.04)	⊕○○○ VERY LOW

¹ Downgrade for serious inconsistency as there was evidence of substantial inter-study heterogeneity ($I^2=68\%$, $p<0.001$) which could not be explained by sensitivity analyses.

² Upgrade for a dose-response gradient, as the GLST analysis revealed a significant linear inverse relationship between fruit and vegetable intake and CVD mortality ($p<0.011$). The MKSPLINE procedure indicated a departure from linearity ($p<0.001$) at a threshold of 4 servings/day as observed by visual inspection.

³ Downgrade for serious inconsistency as there was evidence of substantial inter-study heterogeneity ($I^2=79\%$, $p<0.001$), which could not be explained by sensitivity analyses.

⁴ Upgrade for a dose-response gradient, as the GLST analysis revealed a significant linear inverse relationship between fruit intake and CVD mortality ($p=0.005$).

⁵ Downgrade for serious inconsistency as there was evidence of substantial inter-study heterogeneity ($I^2=59\%$, $p<0.001$), which could not be explained by sensitivity analyses.

⁶ Upgrade for a dose-response gradient, as the GLST analysis revealed a significant linear inverse relationship between fruit intake and CVD mortality ($p<0.001$).

⁷ Downgrade for serious risk of bias as the effect estimate is based on Saglimbene et al. 2017, which presented with a high risk of bias (Newcastle-Ottawa Score: 1/9)

⁸ No downgrade for inconsistency as analyses for inconsistency could not be performed due to <2 observations available

⁹ Downgrade for serious indirectness as evidence is based on 1 cohort of patients receiving hemodialysis and may not be generalizable to different populations.

¹⁰ No downgrade for publication bias as publication bias could not be assessed due to lack of power for assessing funnel plot asymmetry and small study effects (i.e. <10 observations available).

¹¹ No downgrade for inconsistency as analyses for inconsistency could not be performed due to <2 observations available

¹² Downgrade for serious indirectness as evidence is based on 1 male cohort and may not be generalizable to different populations

¹³ Downgrade for serious imprecision, as the lower and upper bound of the 95% CIs (RR, 0.87 to 1.29) includes both clinically important benefit (RR <0.95) and harm (RR ≥ 1.05).

¹⁴ Downgrade for serious indirectness as evidence is based on a predominately (91%) female population and may not be generalizable to different populations.

¹⁵ Downgrade for serious imprecision, as the lower bound of the 95% CI (RR, 0.92) includes the minimally important difference (MID) of 5% while the upper bound of the 95% CI (RR, 1.03) crosses the MID.

¹⁶ No downgrade for inconsistency as the presence of inter-study heterogeneity ($I^2=62\%$, $p=0.05$) was explained by the removal of Lai et al. 2015 ($I^2=0\%$, $p=0.63$) during sensitivity analysis.













¹⁷ Downgrade for serious indirectness as the evidence is based on a predominately (87%) female population and may not be generalizable to different populations.



¹⁸ Downgrade for serious imprecision, as upper bound of the 95% CIs (RR 1.02) crosses the MID (RR <0.95).

¹⁹ Downgrade for serious imprecision, as upper bound of the 95% CIs (RR 1.37) crosses the MID (RR <0.95).

- ²⁰ Downgrade for serious indirectness as evidence is based on 1 female cohort residing in the United Kingdom and may not be generalizable to different populations.
- ²¹ Downgrade for serious imprecision, as the lower and upper bound of the 95% CIs (RR, 0.58 to 1.13) includes both clinically important benefit (RR<0.95) and harm (RR≥1.05).
- ²² No downgrade for inconsistency as the presence of inter-study heterogeneity ($I^2=61\%$, $p=0.08$) was explained by the removal of Lai et al. 2015 ($I^2=0\%$, $p=0.93$) during sensitivity analysis.
- ²³ Downgrade for serious indirectness as evidence is based on a predominately (87%) female population and may not be generalizable to different populations.
- ²⁴ Downgrade for serious imprecision, as the upper bound of the 95% CIs (RR, 1.01) crosses the MID (RR<0.95).
- ²⁵ Downgrade for serious indirectness as evidence is based on a predominately (87%) female population and may not be generalizable to different populations.
- ²⁶ Downgrade for serious indirectness as evidence is based on 1 female cohort and may not be generalizable to different populations.
- ²⁷ Downgrade for serious indirectness as evidence is based on 2 male cohorts and may not be generalizable to different populations.
- ²⁸ Downgrade for serious imprecision, as the lower bound of the 95% CI (RR, 0.85) includes the minimally important difference (MID) of 5% while the upper bound of the 95% CI (RR, 1.01) crosses the MID.
- ²⁹ No downgrade for inconsistency as analyses for inconsistency could not be performed due to <2 observations available
- ³⁰ Downgrade for serious imprecision, as the lower bound of the 95% CI (RR, 0.76) includes the minimally important difference (MID) of 5% while the upper bound of the 95% CI (RR, 0.99) crosses the MID.
- ³¹ Downgrade for serious inconsistency as there was evidence for substantial inter-study heterogeneity ($I^2=86\%$, $p<0.00001$), which could not be explained by sensitivity analyses.
- ³² Downgrade for serious inconsistency as there was evidence of substantial inter-study heterogeneity ($I^2=88\%$, $p<0.00001$), which could not be explained by sensitivity analyses.
- ³³ Downgrade for serious indirectness as evidence is based on only 3 isolated geographical regions (Norway and Massachusetts and Iowa, USA) and may not be generalizable to different populations.
- ³⁴ Downgrade for serious imprecision, as the upper bound of the 95% CIs (RR, 1.04) includes crosses the MID (RR<0.95).

Table S6. GRADE Assessment for Fruits and Vegetables and Coronary Heart Disease Incidence

Quality Assessment								Study Event Rates (%)	Relative Risk (95% CI)	Certainty
No. of Cohorts	Design	Risk of Bias	Inconsistency	Indirectness	Imprecision	Publication Bias	Other			
Fruit and Vegetable Consumption on Coronary Heart Disease Incidence (follow-up median 10 years)										
19	observational	not serious	not serious	not serious	not serious	undetected	dose-response gradient ¹	17,987/619,182 (2.9%)	0.88 (0.83, 0.92)	 MODERATE
Fruit Consumption on Coronary Heart Disease Incidence (follow-up median 10 years)										
20	observational	not serious	not serious	not serious	not serious	undetected	dose-response gradient ²	23,856/1,170,021 (2.0%)	0.88 (0.84, 0.92)	 MODERATE
Vegetable Consumption on Coronary Heart Disease Incidence (follow-up median 10 years)										
18	observational	not serious	not serious ³	not serious	serious ⁴	undetected	dose-response gradient ⁵	17,172/696,330 (2.5%)	0.92 (0.87, 0.96)	 LOW
Bananas Consumption on Coronary Heart Disease Incidence (follow-up median 7.6 years)										
1	observational	not serious	not serious ⁶	serious ⁷	serious ⁸	undetected ⁹	none	365/122,635 (0.3%)	0.76 (0.56, 1.02)	 VERY LOW
Berries Consumption on Coronary Heart Disease Incidence (follow-up median 8 years)										
4	observational	not serious	serious ¹⁰	not serious	serious ¹¹	undetected ⁹	none	2,233/100,296 (2.2%)	0.94 (0.82, 1.09)	 VERY LOW
Citrus Fruit Consumption on Coronary Heart Disease Incidence (follow-up median 9 years)										
10	observational	not serious	not serious	not serious	serious ¹²	undetected	dose-response gradient ¹²	8,333/364,978 (2.3%)	0.91 (0.85, 0.98)	 LOW
Fruit Juice Consumption on Coronary Heart Disease Incidence (follow-up median 15 years)										
4	observational	not serious	not serious	not serious	serious ¹⁴	undetected ⁹	none	7,589/109,898 (6.9%)	0.99 (0.92, 1.07)	 VERY LOW
Grapes Consumption on Coronary Heart Disease Incidence (follow-up median 12 years)										
1	observational	not serious	not serious ⁶	serious ¹⁵	serious ¹⁶	undetected ⁹	none	8,333/364,978 (2.3%)	0.91 (0.85, 0.98)	 VERY LOW
Pommes Consumption on Coronary Heart Disease Incidence (follow-up median 8 years)										
8	observational	not serious	not serious	not serious	serious ¹⁷	undetected ⁹	none	4,886/371,684 (1.3%)	0.90 (0.84, 0.97)	 VERY LOW
Watermelon Consumption on Coronary Heart Disease Incidence (follow-up median 7.6 years)										
1	observational	not serious	not serious	serious ¹⁶	serious ¹⁹	undetected ⁹	none	365/122,635 (0.3%)	0.87 (0.64, 1.18)	 VERY LOW
Allium Vegetables Consumption on Coronary Heart Disease Incidence(follow-up median 10 years)										
5	observational	not serious	not serious	not serious	serious ²⁰	undetected ⁹	none	1,734/210,964 (0.8%)	0.93 (0.80, 1.09)	 VERY LOW
Cruciferous Vegetables Consumption on Coronary Heart Disease Incidence(follow-up median 11 years)										
8	observational	not serious	not serious	not serious	not serious	undetected ⁹	none	9,383/347,453 (2.7%)	1.01 (0.95, 1.07)	 LOW

Green Leafy Vegetables Consumption on Coronary Heart Disease Incidence(follow-up median 16 years)										
5	observational	not serious	not serious	not serious	not serious	undetected ⁹	dose-response gradient ²¹	6,696/170,250 (3.9%)	0.82 (0.76, 0.89)	 MODERATE
Tomatoes Consumption on Coronary Heart Disease Incidence(follow-up median 8 years)										
3	observational	not serious	not serious	serious ²²	serious ²³	undetected ⁹	none	1,283/134,494 (1.0%)	0.80 (0.57, 1.13)	 VERY LOW

¹ Upgrade for a dose-response gradient, as the GLST analysis revealed a significant linear inverse relationship between fruit and vegetable intake and coronary heart disease incidence (CHD) ($p<0.001$).

² Upgrade for a dose-response gradient, as the GLST analysis revealed a significant linear inverse relationship between fruit intake and CHD ($p=0.005$).

³ No downgrade for inconsistency as the presence of inter-study heterogeneity ($I^2=53\%$, $p=0.002$) was explained by the removal of Dauchet et al. 2010 ($I^2=0\%$, $p=0.5$)

⁴ Downgrade for serious imprecision, as the lower bound of the 95% CI (RR, 0.87) includes the minimally important difference (MID) of 5% while the upper bound of the 95% CI (RR, 0.96) crosses the MID.

⁵ Upgrade for a dose-response gradient, as the GLST analysis revealed a significant linear inverse relationship between vegetable intake and CHD ($p<0.001$).

⁶ No downgrade for inconsistency as analyses for inconsistency could not be performed due to <2 observations available

⁷ Downgrade for serious indirectness as evidence is based on only 1 geographical regions (China) and may not be generalizable to different populations.

⁸ Downgrade for serious imprecision, as the upper bound of the 95% CIs (RR, 1.02) crosses the MID (RR <0.95).

⁹ No downgrade for publication bias as publication bias could not be assessed due to lack of power for assessing funnel plot asymmetry and small study effects (i.e. <10 observations available).

¹⁰ Downgrade for serious inconsistency as there was evidence of substantial inter-study heterogeneity ($I^2=74\%$, $p=0.008$), which could not be explained by sensitivity analyses.

¹¹ Downgrade for serious imprecision, as the lower and upper bound of the 95% CIs (RR, 0.82 to 1.09) includes both clinically important benefit (RR <0.95) and harm (RR ≥ 1.05).

¹² Downgrade for serious imprecision, as the lower bound of the 95% CI (RR, 0.85) includes the minimally important difference (MID) of 5% while the upper bound of the 95% CI (RR, 0.98) crosses the MID.

¹³ Upgrade for a dose-response gradient, as the MKSPLINE analysis indicated a significant non-linear inverse relationship between citrus intake and incident CHD ($p=0.005$).

¹⁴ Downgrade for serious imprecision, as the lower and upper bound of the 95% CIs (RR, 0.92 to 1.07) includes both clinically important benefit (RR <0.95) and harm (RR ≥ 1.05).

¹⁵ Downgrade for serious indirectness as evidence is based on 1 female cohort of health professionals and may not be generalizable to different populations.

¹⁶ Downgrade for serious imprecision, as the lower bound of the 95% CI (RR, 0.85) includes the minimally important difference (MID) of 5% while the upper bound of the 95% CI (RR, 0.98) crosses the MID.

¹⁷ Downgrade for serious imprecision, as the lower bound of the 95% CI (RR, 0.84) includes the minimally important difference (MID) of 5% while the upper bound of the 95% CI (RR, 0.97) crosses the MID.

¹⁸ Downgrade for serious imprecision, as the lower and upper bound of the 95% CIs (RR, 0.64 to 1.18) includes both clinically important benefit (RR <0.95) and harm (RR ≥ 1.05).





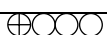






¹⁹ Downgrade for serious imprecision, as the lower and upper bound of the 95% CIs (RR, 0.80 to 1.09) includes both clinically important benefit (RR <0.95) and harm (RR ≥ 1.05).

²⁰ Upgrade for a dose-response gradient, as the GLST analysis revealed a significant linear inverse relationship between fruit intake and CVD mortality ($p=0.002$). The MKSPLINE procedure indicated a departure from linearity ($p=0.004$) at threshold of 0.5 servings/day as observed by visual inspection.

²¹ Downgrade for serious indirectness as the evidence is based only on female populations, predominately (77.9%) of which reside in USA, and may not be generalizable to different populations.

²² Downgrade for serious imprecision, as the lower and upper bound of the 95% CIs (RR, 0.57 to 1.13) includes both clinically important benefit ($RR < 0.95$) and harm ($RR \geq 1.05$)

Table S7. GRADE Assessment for Fruits and Vegetables and Coronary Heart Disease Mortality

Quality Assessment								Study Event Rates (%)	Relative Risk (95% CI)	Certainty
No. of Cohorts	Design	Risk of Bias	Inconsistency	Indirectness	Imprecision	Publication Bias	Other			
Fruit and Vegetable Consumption on Coronary Heart Disease Mortality (follow-up median 18 years)										
5	observational	not serious	not serious	not serious	not serious	undetected ¹	dose-response gradient ²	3,240/489,635 (0.7%)	0.81 (0.72, 0.92)	 MODERATE
Fruit Consumption on Coronary Heart Disease Mortality (follow-up median 13 years)										
21	observational	not serious	serious ³	not serious	not serious	undetected	dose-response gradient ⁴	14,786/1,398,863 (1.1%)	0.86 (0.82, 0.90)	 LOW
Vegetable Consumption on Coronary Heart Disease Mortality (follow-up median 13 years)										
18	observational	not serious	not serious	not serious	not serious	undetected	dose-response gradient ⁵	26,007/1,968,325 (1.3%)	0.86 (0.83, 0.89)	 MODERATE
Bananas Consumption on Coronary Heart Disease Mortality (follow-up median 20 years)										
1	observational	not serious	not serious ⁶	serious ⁷	serious ⁸	undetected ¹	none	2,384/9,964 (4.9%)	1.04 (0.81, 1.34)	 VERY LOW
Berries Consumption on Coronary Heart Disease Mortality (follow-up median 17 years)										
5	observational	not serious	not serious	not serious	serious ⁹	undetected ¹	none	5,141/105,420 (4.9%)	0.98 (0.91, 1.05)	 VERY LOW
Citrus Fruit Consumption on Coronary Heart Disease Mortality (follow-up median 16 years)										
6	observational	not serious	not serious	serious ¹⁰	serious ¹¹	undetected ¹	none	5,309/180,574 (2.9%)	0.91 (0.85, 0.96)	 VERY LOW
Dried Fruit Consumption on Coronary Heart Disease Mortality (follow-up median 17 years)										
1	observational	not serious	not serious ⁶	serious ¹²	serious ¹³	undetected ¹	none	38/30,458 (0.1%)	0.79 (0.47, 1.31)	 VERY LOW
Fruit Juice Consumption on Coronary Heart Disease Mortality (follow-up median 17 years)										
3	observational	serious ¹⁴	not serious	not serious ¹⁵	serious ¹⁶	undetected ¹	none	1,249/141,170 (0.9%)	0.87 (0.75, 1.01)	 VERY LOW
Grapes Consumption on Coronary Heart Disease Mortality (follow-up median 17 years)										
3	observational	not serious	not serious	serious ¹⁷	serious ¹⁸	undetected ¹	none	2,846/106,782 (2.7%)	0.97 (0.77, 1.21)	 VERY LOW
Pommes Consumption on Coronary Heart Disease Mortality (follow-up median 19 years)										
5	observational	not serious	not serious	serious ¹⁹	not serious	undetected ¹	none	4,650/146,407 (3.2%)	0.84 (0.76, 0.92)	 VERY LOW
Allium Vegetables Consumption on Coronary Heart Disease Mortality (follow-up median 15 years)										
4	observational	not serious	serious ²⁰	serious ²¹	not serious	undetected ¹	none	1,280/75,434 (1.7%)	0.67 (0.57, 0.79)	 VERY LOW
Carrots Consumption on Coronary Heart Disease Mortality (follow-up median 13years)										

1	observational	not serious	not serious ⁶	serious ²²	serious ²³	undetected ¹	none	64/10,802 (0.6%)	0.76 (0.37, 1.58)	⊕○○○ VERY LOW
Celery Consumption on Coronary Heart Disease Mortality (follow-up median 16 years)										
1	observational	not serious	not serious ²⁴	serious ²⁵	serious ²⁶	undetected ¹	none	1,329/34,492 (3.9%)	0.92 (0.80, 1.06)	⊕○○○ VERY LOW
Cruciferous Vegetables Consumption on Coronary Heart Disease Mortality (follow-up median 16 years)										
6	observational	serious ²⁷	serious ²⁸	not serious	serious ²⁹	undetected ¹	none	7,420/296,772 (2.5%)	0.91 (0.85, 0.98)	⊕○○○ VERY LOW
Green Leafy Vegetables Consumption on Coronary Heart Disease Mortality (follow-up median 17 years)										
5	observational	serious ³⁰	not serious	not serious	not serious	undetected ¹	none	4,591/148,133 (3.1%)	0.86 (0.78, 0.94)	⊕○○○ VERY LOW
Tomatoes Consumption on Coronary Heart Disease Mortality (follow-up median 16 years)										
3	observational	serious ³¹	not serious	not serious	serious ³²	undetected ¹	none	3,657/175,088 (2.1%)	0.92 (0.82, 1.04)	⊕○○○ VERY LOW

¹ No downgrade for publication bias as publication bias could not be assessed due to lack of power for assessing funnel plot asymmetry and small study effects (i.e. <10 observations available).

² Upgrade for a dose-response gradient, as the MKSPLINE analysis revealed a significant non-linear inverse relationship between fruit and vegetable intake and CHD mortality (p=0.044)

³ Downgrade for serious inconsistency as there was evidence of substantial inter-study heterogeneity ($I^2=62\%$, $p<0.0001$). Although heterogeneity could be partially explained by the removal of Du et al. 2017 ($I^2=44\%$, $p=0.01$) and Hjartaker et al. 2015 ($I^2=46\%$, $p=0.007$) during sensitivity analyses, the presence of residual heterogeneity could not be excluded.

⁴ Upgrade for a dose-response gradient, as the GLST analysis revealed a significant linear inverse relationship between fruit intake and CHD mortality (p<0.001).

⁵ Upgrade for a dose-response gradient, as the GLST analysis revealed a significant linear inverse relationship between vegetable intake and CHD mortality (p=0.005).

⁶ No downgrade for inconsistency as analyses for inconsistency could not be performed due to <2 observations available.

⁷ Downgrade for serious indirectness as evidence is based on 1 male cohort and may not be generalizable to different populations.

⁸ Downgrade for serious imprecision, as the lower and upper bound of the 95% CIs (RR, 0.81 to 1.34) includes both clinically important benefit (RR<0.95) and harm (RR≥1.05).

⁹ Downgrade for serious imprecision, as the lower and upper bound of the 95% CIs (RR, 0.91 to 1.05) includes both clinically important benefit (RR<0.95) and harm (RR≥1.05).

¹⁰ Downgrade for serious indirectness as evidence is based on a predominately (≥69.6%) female populations and may not be generalizable to different populations.

¹¹ Downgrade for serious imprecision, as the lower bound of the 95% CI (RR, 0.85) includes the minimally important difference (MID) of 5% while the upper bound of the 95% CI (RR, 0.96) crosses the MID.

¹² Downgrade for serious indirectness as evidence is based on 1 female cohort and may not be generalizable to different populations.

¹³ Downgrade for serious imprecision, as the lower and upper bound of the 95% CIs (RR, 0.47 to 1.31) includes both clinically important benefit (RR<0.95) and harm (RR≥1.05).

¹⁴ Downgrade for serious risk of bias as 56% of effect estimate is based on Iso et al. 2007, which presented with a high risk of bias (Newcastle-Ottawa Score: 5/9).

¹⁵ No downgrade for inconsistency as the presence of inter-study heterogeneity ($I^2=71\%$, $p=0.02$) was explained by the removal of Collin et al. 2019 ($I^2=0\%$, $p=0.45$).

¹⁶ Downgrade for serious imprecision, as the upper bound of the 95% CIs (RR, 1.01) crosses the MID (RR<0.95).

¹⁷ Downgrade for serious indirectness as evidence is based on a predominately (91%) female population of which the majority are health professionals and may not be generalizable to different populations.

¹⁸ Downgrade for serious imprecision, as the lower and upper bound of the 95% CIs (RR, 0.77 to 1.21) includes both clinically important benefit (RR<0.95) and harm (RR≥1.05).

¹⁹ Downgrade for serious indirectness as evidence is based on a predominately (82.1%) female populations and may not be generalizable to different populations.

²⁰ Downgrade for serious inconsistency as there was evidence of substantial inter-study heterogeneity ($I^2=88\%$, $p<0.00001$). Although heterogeneity could be partially explained by the removal of Blekkenhorst et al. 2017 ($I^2=47\%$, $p=0.13$) during sensitivity analyses, the presence of residual heterogeneity could not be excluded.

²¹ Downgrade for serious indirectness as evidence is based on a predominately (95.4%) female populations and may not be generalizable to different populations.

²² Downgrade for serious indirectness as evidence is based on 1 female cohort and may not be generalizable to different populations.

²³ Downgrade for serious imprecision, as the lower and upper bound of the 95% CIs (RR, 0.37 to 1.58) includes both clinically important benefit (RR<0.95) and harm (RR≥1.05).

²⁴ No downgrade for inconsistency as analyses for inconsistency could not be performed due to <2 observations available.

²⁵ Downgrade for serious indirectness as evidence is based on 1 female cohort and may not be generalizable to different populations.

²⁶ Downgrade for serious imprecision, as the lower and upper bound of the 95% CIs (RR, 0.80 to 1.06) includes both clinically important benefit (RR<0.95) and harm (RR≥1.05).

²⁷ Downgrade for serious risk of bias as 39.3% of effect estimate is based on Iso et al. 2007, which presented with a high risk of bias (Newcastle-Ottawa Score: 1/9).

²⁸ Downgrade for serious inconsistency as there was evidence of substantial inter-study heterogeneity ($I^2=88\%$, $p<0.00001$) which could not be explained by sensitivity analyses.












²⁹ Downgrade for serious imprecision, as the lower bound of the 95% CI (RR, 0.85) includes the minimally important difference (MID) of 5% while the upper bound of the 95% CI (RR, 0.98) crosses the MID.

³⁰ Downgrade for serious risk of bias as 36.8% of effect estimate is based on Iso et al. 2007, which presented with a high risk of bias (Newcastle-Ottawa Score: 1/9)

³¹ Downgrade for serious risk of bias as 48.0% of effect estimate is based on Iso et al. 2007, which presented with a high risk of bias (Newcastle-Ottawa Score: 1/9)

³² Downgrade for serious imprecision, as the lower bound of the 95% CI (RR, 0.82) includes the minimally important difference (MID) of 5% while the upper bound of the 95% CI (RR, 1.04) crosses the MID.

Table S8. GRADE Assessment for Fruits and Vegetables and Stroke Incidence

Quality Assessment								Study Event Rates (%)	Relative Risk (95% CI)	Certainty
No. of Cohorts	Design	Risk of Bias	Inconsistency	Indirectness	Imprecision	Publication Bias	Other			
Fruit and Vegetable Consumption on Stroke Incidence (follow-up median 9 years)										
14	observational	not serious	not serious	not serious	not serious	undetected	dose-response gradient ¹	11,091/532,667 (2.1%)	0.82 (0.77, 0.88)	 MODERATE
Fruit Consumption on Stroke Incidence (follow-up median 14 years)										
17	observational	not serious	not serious	not serious	not serious	undetected	dose-response gradient ²	43,702/987,983 (4.4%)	0.82 (0.79, 0.85)	 MODERATE
Vegetable Consumption on Stroke Incidence (follow-up median 14 years)										
16	observational	not serious	serious ³	not serious	not serious	undetected	dose-response gradient ⁴	13,607/564,531 (2.4%)	0.82 (0.83, 0.93)	 MODERATE
Berries Consumption on Stroke Incidence (follow-up median 10 years)										
4	observational	not serious	not serious ⁵	not serious	serious ⁶	undetected ⁷	none	5,967/143,662 (4.2%)	1.03 (0.94, 1.13)	 VERY LOW
Citrus Fruit Consumption on Stroke Incidence (follow-up median 11 years)										
8	observational	not serious	serious ⁸	not serious	not serious	undetected ⁷	dose-response gradient ⁹	7,142/225,613 (3.2%)	0.88 (0.82, 0.94)	 LOW
Fruit Juice Consumption on Stroke Incidence (follow-up median 11 years)										
4	observational	not serious	not serious ¹⁰	not serious	serious ¹¹	undetected ⁷	none	1,705/148,839 (1.2%)	0.82 (0.68, 0.99)	 VERY LOW
Pommes Consumption on Stroke Incidence (follow-up median 14 years)										
5	observational	not serious	not serious	not serious	not serious	undetected ⁷	dose-response gradient ¹²	7,364/146,723 (5.0%)	0.89 (0.84, 0.95)	 MODERATE
Allium Vegetables Consumption on Stroke Incidence (follow-up median 28 years)										
2	Observational	not serious	not serious	serious ¹³	serious ¹⁴	undetected ⁷	none	4,912/84,169 (5.8%)	0.89 (0.80, 0.99)	 VERY LOW
Cruciferous Vegetables Consumption on Stroke Incidence (follow-up median 12 years)										
6	observational	not serious	serious ¹⁵	not serious	serious ¹⁶	undetected ⁷	none	7,706/255,726 (3.0%)	0.98 (0.91, 1.05)	 VERY LOW
Green Leafy Vegetables Consumption on Stroke Incidence (follow-up median 9 years)										
4	observational	not serious	not serious	not serious	serious ¹⁷	undetected ⁷	dose-response gradient ¹⁸	4,798/196,456 (2.4%)	0.88 (0.79, 0.98)	 LOW
Tomatoes Consumption on Stroke Incidence (follow-up median 7 years)										
1	observational	not serious	not serious ¹⁹	serious ²⁰	not serious	undetected ⁷	dose-response gradient ²¹	247/38,445 (0.6%)	0.20 (0.05, 0.82)	 LOW

¹ Upgrade for a dose-response gradient, as the GLST analysis revealed a significant linear inverse relationship between fruit and vegetable intake and stroke incidence ($p=0.002$).

² Upgrade for a dose-response gradient, as the GLST analysis revealed a significant linear inverse relationship between fruit intake and stroke incidence ($p<0.001$).

³ Downgrade for serious inconsistency given evidence of substantial inter-study heterogeneity ($I^2=50\%$, $p=0.006$) that could not be explained during sensitivity analysis.

⁴ Upgrade for a dose-response gradient, as the MKSPLINE analysis revealed a significant non-linear inverse relationship between vegetable intake and stroke incidence with a departure from linearity at 1.5 servings/day ($p=0.012$)

⁵ No downgrade for inconsistency as the presence of inter-study heterogeneity ($I^2=50\%$, $p=0.08$) was explained by the removal of Hirvonen et al. 2000 – cerebral infraction ($I^2=0\%$, $p=0.41$) during sensitivity analysis.

⁶ Downgrade for serious imprecision, as the lower and upper bound of the 95% CIs (RR, 0.94 to 1.13) includes both clinically important benefit (RR<0.95) and harm (RR≥1.05)

⁷ No downgrade for publication bias as publication bias could not be assessed due to lack of power for assessing funnel plot asymmetry and small study effects (i.e. <10 observations available).

⁸ Downgrade for serious inconsistency given evidence of substantial inter-study heterogeneity ($I^2=51\%$, $p=0.04$). Although the removal of Larsson et al. 2013 ($I^2=37\%$, $p=0.14$) or Yamada et al. 2011 ($I^2=39\%$, $p=0.12$) during sensitivity analysis did partially explain the heterogeneity, the presence of residual heterogeneity could not be excluded.

⁹ Upgrade for a dose-response gradient, as the GLST analysis revealed a significant linear inverse relationship between citrus fruit intake and stroke incidence ($p=0.033$) and an MKSPLINE analysis revealed a significant non-linear inverse relationship between citrus fruit intake and stroke incidence ($p=0.039$).

¹⁰ No downgrade for inconsistency as the presence of inter-study heterogeneity ($I^2=73\%$, $p=0.02$) was explained by the removal of Scheffers et al. 2019 ($I^2=0\%$, $p=0.47$)

¹¹ Downgrade for serious imprecision, as the upper bound of the 95% CIs (RR, 0.99) crosses the MID (RR<0.95).

¹² Upgrade for a dose-response gradient, as the GLST analysis revealed a significant linear inverse relationship between pommes intake and stroke incidence ($p=0.003$). MKSPLINE analyses could not be conducted due to small sample size.

¹³ Downgrade for serious indirectness as evidence is based on cohorts residing in Northern Europe and may not be generalizable to different populations.

¹⁴ Downgrade for serious imprecision, as the lower bound of the 95% CI (RR, 0.80) includes the MID of 5% while the upper bound of the 95% CI (RR, 0.99) crosses the MID.

¹⁵ Downgrade for serious inconsistency given evidence of substantial inter-study heterogeneity ($I^2=62\%$, $p=0.02$). Although the removal of Larsson et al. 2013 (during sensitivity analysis did partially explain the heterogeneity ($I^2=40\%$, $p=0.16$), the presence of residual heterogeneity could not be excluded.

¹⁶ Downgrade for serious imprecision, as the lower and upper bound of the 95% CIs (RR, 0.91 to 1.05) includes both clinically important benefit (RR<0.95) and harm (RR≥1.05).

¹⁶ Downgrade for serious imprecision, as the lower bound of the 95% CI (RR, 0.79) includes the MID of 5% while the upper bound of the 95% CI (RR, 0.98) crosses the MID.

¹⁷ Upgrade for a dose-response gradient, as the GLST analysis revealed a significant linear inverse relationship between green leafy vegetable intake and stroke incidence ($p=0.008$). MKSPLINE analyses could not be conducted due to small sample size.




¹⁸ No downgrade for inconsistency as analyses for inconsistency could not be performed due to <2 observations available.

¹⁹ Downgrade for serious indirectness as evidence is based on only 1 cohort of females for USA and may not be generalizable to different populations.

²⁰ Upgrade for a dose-response gradient, as the GLST analysis revealed a significant linear inverse relationship between tomato intake and stroke incidence ($p=0.002$). MKSPLINE analyses could not be conducted due to small sample size.

Table S9. GRADE Assessment for Fruits and Vegetables and Stroke Mortality

Quality Assessment								Study Event Rates (%)	Relative Risk (95% CI)	Certainty
No. of Cohorts	Design	Risk of Bias	Inconsistency	Indirectness	Imprecision	Publication Bias	Other			
Fruit and Vegetable Consumption on Stroke Mortality (follow-up median 19 years)										
6	observational	not serious	not serious	not serious	not serious	undetected ¹	dose-response gradient ²	3,051/499,732 (0.6%)	0.73 (0.65, 0.81)	⊕⊕⊕⊕ MODERATE
Fruit Consumption on Stroke Mortality (follow-up median 20 years)										
14	observational	not serious	serious ³	not serious	not serious	undetected	dose-response gradient ⁴	10,899/1,282,756 (0.8%)	0.87 (0.84, 0.91)	⊕⊕⊕⊕ LOW
Vegetable Consumption on Stroke Mortality (follow-up median 15 years)										
12	observational	not serious	serious ⁵	not serious	serious ⁶	undetected	dose-response gradient ⁷	7,551/780,441 (1.0%)	0.94 (0.90, 0.99)	⊕⊕⊕⊕ LOW
Bananas Consumption on Stroke Mortality (follow-up median 20 years)										
1	observational	not serious	not serious ⁸	serious ⁹	serious ¹⁰	undetected ¹	none	1,34/9,766 (10.6%)	1.04 (0.70, 1.54)	⊕⊕⊕⊕ VERY LOW
Berries Consumption on Stroke Mortality (follow-up median 19 years)										
2	observational	not serious	not serious	serious ¹¹	serious ¹²	undetected ¹	none	1,182/40,224 (2.9%)	0.97 (0.82, 1.15)	⊕⊕⊕⊕ VERY LOW
Citrus Fruit Consumption on Stroke Mortality (follow-up median 20 years)										
4	observational	serious ¹³	serious ¹⁴	not serious	not serious	undetected ¹	dose-response gradient ¹⁵	3,869/145,204 (2.7%)	0.90 (0.86, 0.95)	⊕⊕⊕⊕ LOW
Dried Fruit Consumption on Stroke Mortality (follow-up median 17 years)										
1	observational	not serious	not serious	serious ¹⁶	serious ¹⁷	undetected ¹	none	152/30,458 (0.5%)	0.95 (0.80, 1.13)	⊕⊕⊕⊕ VERY LOW
Fruit Juice Consumption on Stroke Mortality (follow-up median 17 years)										
2	observational	serious ¹⁸	not serious	not serious	not serious	undetected ¹	dose-response gradient ¹⁹	2,232/128,270 (1.7%)	0.67 (0.60, 0.76)	⊕⊕⊕⊕ LOW
Grapes Consumption on Stroke Mortality (follow-up median 19 years)										
2	observational	not serious	not serious	serious ²⁰	serious ²¹	undetected ¹	none	1,182/40,224 (2.9%)	0.74 (0.53, 1.02)	⊕⊕⊕⊕ VERY LOW
Pommes Consumption on Stroke Mortality (follow-up median 17 years)										
3	observational	not serious	not serious	serious ²²	serious ²³	undetected ¹	none	1,651/74,716 (2.2%)	0.91 (0.77, 1.09)	⊕⊕⊕⊕ VERY LOW
Allium Vegetable Consumption on Stroke Mortality (follow-up median 19 years)										
2	observational	not serious	serious ²⁴	not serious	serious ²⁵	undetected ¹	none	544/3,671 (14.8%)	0.99 (0.79, 1.24)	⊕⊕⊕⊕ VERY LOW
Carrots Consumption on Stroke Mortality (follow-up median 20 years)										
1	observational	not serious	not serious ⁸	serious ⁹	not serious	undetected ¹	dose-response gradient ²⁶	1,034/9,766 (10.6%)	0.54 (0.48, 0.61)	⊕⊕⊕⊕ LOW

Cruciferous Vegetables Consumption on Stroke Mortality (follow-up median 20 years)										
5	observational	serious ²⁷	not serious	not serious	serious ²⁸	undetected ¹	none	5,065/195,452 (2.6%)	0.92 (0.85, 1.01)	 VERY LOW
Green Leafy Vegetables Consumption on Stroke Mortality (follow-up median 21 years)										
4	observational	serious ²⁹	serious ³⁰	not serious	serious ³¹	undetected ¹	dose-response gradient ³²	4,103/126,971 (3.2%)	0.90 (0.83, 0.97)	 LOW
Tomatoes Consumption on Stroke Mortality (follow-up median 20 years)										
2	observational	serious ³³	not serious	not serious	serious ³³	undetected ¹	none ³⁴	3,107/108,260 (2.9%)	1.03 (0.94, 1.12)	 VERY LOW

¹ No downgrade for publication bias as publication bias could not be assessed due to lack of power for assessing funnel plot asymmetry and small study effects (i.e. <10 observations available).

² Upgrade for a dose-response gradient, as the GLST analysis revealed a significant linear inverse relationship between fruit and vegetable intake and stroke mortality (p=0.005).

³ Downgrade for serious inconsistency as there was evidence of substantial inter-study heterogeneity ($I^2=75\%$, p<0.00001) which could not be explained by sensitivity analyses.

⁴ Upgrade for a dose-response gradient, as the GLST analysis revealed a significant linear inverse relationship between fruit intake and stroke mortality (p<0.001) and an MKSPLINE analysis revealed a significant non-linear inverse relationship between fruit intake and stroke mortality (p<0.001)

⁵ Downgrade for serious inconsistency given evidence of substantial inter-study heterogeneity ($I^2=62\%$, p=0.0010). Although the removal of Wang et al. 2013 ($I^2=43\%$, p=0.05) or Leeanders et al. 2014 ($I^2=48\%$, p=0.02) during sensitivity analysis did partially explain the heterogeneity, the presence of residual heterogeneity could not be excluded.

⁶ Downgrade for serious imprecision, as the lower bound of the 95% CI (RR, 0.90) includes the MID of 5% while the upper bound of the 95% CI (RR, 0.99) crosses the MID.

⁷ Upgrade for a dose-response gradient, as the GLST analysis revealed a significant linear inverse relationship between vegetable intake and stroke mortality (p=0.025).

⁸ No downgrade for inconsistency as analyses for inconsistency could not be performed due to <2 observations available.

⁹ Downgrade for serious indirectness as evidence is based on 1 male cohort and may not be generalizable to different populations

¹⁰ Downgrade for serious imprecision, as the lower and upper bound of the 95% CIs (RR, 0.70 to 1.54) includes both clinically important benefit (RR<0.95) and harm (RR≥1.05).

¹¹ Downgrade for serious indirectness as evidence is based on a predominately (76%) female population and may not be generalizable to different populations.

¹² Downgrade for serious imprecision, as the lower bound of the 95% CI (RR, 0.82) includes the MID of 5% while the upper bound of the 95% CI (RR, 1.15) crosses the MID.

¹³ Downgrade for serious risk of bias as 75.3% of effect estimate is based on Iso et al. 2007, which presented with a high risk of bias (Newcastle-Ottawa Score: 5/9).

¹⁴ Downgrade for serious inconsistency given evidence of substantial inter-study heterogeneity ($I^2=82\%$, p=0.0001). Although the removal of Wang et al. 2016 ($I^2=40\%$, p=0.17) during sensitivity analysis did partially explain the heterogeneity, the presence of residual heterogeneity could not be excluded.

¹⁵ Upgrade for a dose-response gradient, as the GLST analysis revealed a significant linear inverse relationship between citrus fruit intake and stroke mortality (p<0.001).

¹⁶ Downgrade for serious indirectness as evidence is based on one female population and may not be generalizable to different populations.

¹⁷ Downgrade for serious imprecision, as the lower and upper bound of the 95% CIs (RR, 0.80 to 1.13) includes both clinically important benefit (RR<0.95) and harm (RR≥1.05).

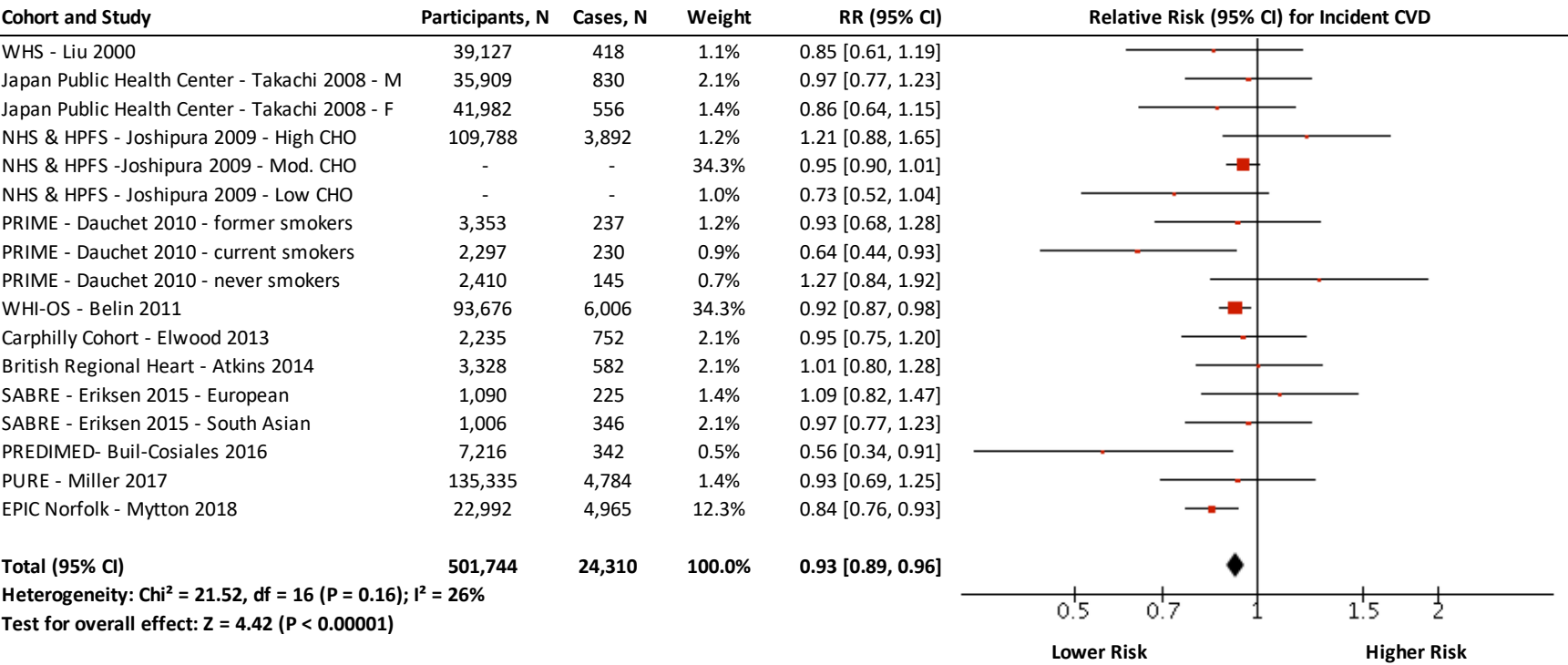
¹⁸ Downgrade for serious risk of bias as 62% of effect estimate is based on Iso et al. 2007, which presented with a high risk of bias (Newcastle-Ottawa Score: 5/9).

- ¹⁹ Upgrade for a dose-response gradient, as the GLST analysis revealed a significant linear inverse relationship between fruit juice intake and CHD mortality ($p=0.002$). MKSPLINE analyses could not be conducted due to small sample size.
- ²⁰ Downgrade for serious indirectness as evidence is based on a predominately (76%) female population and may not be generalizable to different populations.
- ²¹ Downgrade for serious imprecision, as the lower and upper bound of the 95% CIs (RR, 0.53 to 1.02) includes both clinically important benefit ($RR<0.95$) and harm ($RR\geq 1.05$).
- ²² Downgrade for serious indirectness as evidence is based on a predominately (87%) female population and may not be generalizable to different populations.
- ²³ Downgrade for serious imprecision, as the lower bound of the 95% CI (RR, 0.77) includes the MID of 5% while the upper bound of the 95% CI (RR, 1.09) crosses the MID.
- ²⁴ Downgrade for serious inconsistency given evidence of substantial inter-study heterogeneity ($I^2=96\%$, $p<0.00001$).
- ²⁵ Downgrade for serious imprecision, as the lower and upper bound of the 95% CIs (RR, 0.79 to 1.24) includes both clinically important benefit ($RR<0.95$) and harm ($RR\geq 1.05$).
- ²⁶ Upgrade for a dose-response gradient, as the GLST analysis revealed a significant linear inverse relationship between carrots intake and stroke mortality ($p<0.001$).
- ²⁷ Downgrade for serious risk of bias as 79.4% of effect estimate is based on Iso et al. 2007, which presented with a high risk of bias (Newcastle-Ottawa Score: 5/9).
- ²⁸ Downgrade for serious imprecision, as the lower bound of the 95% CI (RR, 0.85) includes the MID of 5% while the upper bound of the 95% CI (RR, 1.01) crosses the MID.
- ²⁹ Downgrade for serious risk of bias as 50.0% of effect estimate is based on Iso et al. 2007, which presented with a high risk of bias (Newcastle-Ottawa Score: 5/9).
- ³⁰ Downgrade for serious inconsistency given evidence of substantial inter-study heterogeneity ($I^2=50\%$, $p=0.09$). Although the removal of Appleby et al. 2002 ($I^2=36\%$, $p=0.20$) or Wang et al. 2016 ($I^2=25\%$, $p=0.05$) during sensitivity analysis did partially explain the heterogeneity, the presence of residual heterogeneity could not be excluded.
- ³¹ Downgrade for serious imprecision, as the lower bound of the 95% CI (RR, 0.83) includes the MID of 5% while the upper bound of the 95% CI (RR, 0.97) crosses the MID.
- ³² Upgrade for a dose-response gradient, as the GLST analysis revealed a significant linear inverse relationship between green leafy vegetable intake and CHD mortality ($p=0.032$). MKSPLINE analyses could not be conducted due to small sample size.
- ³³ Downgrade for serious risk of bias as 60.4% of effect estimate is based on Iso et al. 2007, which presented with a high risk of bias (Newcastle-Ottawa Score: 5/9).
- ³⁴ Downgrade for serious imprecision, as the lower bound of the 95% CI (RR, 0.94) includes the MID of 5% while the upper bound of the 95% CI (RR, 1.12) crosses the MID.
- ³⁵ Dose-response gradient could not be assessed due to insufficient dose ranges available to determine the presence of a linear/non-linear dose response.

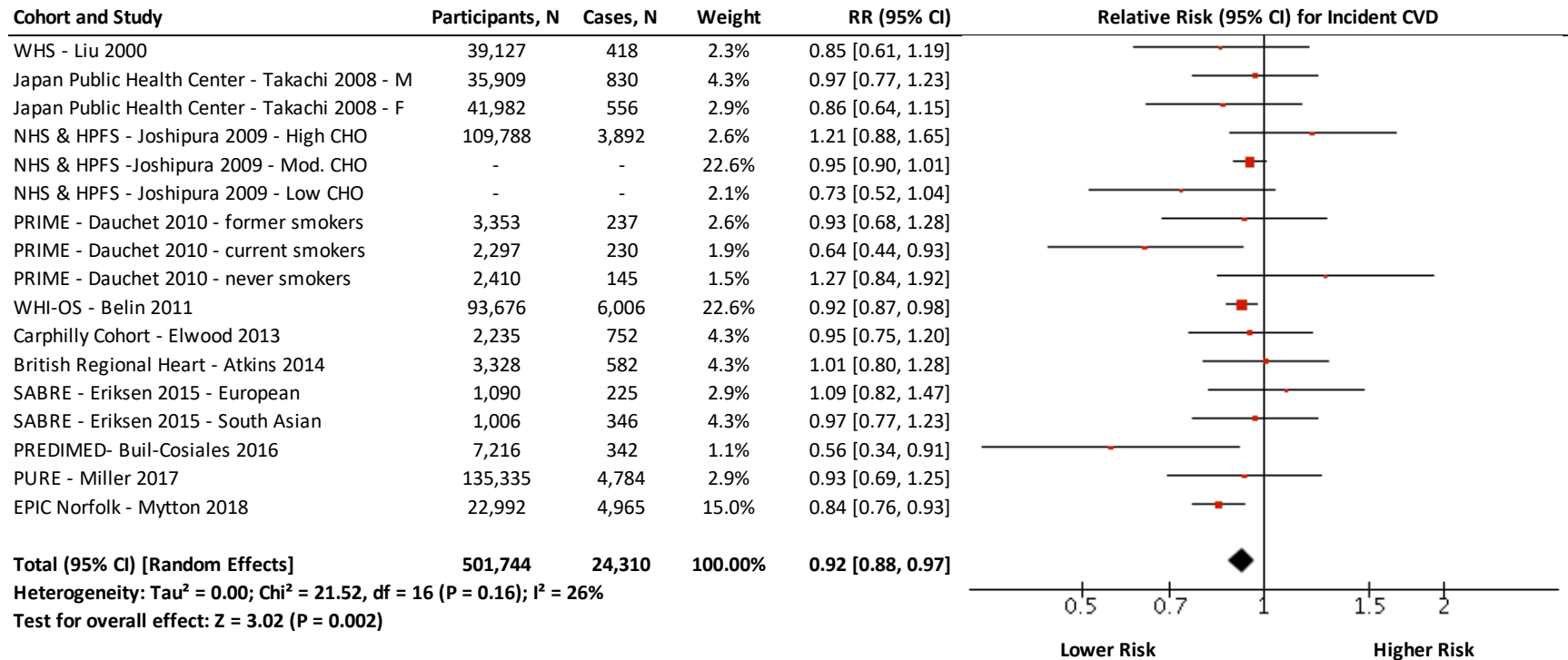
Figure S1. Relation between total fruit and vegetable intake and cardiovascular disease incidence (highest vs. lowest level of intake).

TOTAL FRUIT AND VEGETABLES AND CARDIOVASCULAR DISEASE INCIDENCE

A. Fixed Effects



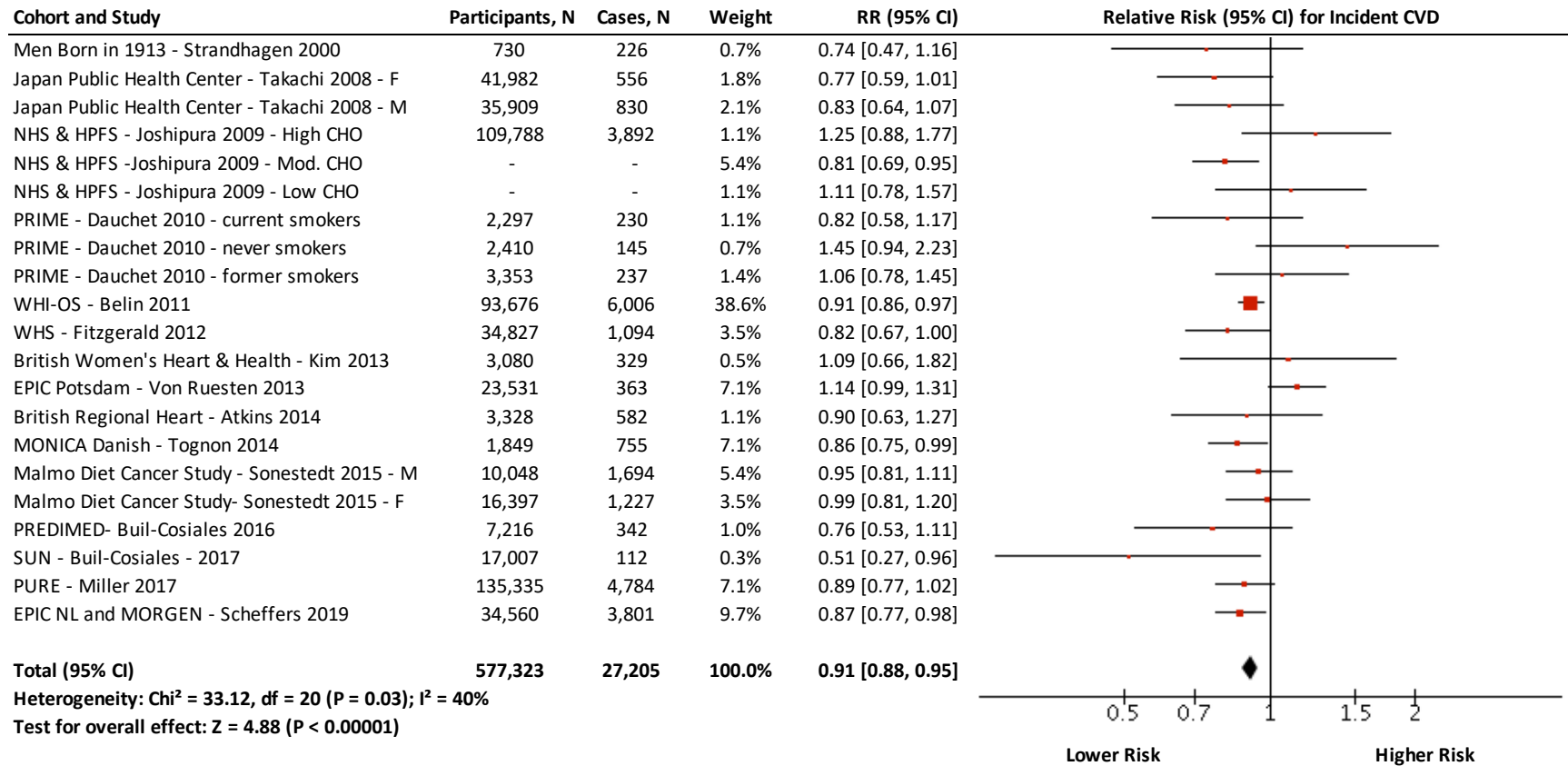
B. Random Effects



All results are presented as relative risk (RR) with 95% confidence intervals (95% CI). Pooled risk estimate is represented by the black diamond using (A) fixed effects and (B) random effects models. Inter-study heterogeneity was assessed using the Cochran Q statistic (Chi²) at a significance level of $p < 0.10$, and quantified by I², with values $\geq 50\%$ indicating substantial heterogeneity.

FRUIT AND CARDIOVASCULAR DISEASE INCIDENCE

A. Fixed Effects



B. Random Effects

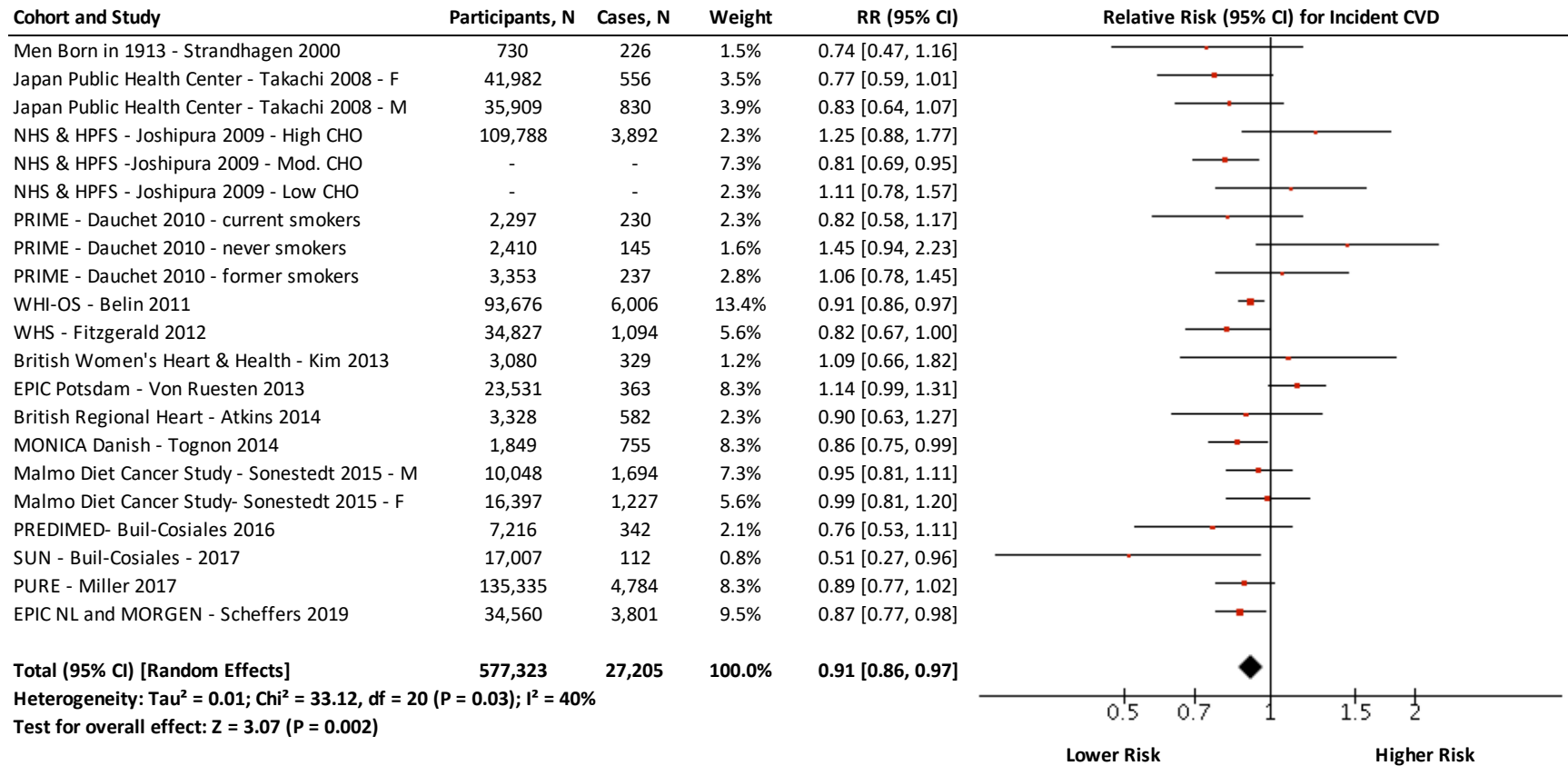
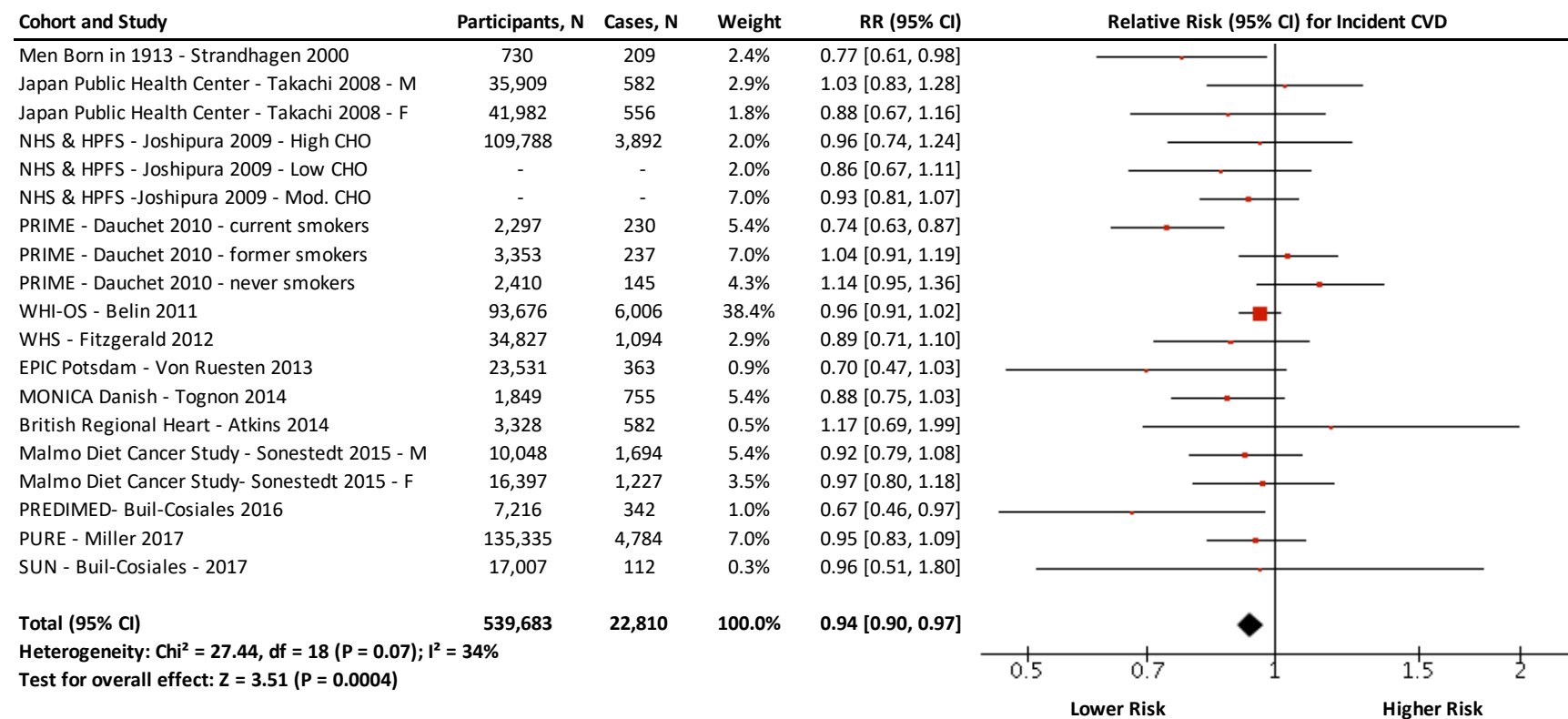


Figure S2. Relation between fruit intake and cardiovascular disease incidence (highest vs. lowest level of intake). All results are presented as relative risk (RR) with 95% confidence intervals (95% CI). Pooled risk estimate is represented by the black diamond using (A) fixed effects and (B) random effects models. Inter-study heterogeneity was assessed using the Cochran Q statistic (Chi²) at a significance level of p<0.10, and quantified by I², with values ≥ 50% indicating substantial heterogeneity.

VEGETABLES AND CARDIOVASCULAR DISEASE INCIDENCE

A. Fixed Effects



B. Random Effects

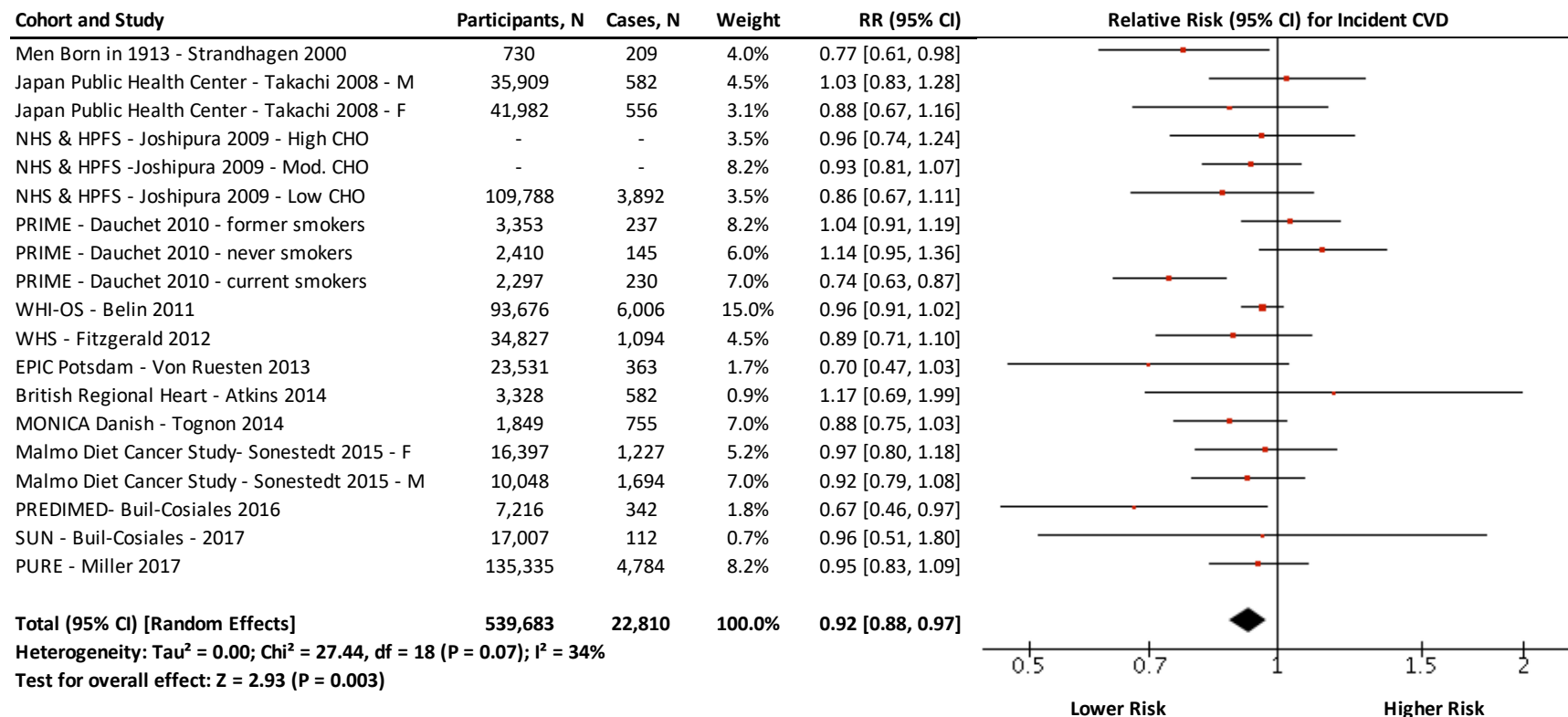


Figure S3. Relation between vegetable intake and cardiovascular disease incidence (highest vs. lowest level of intake). All results are presented as relative risk (RR) with 95% confidence intervals (95% CI). Pooled risk estimate is represented by the black diamond using (A) fixed effects and (B) random effects models. Inter-study heterogeneity was assessed using the Cochran Q statistic (Chi²) at a significance level of p<0.10, and quantified by I², with values ≥ 50% indicating substantial heterogeneity.

BERRIES AND CARDIOVASCULAR DISEASE INCIDENCE

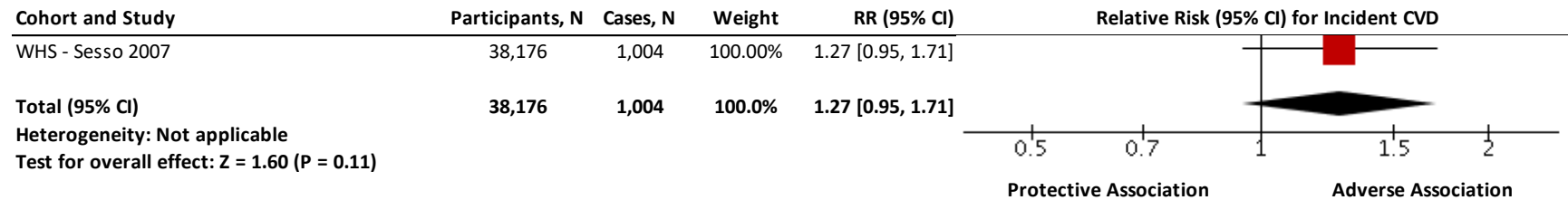
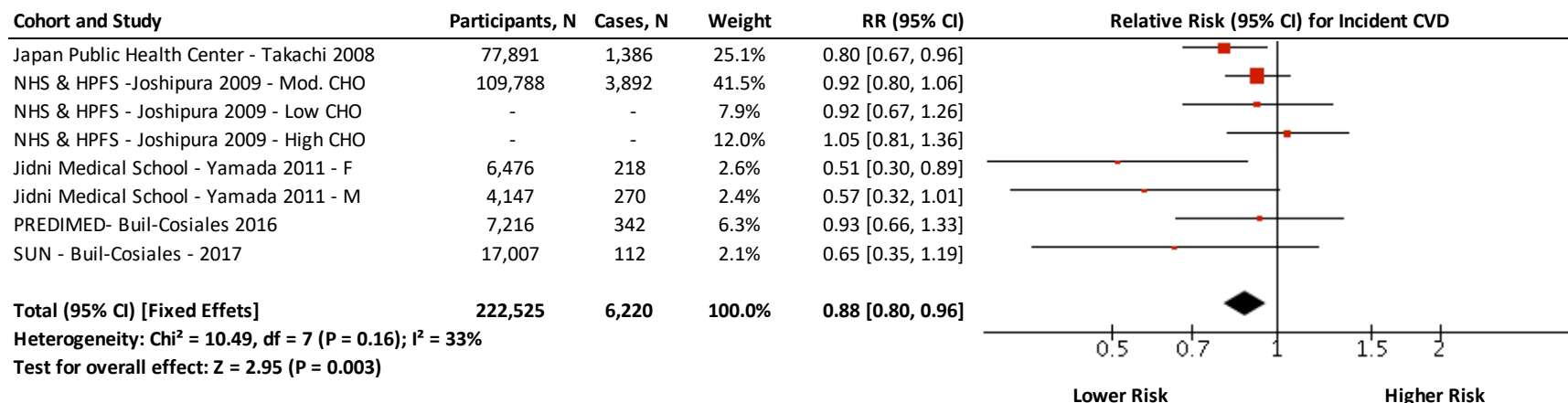


Figure S4. Relation between intake of berries and cardiovascular disease incidence (highest vs. lowest level of intake). All results are presented as relative risk (RR) with 95% confidence intervals (95% CI). Pooled risk estimate is represented by the black diamond. Inter-study heterogeneity was assessed using the Cochran Q statistic (χ^2) at a significance level of $p < 0.10$, and quantified by I^2 , with values $\geq 50\%$ indicating substantial heterogeneity.

CITRUS FRUIT AND CARDIOVASCULAR DISEASE INCIDENCE

A. Fixed Effects



B. Random Effects

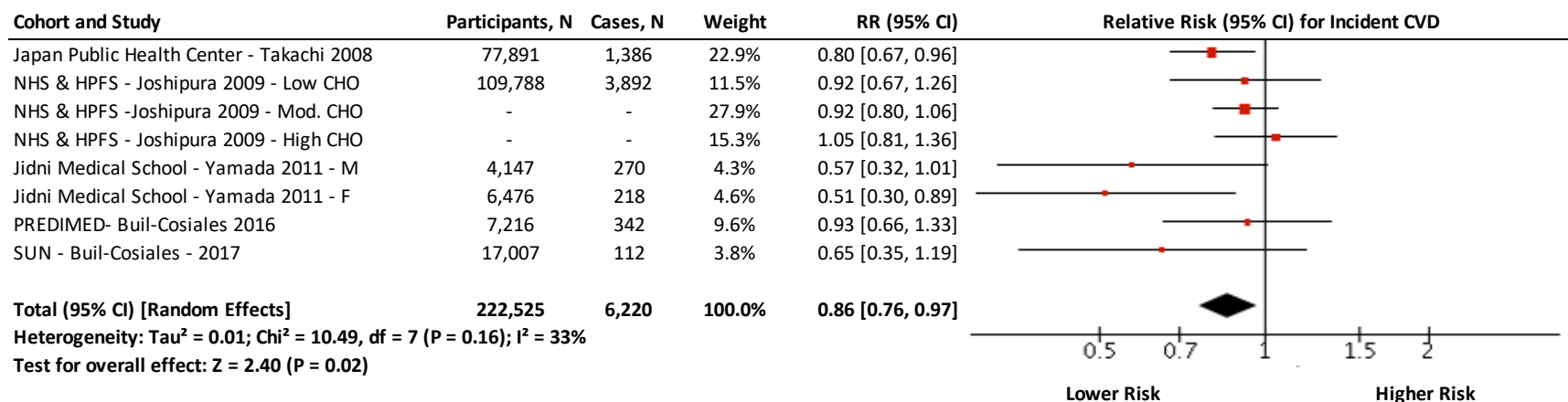


Figure S5. Relation between citrus fruit intake and cardiovascular disease incidence (highest vs. lowest level of intake). All results are presented as relative risk (RR) with 95% confidence intervals (95% CI). Pooled risk estimate is represented by the black diamond using (A) fixed effects and (B) random effects models. Inter-study heterogeneity was assessed using the Cochran Q statistic (χ^2) at a significance level of $p < 0.10$, and quantified by I^2 , with values $\geq 50\%$ indicating substantial heterogeneity.

FRUIT JUICE AND CARDIOVASCULAR DISEASE INCIDENCE

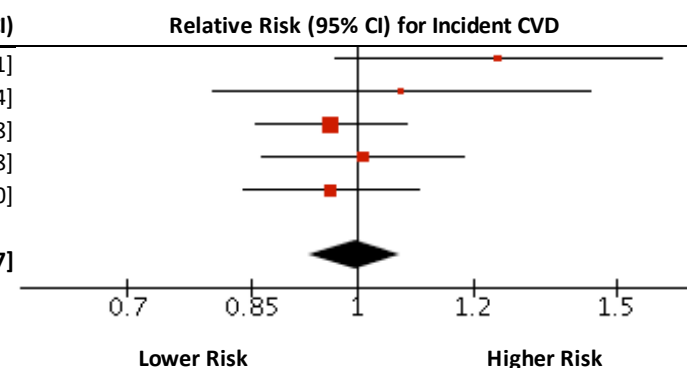
A. Fixed Effects

Cohort and Study	Participants, N	Cases, N	Weight	RR (95% CI)
NHS & HPFS - Joshipura 2009 - High CHO	109,788	3,892	8.0%	1.25 [0.97, 1.61]
NHS & HPFS - Joshipura 2009 - Low CHO	-	-	6.0%	1.07 [0.80, 1.44]
NHS & HPFS -Joshipura 2009 - Mod. CHO	-	-	37.5%	0.96 [0.85, 1.08]
EPIC Potsdam - Von Ruesten 2013	23,531	363	21.1%	1.01 [0.86, 1.18]
EPIC NL and MORGEN - Scheffers 2019	34,560	3,801	27.5%	0.96 [0.84, 1.10]

Total (95% CI) 167,879 8,056 100.0% 1.00 [0.93, 1.07]

Heterogeneity: $\tau^2 = 0.00$; $\chi^2 = 3.86$, $df = 4$ ($P = 0.42$); $I^2 = 0\%$

Test for overall effect: $Z = 0.06$ ($P = 0.95$)



B. Random Effects

Cohort and Study	Participants, N	Cases, N	Weight	RR (95% CI)
NHS & HPFS - Joshipura 2009 - High CHO	109,788	3,892	8.0%	1.25 [0.97, 1.61]
NHS & HPFS - Joshipura 2009 - Low CHO	-	-	6.0%	1.07 [0.80, 1.44]
NHS & HPFS -Joshipura 2009 - Mod. CHO	-	-	37.5%	0.96 [0.85, 1.08]
EPIC Potsdam - Von Ruesten 2013	23,531	363	21.1%	1.01 [0.86, 1.18]
EPIC NL and MORGEN - Scheffers 2019	34,560	3,801	27.5%	0.96 [0.84, 1.10]

Total (95% CI) 167,879 8,056 100.0% 1.00 [0.93, 1.07]

Heterogeneity: $\tau^2 = 0.00$; $\chi^2 = 3.86$, $df = 4$ ($P = 0.42$); $I^2 = 0\%$

Test for overall effect: $Z = 0.06$ ($P = 0.95$)

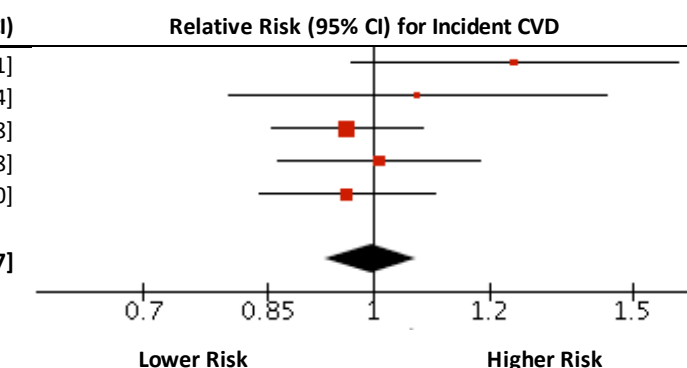
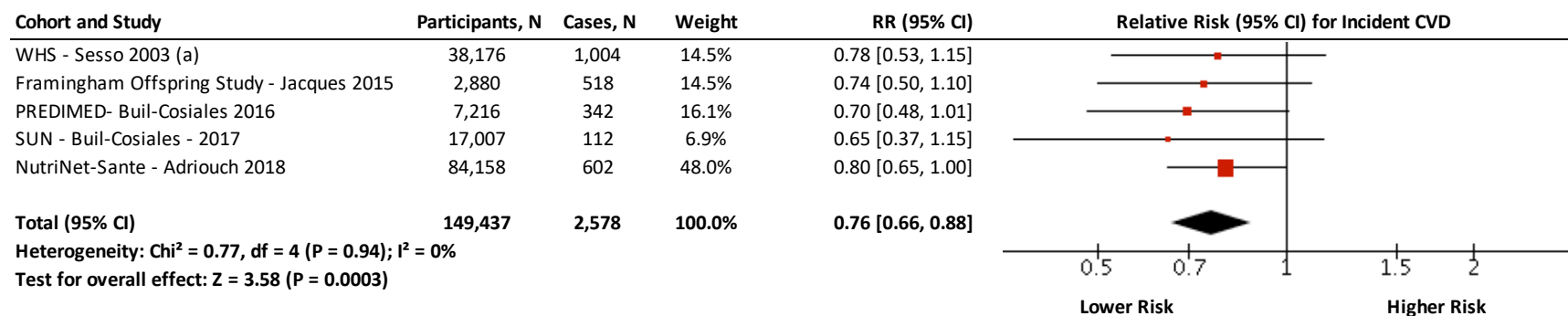


Figure S6. Relation between fruit juice intake and cardiovascular disease incidence (highest vs. lowest level of intake). All results are presented as relative risk (RR) with 95% confidence intervals (95% CI). Pooled risk estimate is represented by the black diamond using (A) fixed effects and (B) random effects models. Inter-study heterogeneity was assessed using the Cochran Q statistic (χ^2) at a significance level of $p < 0.10$, and quantified by I^2 , with values $\geq 50\%$ indicating substantial heterogeneity.

POMMES AND CARDIOVASCULAR DISEASE INCIDENCE

A. Fixed Effects



B. Random Effects

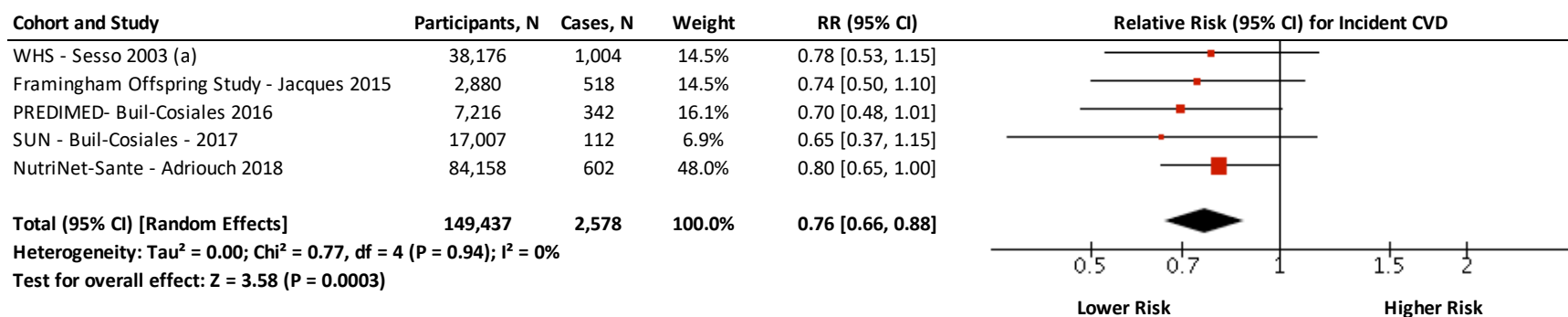
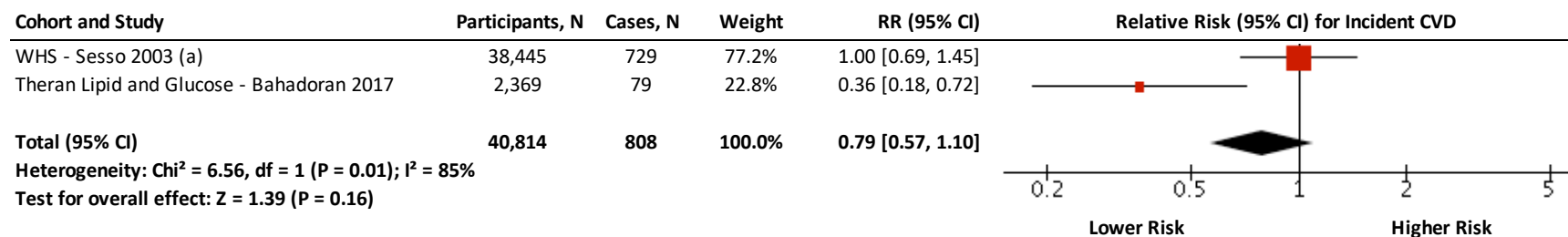


Figure S7. Relation between pommes intake and cardiovascular disease incidence (highest vs. lowest level of intake). All results are presented as relative risk (RR) with 95% confidence intervals (95% CI). Pooled risk estimate is represented by the black diamond using (A) fixed effects and (B) random effects models. Inter-study heterogeneity was assessed using the Cochran Q statistic (χ^2) at a significance level of $p < 0.10$, and quantified by I^2 , with values $\geq 50\%$ indicating substantial heterogeneity.

ALLIUM VEGETABLES AND CARDIOVASCULAR DISEASE INCIDENCE

A. Fixed Effects



B. Random Effects

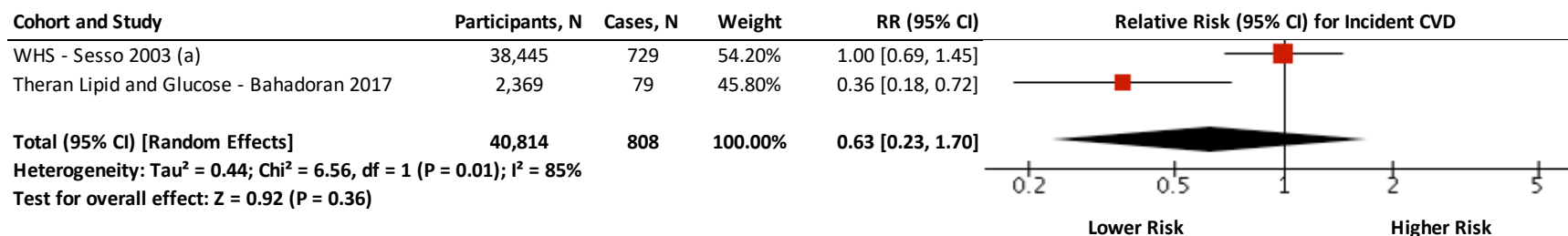


Figure S8. Relation between intake of allium vegetables and cardiovascular disease incidence (highest vs. lowest level of intake). All results are presented as relative risk (RR) with 95% confidence intervals (95% CI). Pooled risk estimate is represented by the black diamond using (A) fixed effects and (B) random effects models. Inter-study heterogeneity was assessed using the Cochran Q statistic (χ^2) at a significance level of $p < 0.10$, and quantified by I^2 , with values $\geq 50\%$ indicating substantial heterogeneity.

CRUCIFEROUS VEGETABLES AND CARDIOVASCULAR DISEASE INCIDENCE

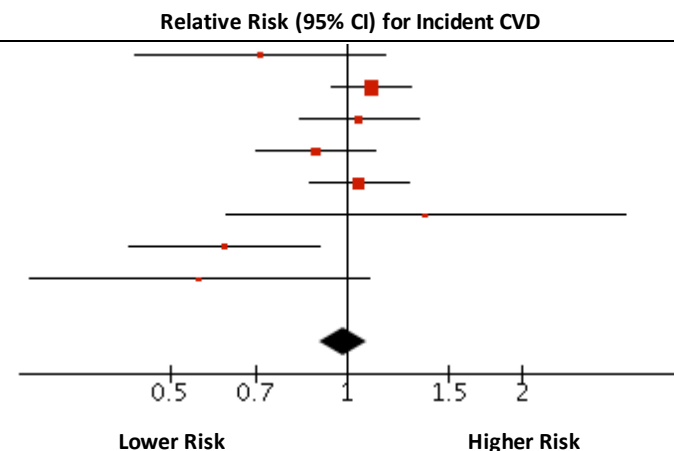
A. Fixed Effects

Cohort and Study	Participants, N	Cases, N	Weight	RR (95% CI)
WHS - Sesso 2003 (a)	38,445	729	3.5%	0.71 [0.44, 1.16]
Japan Public Health Center - Takachi 2008	77,891	1,386	34.4%	1.11 [0.94, 1.29]
NHS & HPFS - Josophura 2009 - Low CHO	109,788	3,892	15.3%	1.05 [0.83, 1.33]
NHS & HPFS - Josophura 2009 - High CHO	-	-	15.3%	0.89 [0.70, 1.12]
NHS & HPFS -Josophura 2009 - Mod. CHO	-	-	22.0%	1.05 [0.86, 1.28]
EPIC Potsdam - Von Ruesten 2013	23,531	363	1.4%	1.36 [0.62, 2.99]
PREDIMED- Buil-Cosiales 2016	7,216	342	6.1%	0.62 [0.43, 0.90]
SUN - Buil-Cosiales - 2017	17,007	112	1.9%	0.56 [0.29, 1.09]

Total (95% CI) 273,878 6,824 100.0% **0.99 [0.90, 1.08]**

Heterogeneity: Chi² = 14.65, df = 7 (P = 0.04); I² = 52%

Test for overall effect: Z = 0.28 (P = 0.78)



B. Random Effects

Cohort and Study	Participants, N	Cases, N	Weight	RR (95% CI)
WHS - Sesso 2003 (a)	38,445	729	7.2%	0.71 [0.44, 1.16]
Japan Public Health Center - Takachi 2008	77,891	1,386	21.7%	1.11 [0.94, 1.29]
NHS & HPFS - Josophura 2009 - High CHO	-	-	16.8%	0.89 [0.70, 1.12]
NHS & HPFS -Josophura 2009 - Mod. CHO	-	-	19.2%	1.05 [0.86, 1.28]
NHS & HPFS - Josophura 2009 - Low CHO	109,788	3,892	16.8%	1.05 [0.83, 1.33]
EPIC Potsdam - Von Ruesten 2013	23,531	363	3.3%	1.36 [0.62, 2.99]
PREDIMED- Buil-Cosiales 2016	7,216	342	10.5%	0.62 [0.43, 0.90]
SUN - Buil-Cosiales - 2017	17,007	112	4.4%	0.56 [0.29, 1.09]

Total (95% CI) [Random Effects] 273,878 6,824 100.0% **0.93 [0.80, 1.09]**

Heterogeneity: Tau² = 0.02; Chi² = 14.65, df = 7 (P = 0.04); I² = 52%

Test for overall effect: Z = 0.91 (P = 0.36)

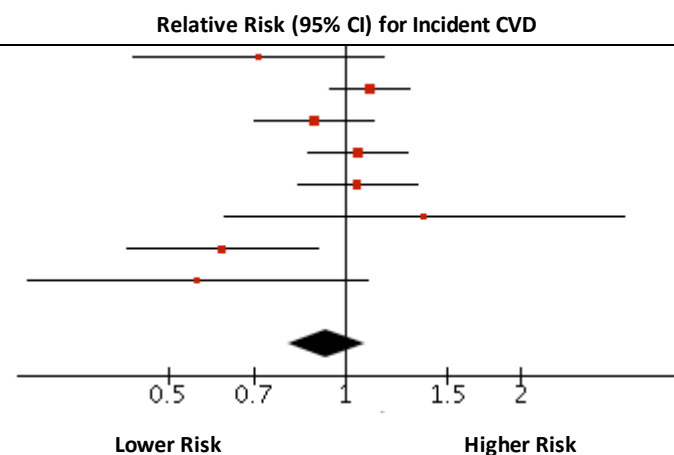
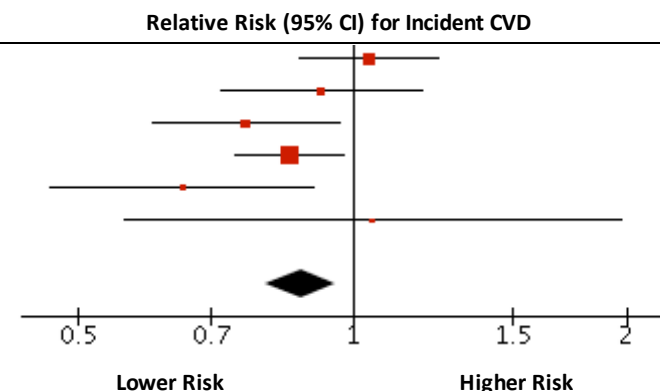


Figure S9. Relation between intake of cruciferous vegetables and cardiovascular disease incidence (highest vs. lowest level of intake). All results are presented as relative risk (RR) with 95% confidence intervals (95% CI). Pooled risk estimate is represented by the black diamond using (A) fixed effects and (B) random effects models. Inter-study heterogeneity was assessed using the Cochran Q statistic (Chi²) at a significance level of p<0.10, and quantified by I², with values ≥ 50% indicating substantial heterogeneity.

GREEN LEAFY VEGETABLES AND CARDIOVASCULAR DISEASE INCIDENCE

A. Fixed Effects

Cohort and Study	Participants, N	Cases, N	Weight	RR (95% CI)
Japan Public Health Center - Takachi 2008	77,891	1,386	24.7%	1.04 [0.87, 1.24]
NHS & HPFS - Josophura 2009 - High CHO	109,788	3,892	11.8%	0.92 [0.72, 1.19]
NHS & HPFS -Josophura 2009 - Low. CHO	-	-	13.9%	0.76 [0.60, 0.97]
NHS & HPFS -Josophura 2009 - Mod. CHO	-	-	40.8%	0.85 [0.74, 0.98]
PREDIMED- Buil-Cosiales 2016	7,216	342	6.9%	0.65 [0.47, 0.91]
SUN - Buil-Cosiales - 2017	17,007	112	2.0%	1.05 [0.56, 1.97]
Total (95% CI)	211,902	5,732	100.0%	0.87 [0.76, 0.99]
Heterogeneity: Chi² = 8.69, df = 5 (P = 0.12); I² = 42%				
Test for overall effect: Z = 2.93 (P = 0.003)				



B. Random Effects

Cohort and Study	Participants, N	Cases, N	Weight	RR (95% CI)
Japan Public Health Center - Takachi 2008	77,891	1,386	24.7%	1.04 [0.87, 1.24]
NHS & HPFS - Josophura 2009 - High CHO	109,788	3,892	11.8%	0.92 [0.72, 1.19]
NHS & HPFS -Josophura 2009 - Low. CHO	-	-	13.9%	0.76 [0.60, 0.97]
NHS & HPFS -Josophura 2009 - Mod. CHO	-	-	40.8%	0.85 [0.74, 0.98]
PREDIMED- Buil-Cosiales 2016	7,216	342	6.9%	0.65 [0.47, 0.91]
SUN - Buil-Cosiales - 2017	17,007	112	2.0%	1.05 [0.56, 1.97]
Total (95% CI)	211,902	5,732	100.0%	0.87 [0.76, 0.99]
Heterogeneity: Tau² = 0.01; Chi² = 8.69, df = 5 (P = 0.12); I² = 42%				
Test for overall effect: Z = 2.16 (P = 0.03)				

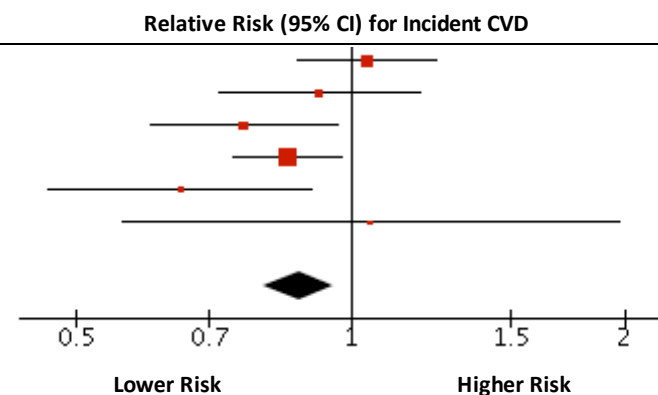
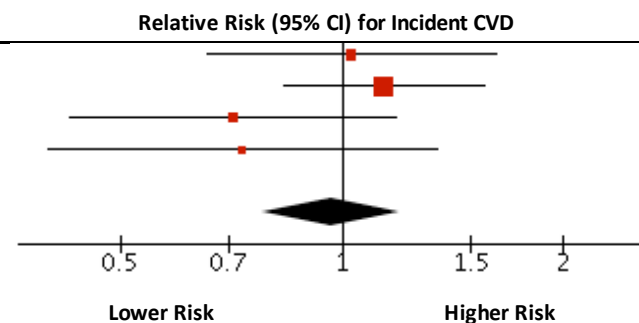


Figure S10. Relation between intake of green leafy vegetables and cardiovascular disease incidence (highest vs. lowest level of intake). All results are presented as relative risk (RR) with 95% confidence intervals (95% CI). Pooled risk estimate is represented by the black diamond using (A) fixed effects and (B) random effects models. Inter-study heterogeneity was assessed using the Cochran Q statistic (Chi²) at a significance level of $p < 0.10$, and quantified by I², with values $\geq 50\%$ indicating substantial heterogeneity.

TOMATOES AND CARDIOVASCULAR DISEASE INCIDENCE

A. Fixed Effects

Cohort and Study	Participants, N	Cases, N	Weight	RR (95% CI)
WHS - Sesso 2003 (b) - tomatoes	38,445	729	22.7%	1.03 [0.66, 1.62]
WHS - Sesso 2003 (b) - tomato juice	-	-	47.0%	0.71 [0.43, 1.18]
WHS - Sesso 2003 (b) - tomato based products	-	-	17.8%	1.14 [0.83, 1.56]
SUN - Buil-Cosiales - 2017	17,007	112	12.5%	0.73 [0.40, 1.35]
Total (95% CI)	55,452	841	100.0%	0.97 [0.78, 1.20]
Heterogeneity: $\chi^2 = 3.31$, $df = 3$ ($P = 0.35$); $I^2 = 9\%$				
Test for overall effect: $Z = 0.29$ ($P = 0.77$)				



B. Random Effects

Cohort and Study	Participants, N	Cases, N	Weight	RR (95% CI)
WHS - Sesso 2003 (b) - tomatoes	38,445	729	23.5%	1.03 [0.66, 1.62]
WHS - Sesso 2003 (b) - tomato based products	-	-	18.8%	0.71 [0.43, 1.18]
WHS - Sesso 2003 (b) - tomato juice	-	-	44.2%	1.14 [0.83, 1.56]
SUN - Buil-Cosiales - 2017	17,007	112	13.5%	0.73 [0.40, 1.35]
Total (95% CI) [Random Effects]	55,452	841	100.0%	0.96 [0.76, 1.21]
Heterogeneity: $\tau^2 = 0.01$; $\chi^2 = 3.31$, $df = 3$ ($P = 0.35$); $I^2 = 9\%$				
Test for overall effect: $Z = 0.35$ ($P = 0.73$)				

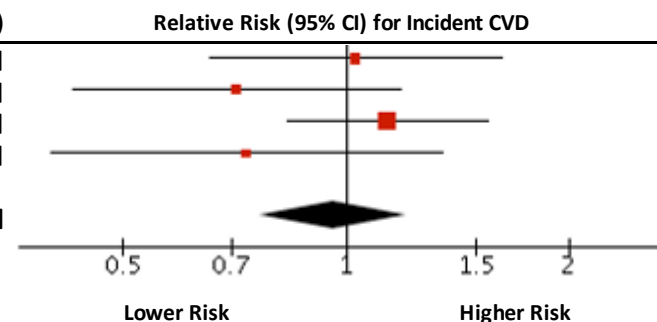
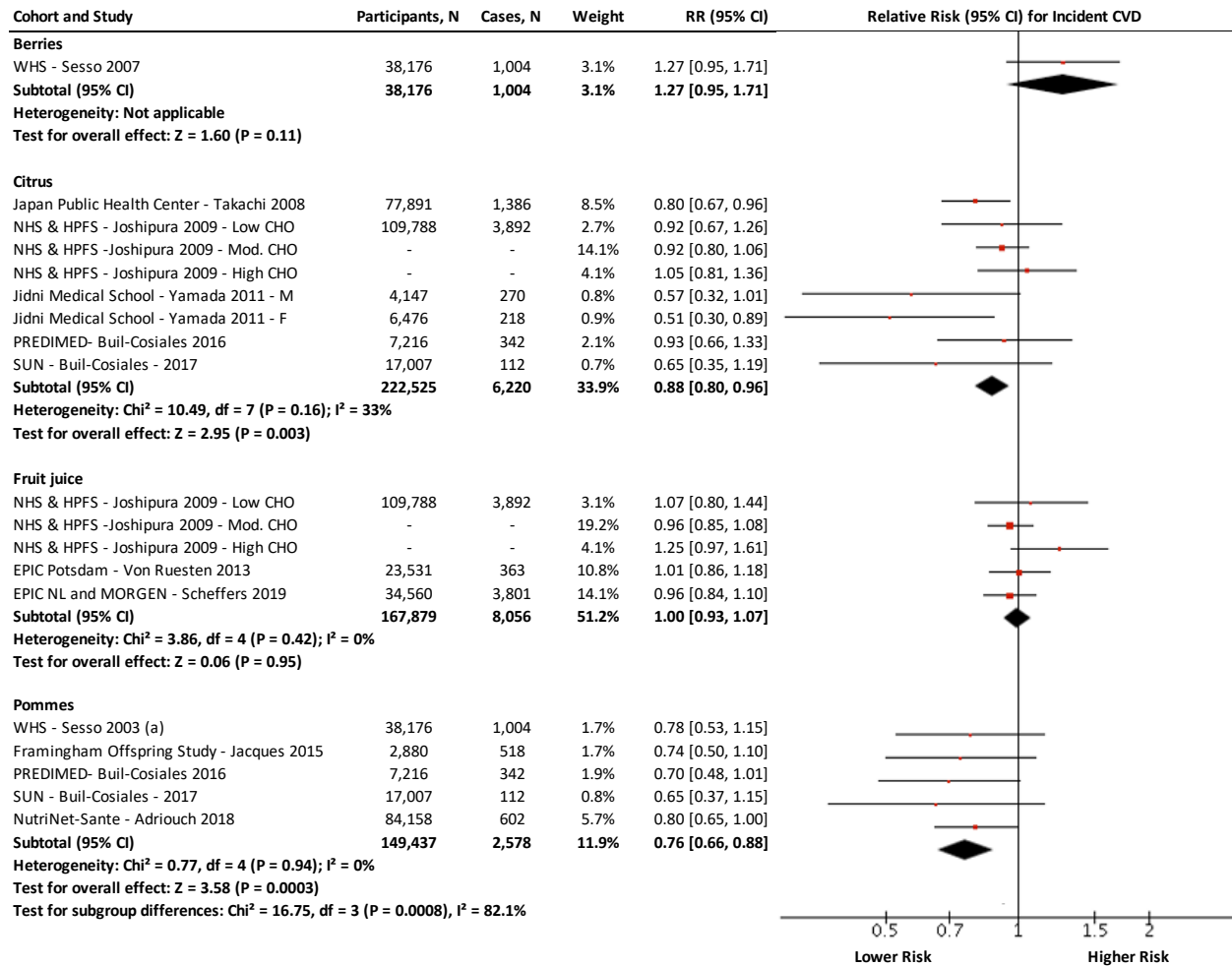


Figure S11. Relation between tomato intake and cardiovascular disease incidence (highest vs. lowest level of intake). All results are presented as relative risk (RR) with 95% confidence intervals (95% CI). Pooled risk estimate is represented by the black diamond using (A) fixed effects and (B) random effects models. Inter-study heterogeneity was assessed using the Cochran Q statistic (χ^2) at a significance level of $p < 0.10$, and quantified by I^2 , with values $\geq 50\%$ indicating substantial heterogeneity.

A. Fixed Effects



B. Random Effects

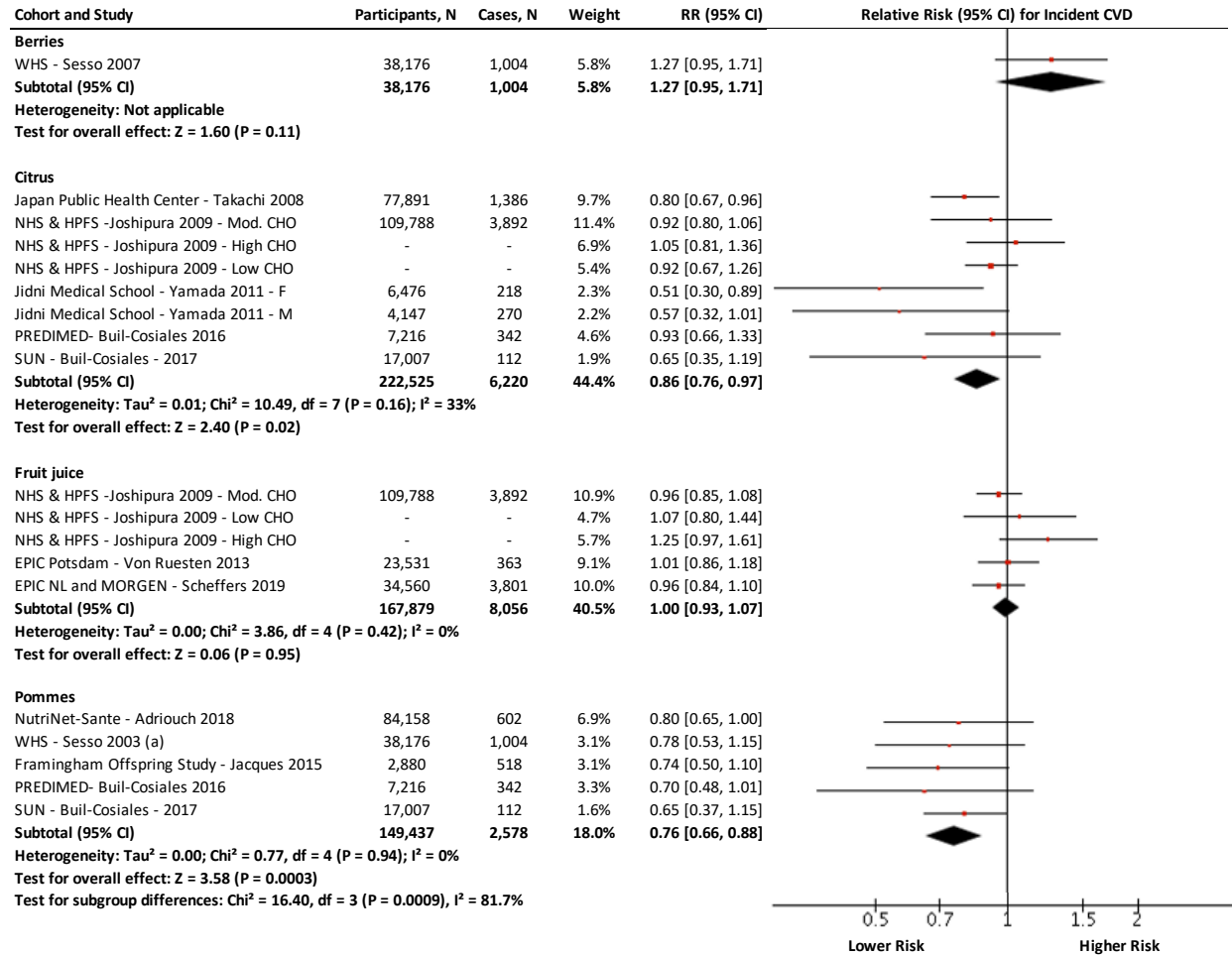
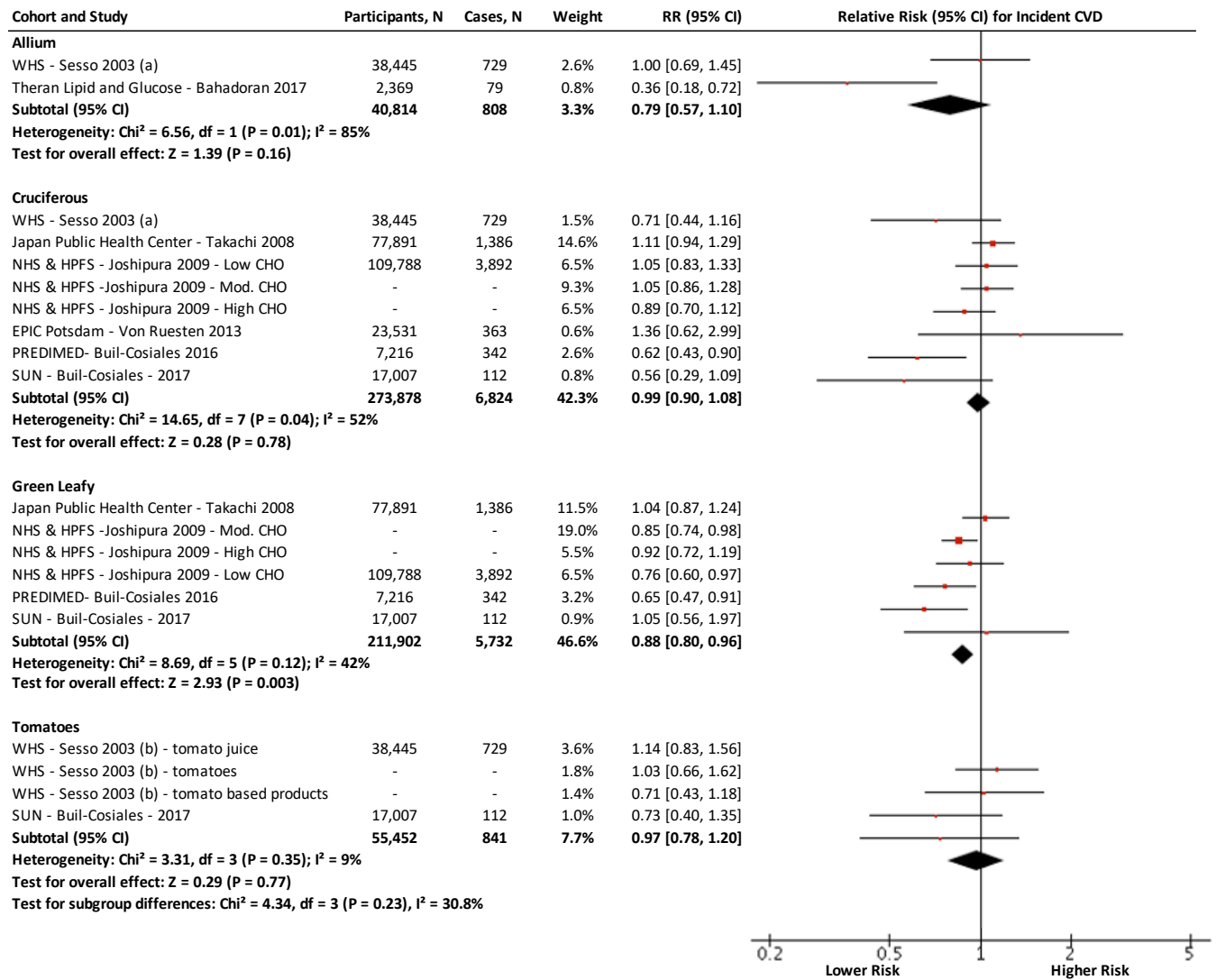


Figure S12. Relation between sources of fruit and CVD incidence (highest vs. lowest level of intake). All results are presented as relative risk (RR) with 95% confidence intervals (95% CI). Pooled risk estimate is represented by the black diamond using (A) fixed effects and (B) random effects models. Inter-study heterogeneity was assessed using the Cochran Q statistic (Chi²) at a significance level of p<0.10, and quantified by I², with values ≥ 50% indicating substantial heterogeneity.

A. Fixed Effects



B. Random Effects

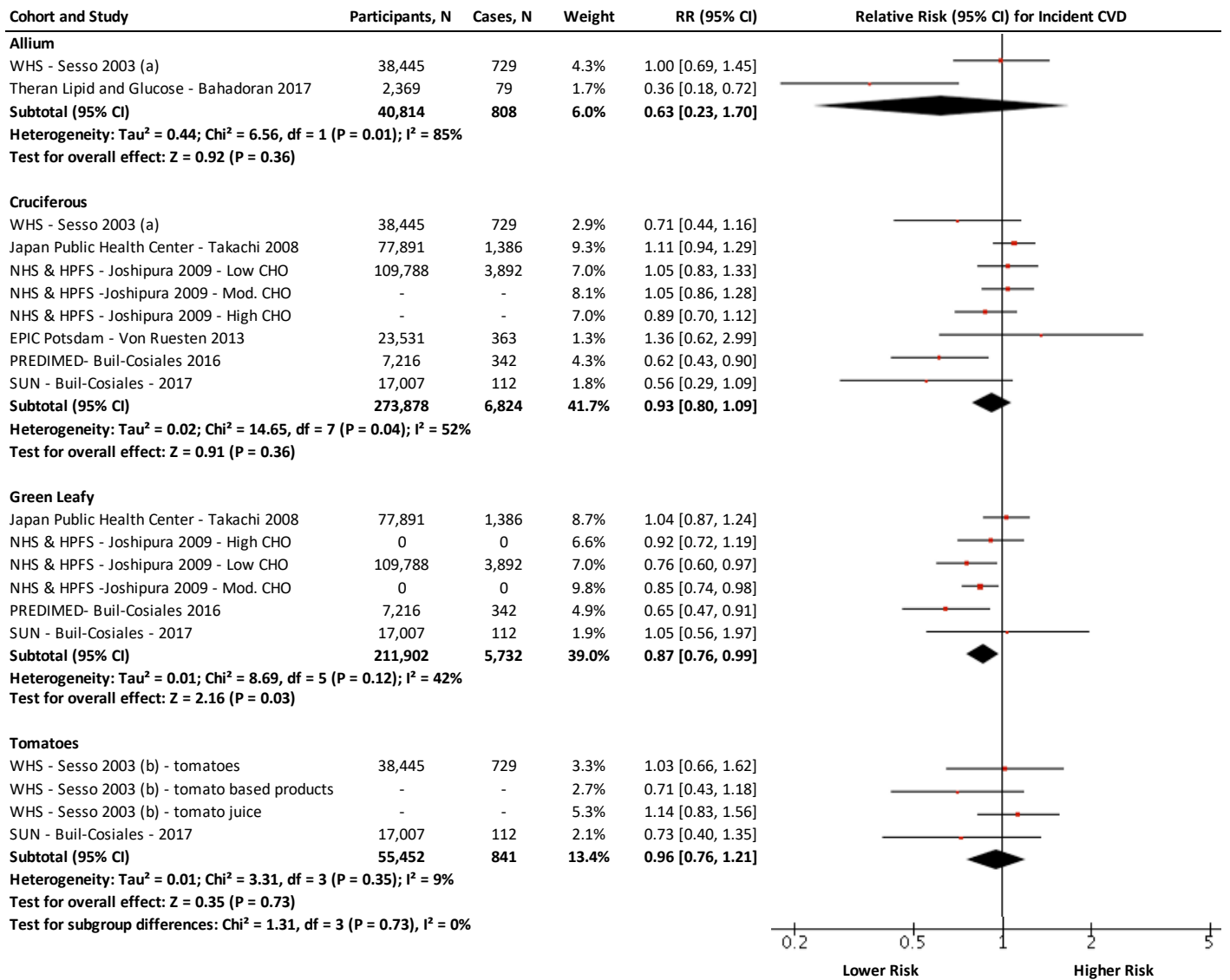
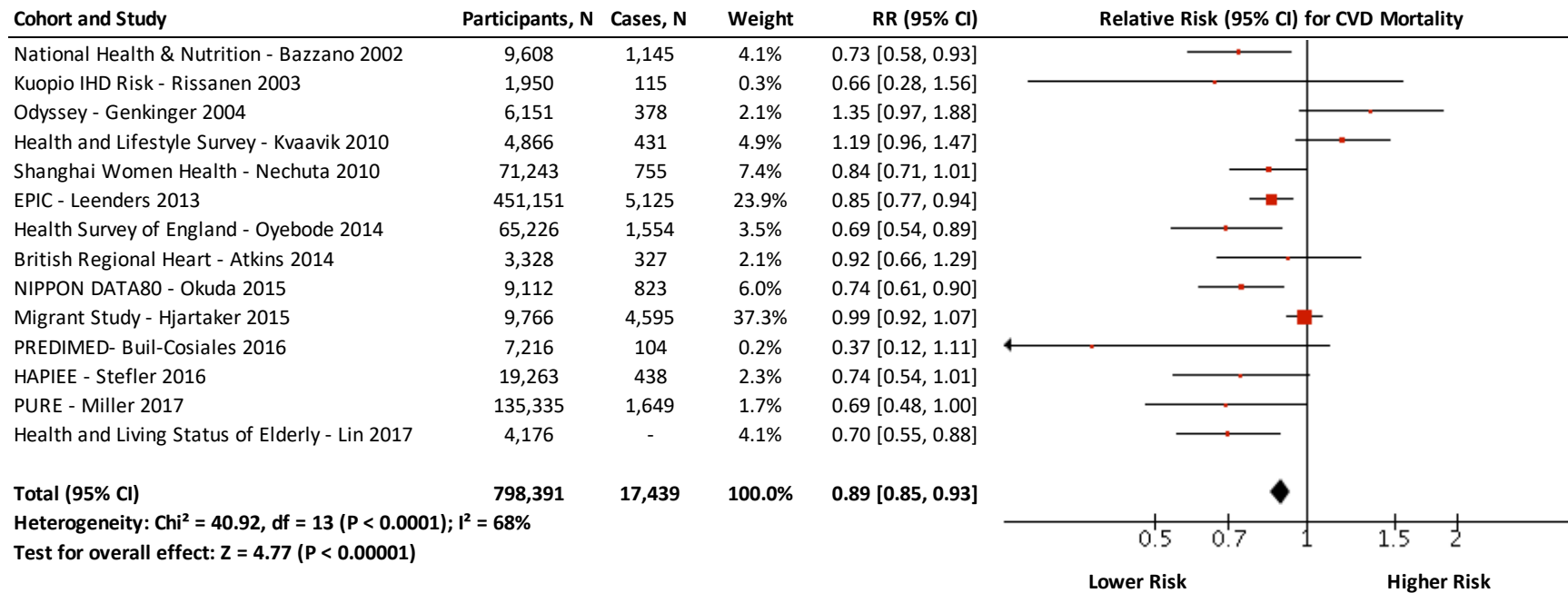


Figure S13. Relation between sources of vegetables and CVD incidence (highest vs. lowest level of intake). All results are presented as relative risk (RR) with 95% confidence intervals (95% CI). Pooled risk estimate is represented by the black diamond using (A) fixed effects and (B) random effects models. Inter-study heterogeneity was assessed using the Cochran Q statistic (χ^2) at a significance level of $p < 0.10$, and quantified by I^2 , with values $\geq 50\%$ indicating substantial heterogeneity.

TOTAL FRUIT AND VEGETABLES AND CARDIOVASCULAR DISEASE MORTALITY

A. Fixed Effects



B. Random Effects

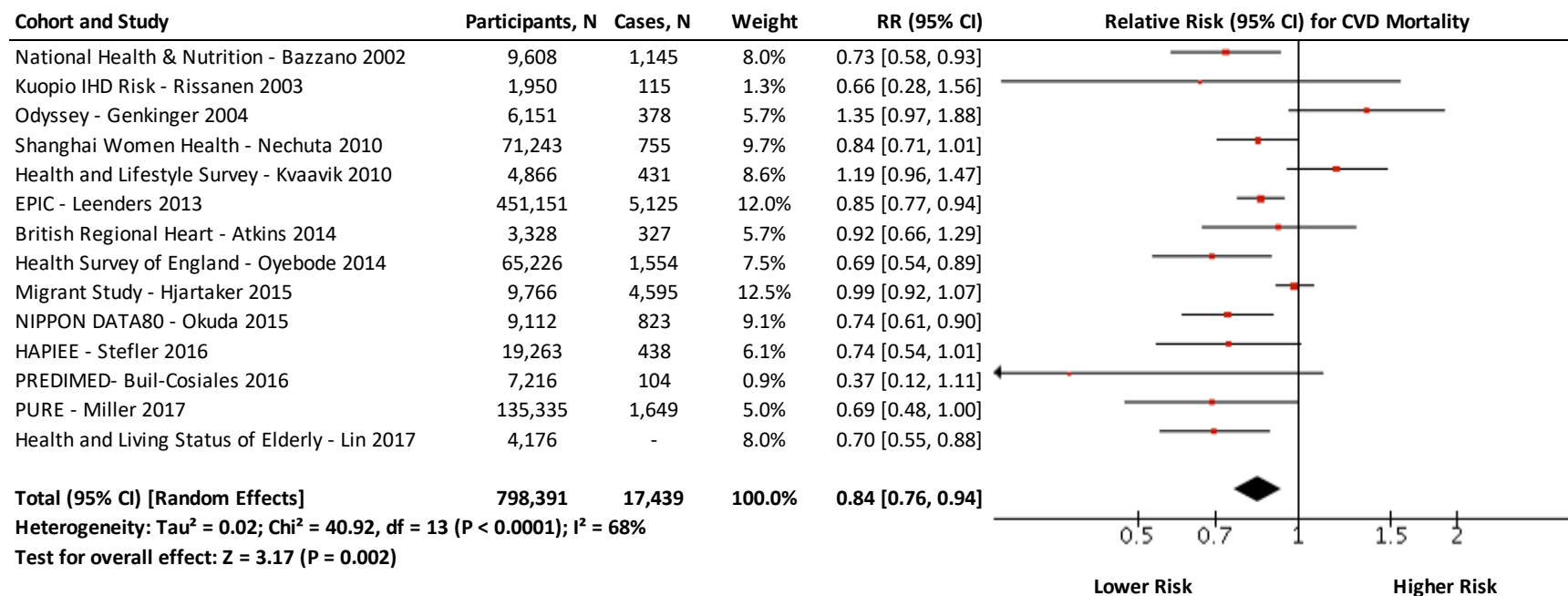
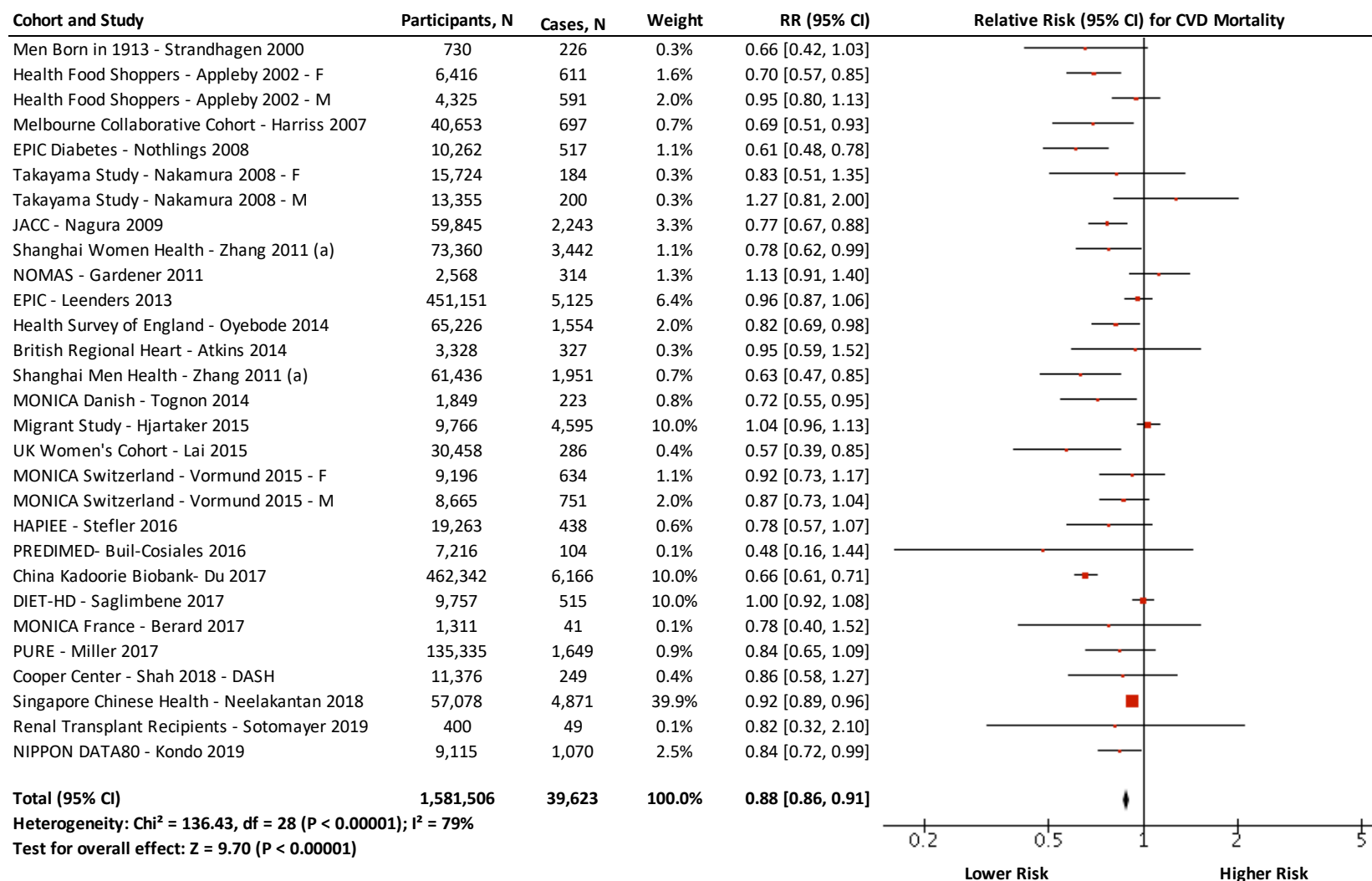


Figure S14. Relation between total fruit and vegetable intake and cardiovascular disease mortality (highest vs. lowest level of intake). All results are presented as relative risk (RR) with 95% confidence intervals (95% CI). Pooled risk estimate is represented by the black diamond using (A) fixed effects and (B) random effects models. Inter-study heterogeneity was assessed using the Cochran Q statistic (Chi²) at a significance level of p<0.10, and quantified by I², with values ≥ 50% indicating substantial heterogeneity.

FRUIT AND CARDIOVASCULAR DISEASE MORTALITY

A. Fixed Effects



B. Random Effect

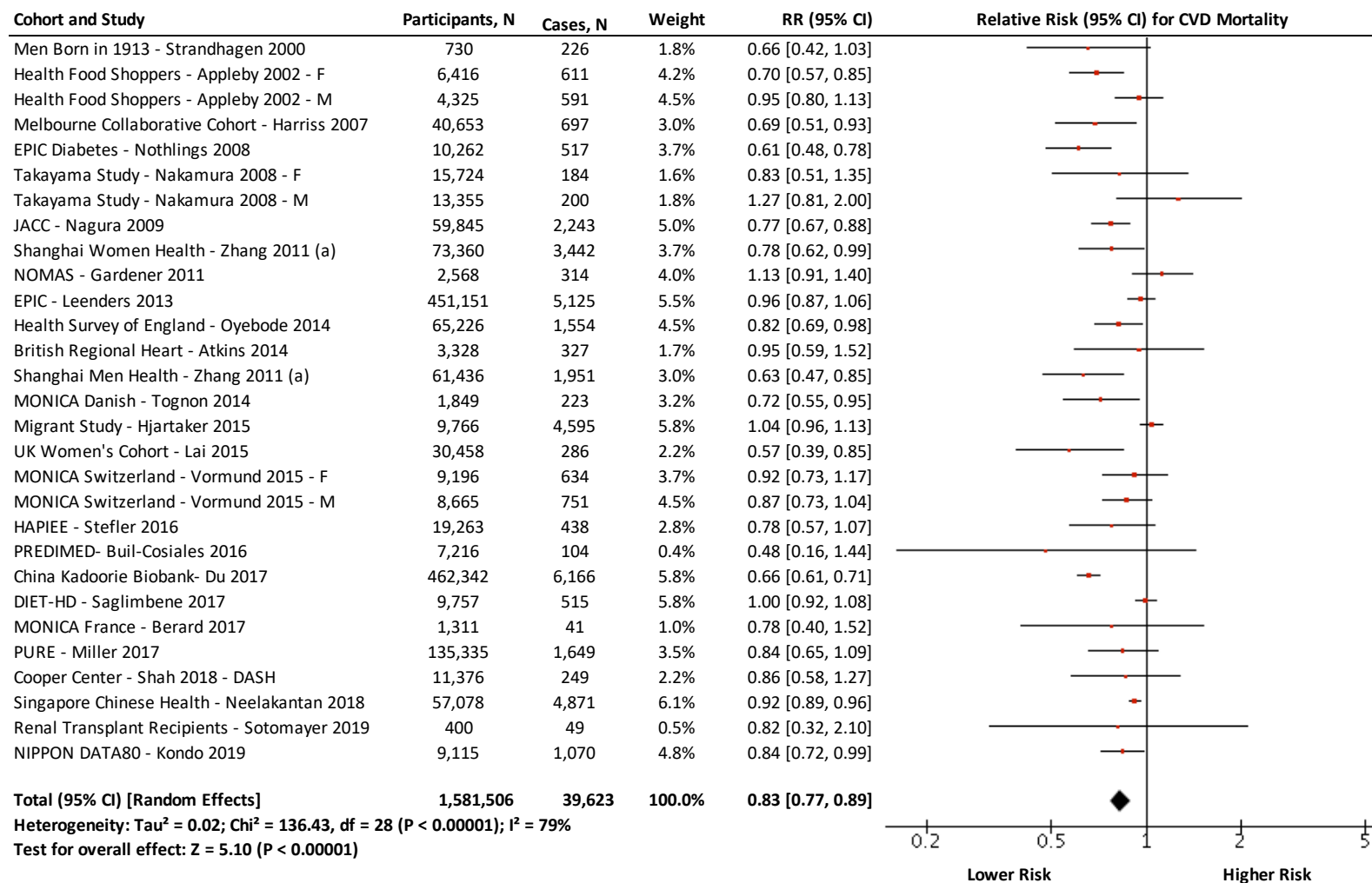
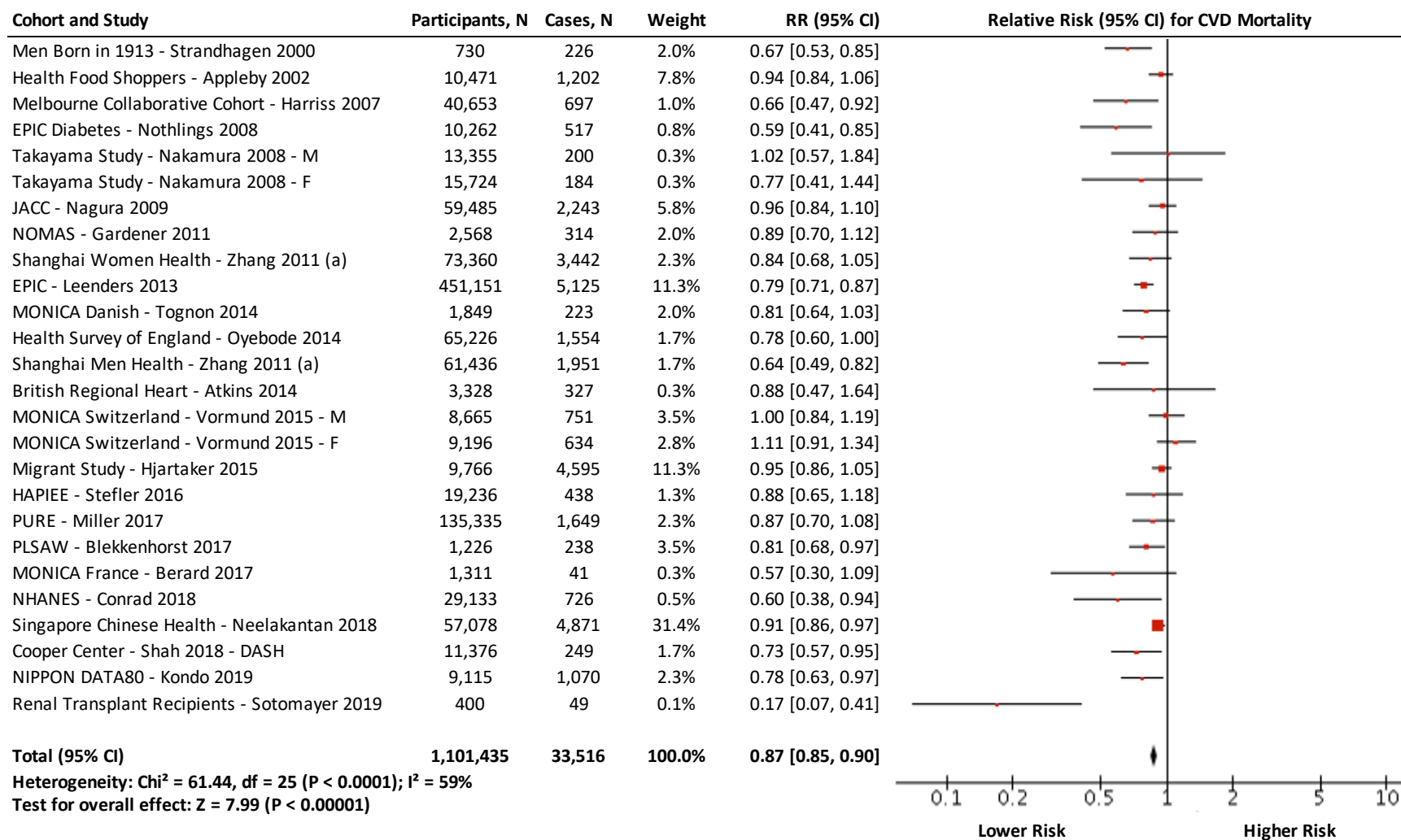


Figure S15. Relation between fruit intake and cardiovascular disease mortality (highest vs. lowest level of intake). All results are presented as relative risk (RR) with 95% confidence intervals (95% CI). Pooled risk estimate is represented by the black diamond using (A) fixed effects and (B) random effects models. Inter-study heterogeneity was assessed using the Cochran Q statistic (χ^2) at a significance level of $p < 0.10$, and quantified by I^2 , with values $\geq 50\%$ indicating substantial heterogeneity.

VEGETABLES AND CARDIOVASCULAR DISEASE MORTALITY

A. Fixed Effects



B. Random Effects

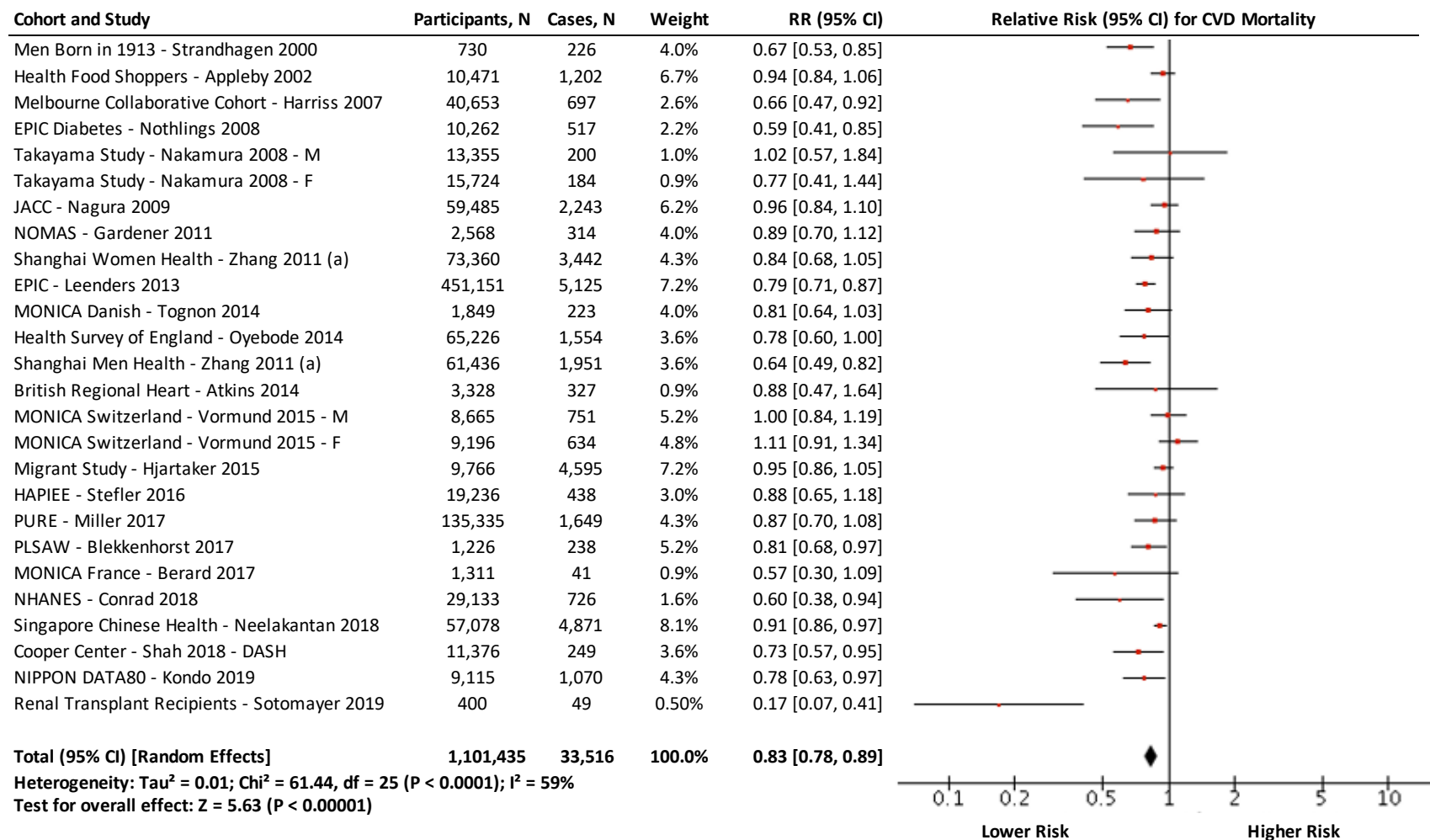
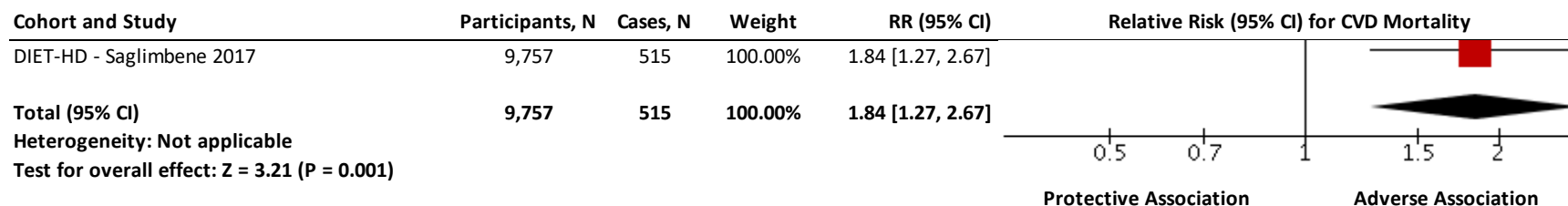


Figure S16. Relation between vegetable intake and cardiovascular disease mortality (highest vs. lowest level of intake). All results are presented as relative risk (RR) with 95% confidence intervals (95% CI). Pooled risk estimate is represented by the black diamond using (A) fixed effects and (B) random effects models. Inter-study heterogeneity was assessed using the Cochran Q statistic (Chi²) at a significance level of p<0.10, and quantified by I², with values ≥ 50% indicating substantial heterogeneity.

APRICOTS AND CARDIOVASCULAR DISEASE MORTALITY



Supplementary Figure 17. Relation between intake of apricots and cardiovascular disease mortality (highest vs. lowest level of intake). All results are presented as relative risk (RR) with 95% confidence intervals (95% CI). Pooled risk estimate is represented by the black diamond. Inter-study heterogeneity was assessed using the Cochran Q statistic (χ^2) at a significance level of $p < 0.10$, and quantified by I^2 , with values $\geq 50\%$ indicating substantial heterogeneity.

BANANAS AND CARDIOVASCULAR DISEASE MORTALITY

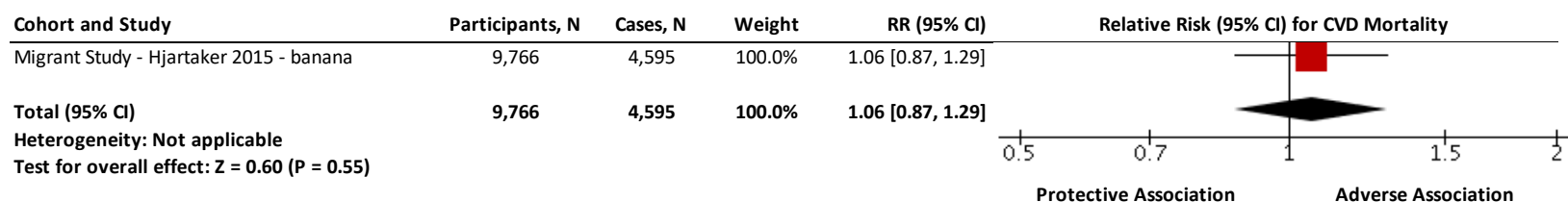
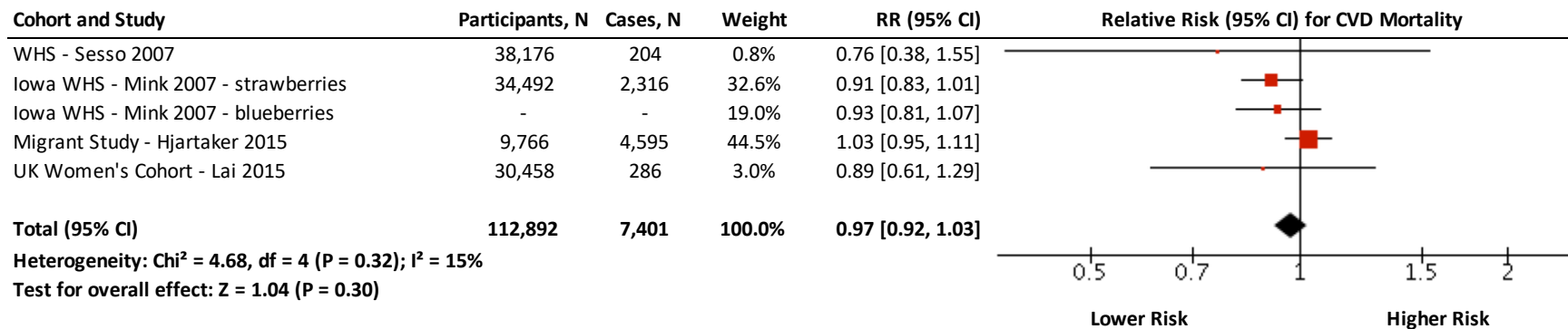


Figure S18. Relation between intake of bananas and cardiovascular disease mortality (highest vs. lowest level of intake). All results are presented as relative risk (RR) with 95% confidence intervals (95% CI). Pooled risk estimate is represented by the black diamond. Inter-study heterogeneity was assessed using the Cochran Q statistic (χ^2) at a significance level of $p < 0.10$, and quantified by I^2 , with values $\geq 50\%$ indicating substantial heterogeneity.

BERRIES AND CARDIOVASCULAR DISEASE MORTALITY

A. Fixed Effects



B. Random Effects

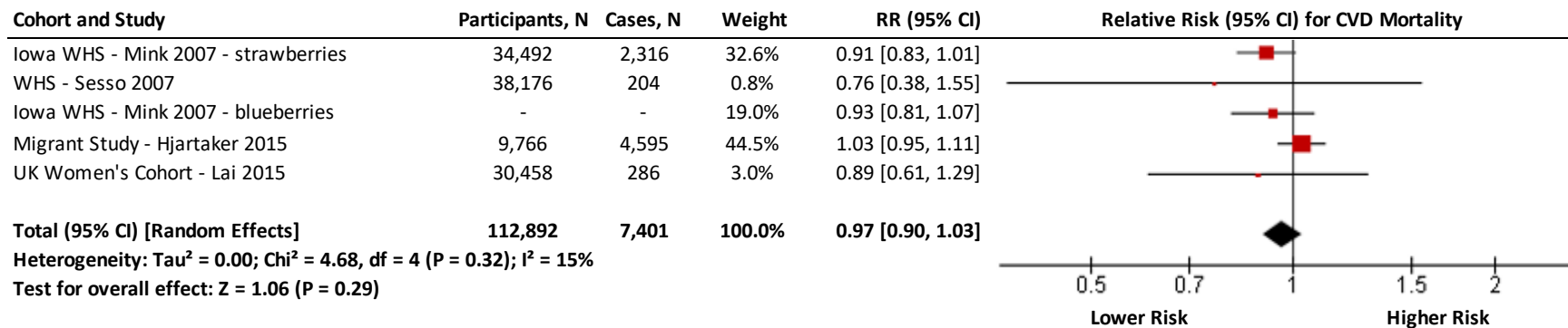
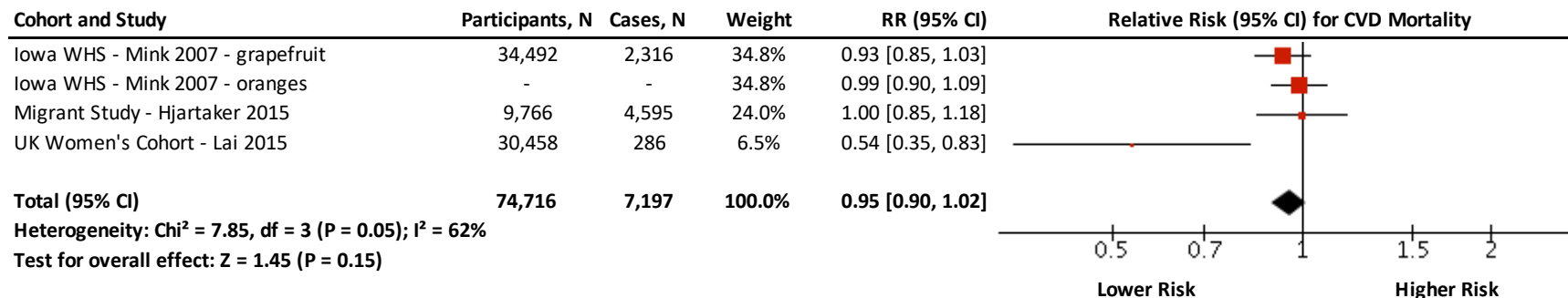


Figure S19. Relation between intake of berries and cardiovascular disease mortality (highest vs. lowest level of intake). All results are presented as relative risk (RR) with 95% confidence intervals (95% CI). Pooled risk estimate is represented by the black diamond using (A) fixed effects and (B) random effects models. Inter-study heterogeneity was assessed using the Cochran Q statistic (χ^2) at a significance level of $p < 0.10$, and quantified by I^2 , with values $\geq 50\%$ indicating substantial heterogeneity.

CITRUS FRUIT AND CARDIOVASCULAR DISEASE MORTALITY

A. Fixed Effects



B. Random Effects

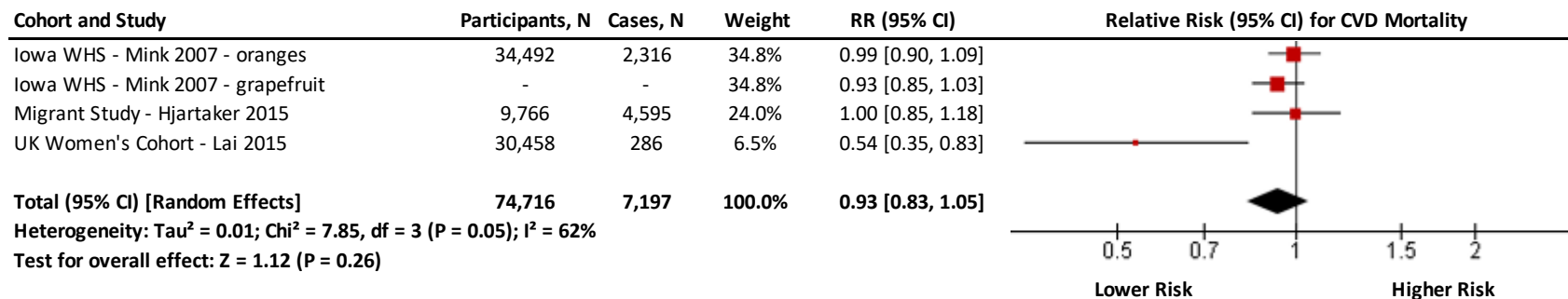
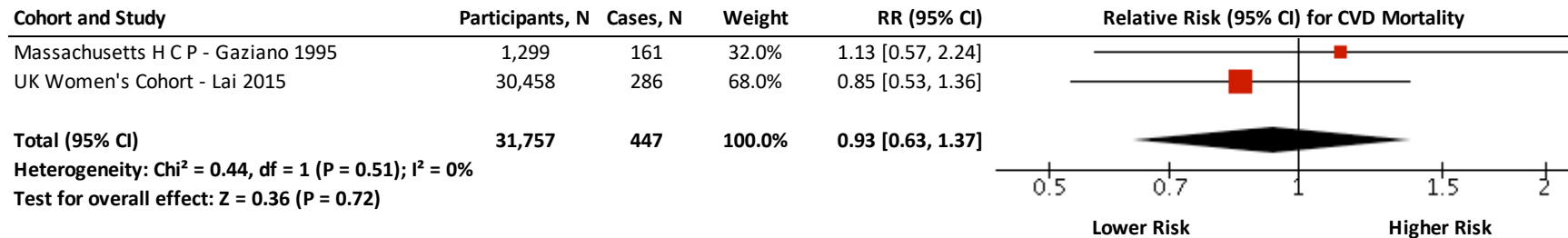


Figure S20. Relation between citrus fruit intake and cardiovascular disease mortality (highest vs. lowest level of intake). All results are presented as relative risk (RR) with 95% confidence intervals (95% CI). Pooled risk estimate is represented by the black diamond using (A) fixed effects and (B) random effects models. Inter-study heterogeneity was assessed using the Cochran Q statistic (χ^2) at a significance level of $p < 0.10$, and quantified by I^2 , with values $\geq 50\%$ indicating substantial heterogeneity.

DRIED FRUIT AND CARDIOVASCULAR DISEASE MORTALITY

A. Fixed Effects



B. Random Effects

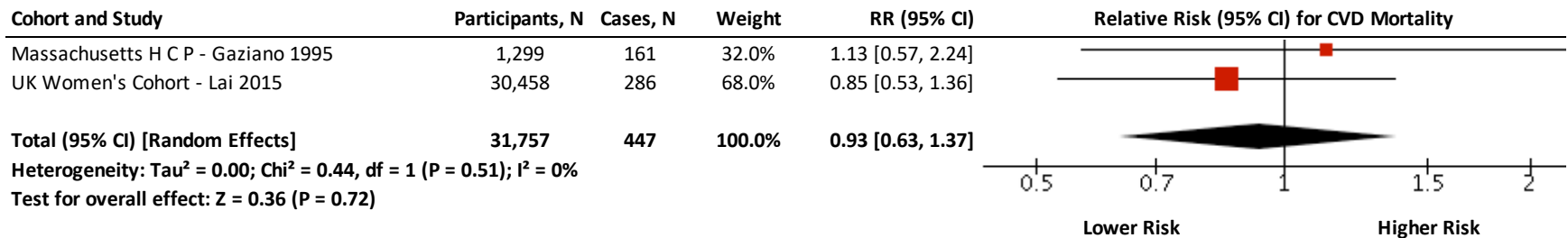


Figure S21. Relation between dried fruit intake and cardiovascular disease mortality (highest vs. lowest level of intake). All results are presented as relative risk (RR) with 95% confidence intervals (95% CI). Pooled risk estimate is represented by the black diamond using (A) fixed effects and (B) random effects models. Inter-study heterogeneity was assessed using the Cochran Q statistic (χ^2) at a significance level of $p < 0.10$, and quantified by I^2 , with values $\geq 50\%$ indicating substantial heterogeneity

FRUIT JUICE AND CARDIOVASCULAR DISEASE MORTALITY

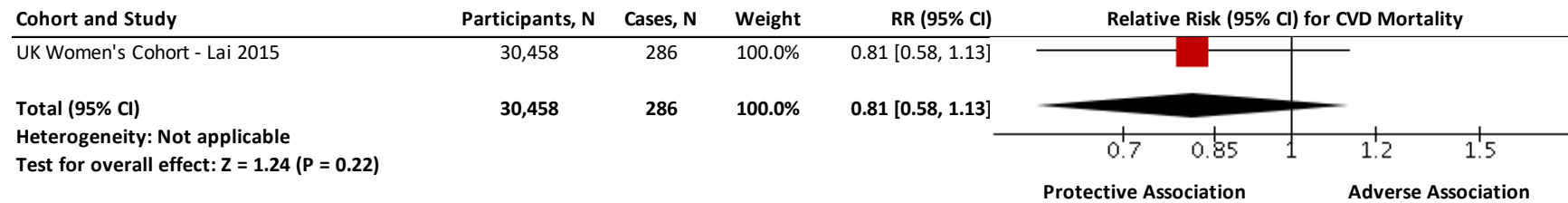
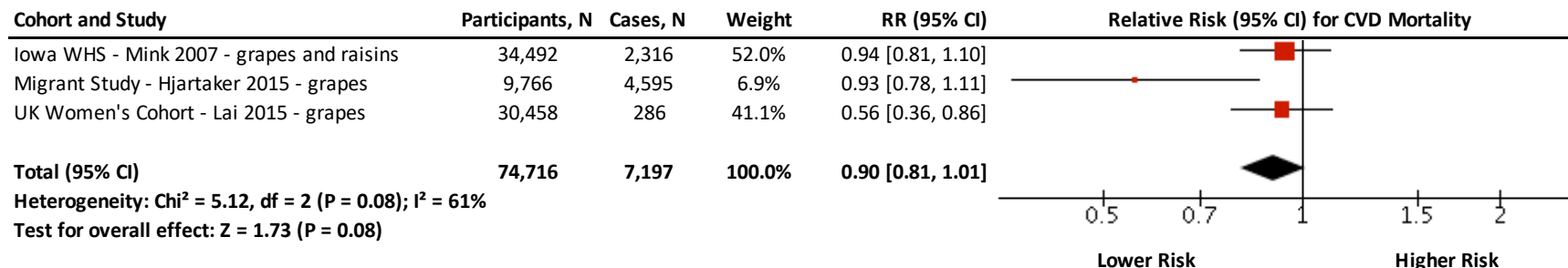


Figure S22. Relation between fruit juice intake and cardiovascular disease mortality (highest vs. lowest level of intake). All results are presented as relative risk (RR) with 95% confidence intervals (95% CI). Pooled risk estimate is represented by the black diamond. Inter-study heterogeneity was assessed using the Cochran Q statistic (χ^2) at a significance level of $p < 0.10$, and quantified by I^2 , with values $\geq 50\%$ indicating substantial heterogeneity.

GRAPES AND CARDIOVASCULAR DISEASE MORTALITY

A. Fixed Effects



B. Random Effects

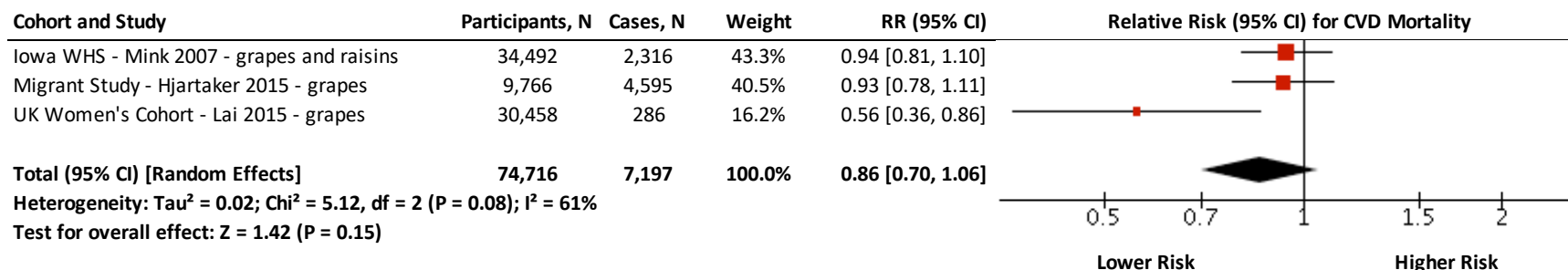
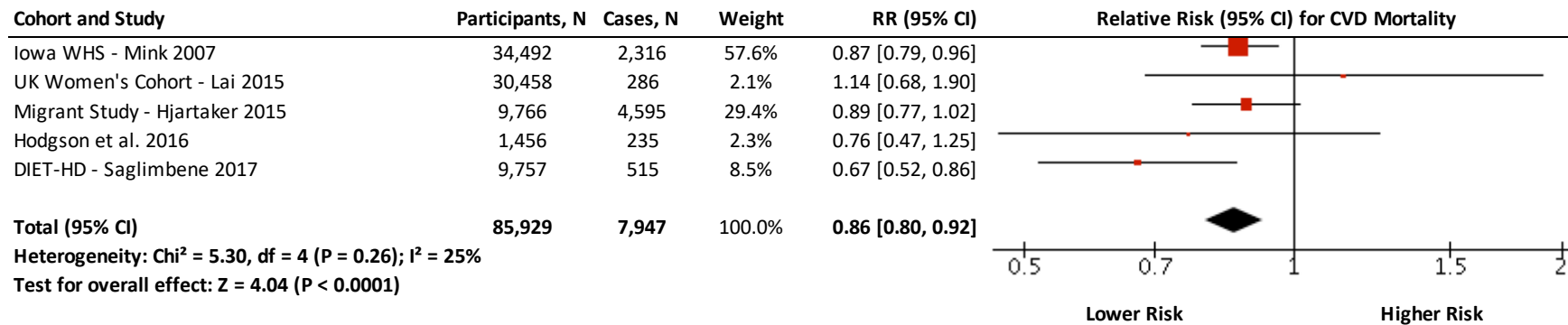


Figure S23. Relation between intake of grapes and cardiovascular disease mortality (highest vs. lowest level of intake). All results are presented as relative risk (RR) with 95% confidence intervals (95% CI). Pooled risk estimate is represented by the black diamond using (A) fixed effects and (B) random effects models. Inter-study heterogeneity was assessed using the Cochran Q statistic (χ^2) at a significance level of $p < 0.10$, and quantified by I^2 , with values $\geq 50\%$ indicating substantial heterogeneity.

POMMES AND CARDIOVASCULAR DISEASE MORTALITY

A. Fixed Effects



B. Random Effects

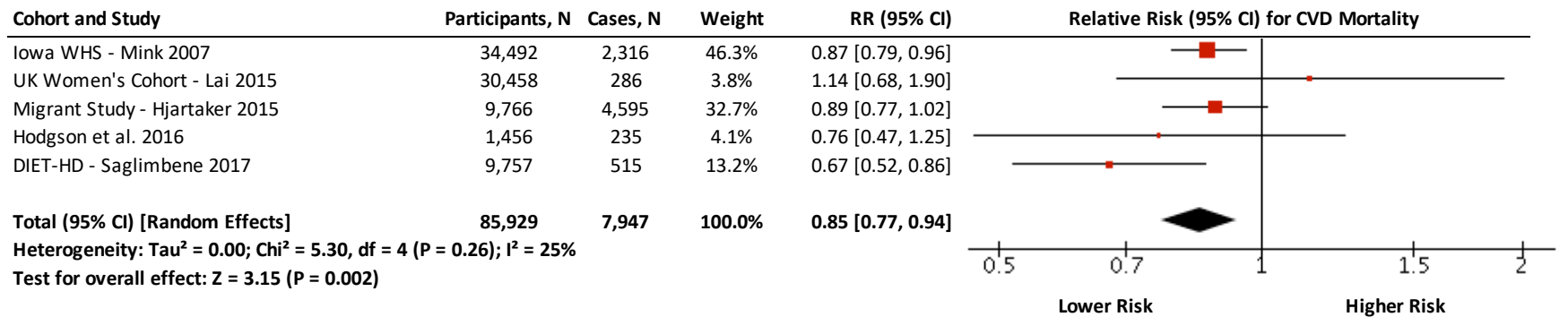


Figure S24. Relation between pomes fruit intake and cardiovascular disease mortality (highest vs. lowest level of intake). All results are presented as relative risk (RR) with 95% confidence intervals (95% CI). Pooled risk estimate is represented by the black diamond using (A) fixed effects and (B) random effects models. Inter-study heterogeneity was assessed using the Cochran Q statistic (χ^2) at a significance level of $p < 0.10$, and quantified by I^2 , with values $\geq 50\%$ indicating substantial heterogeneity.

ALLIUM VEGETABLES AND CARDIOVASCULAR DISEASE MORTALITY

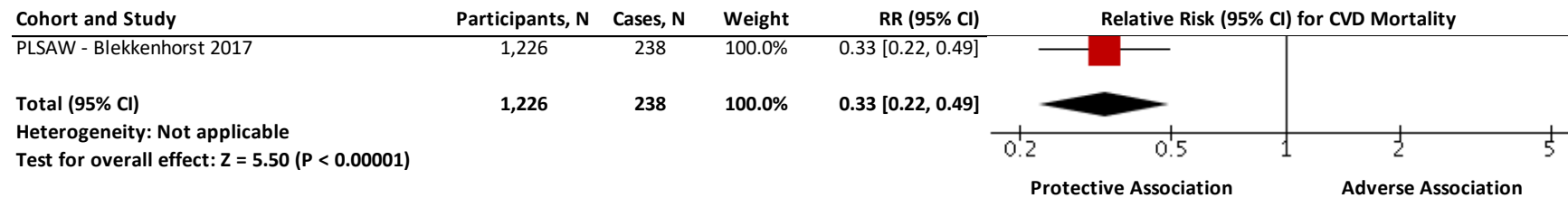
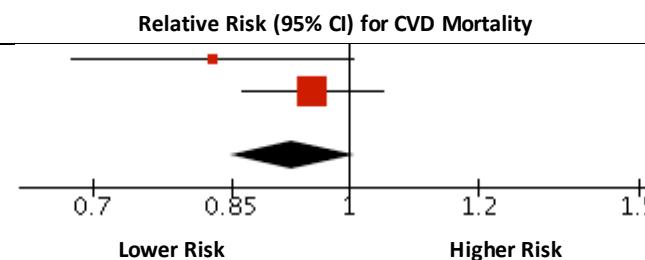


Figure S25. Relation between intake allium vegetables and cardiovascular disease mortality (highest vs. lowest level of intake). All results are presented as relative risk (RR) with 95% confidence intervals (95% CI). Pooled risk estimate is represented by the black diamond. Inter-study heterogeneity was assessed using the Cochran Q statistic (χ^2) at a significance level of $p < 0.10$, and quantified by I^2 , with values $\geq 50\%$ indicating substantial heterogeneity.

CARROTS AND CARDIOVASCULAR DISEASE MORTALITY

A. Fixed Effects

Cohort and Study	Participants, N	Cases, N	Weight	RR (95% CI)
Zutphen Elderly - Buijsse 2008- Carrots	559	197	20.0%	0.83 [0.68, 1.01]
Miigrant Study - Hjartaker 2015 - carrots	9,766	4,595	80.0%	0.95 [0.86, 1.05]
Total (95% CI)	10,325	4,792	100.0%	0.92 [0.85, 1.01]
Heterogeneity: $\chi^2 = 1.57$, $df = 1$ ($P = 0.21$); $I^2 = 36\%$				
Test for overall effect: $Z = 1.74$ ($P = 0.08$)				



B. Random Effects

Cohort and Study	Participants, N	Cases, N	Weight	RR (95% CI)
Zutphen Elderly - Buijsse 2008- Carrots	559	197	30.9%	0.83 [0.68, 1.01]
Miigrant Study - Hjartaker 2015 - carrots	9,766	4,595	69.1%	0.95 [0.86, 1.05]
Total (95% CI) [Random Effects]	10,325	4,792	100.0%	0.91 [0.80, 1.03]
Heterogeneity: $\tau^2 = 0.00$; $\chi^2 = 1.57$, $df = 1$ ($P = 0.21$); $I^2 = 36\%$				
Test for overall effect: $Z = 1.44$ ($P = 0.15$)				

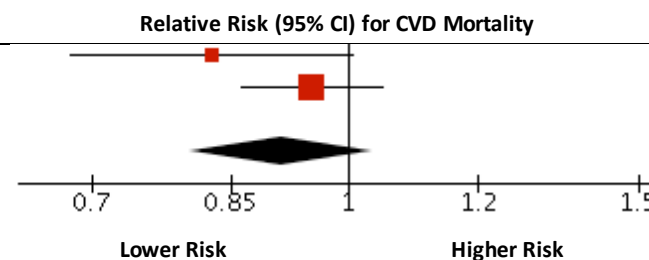


Figure S26. Relation between carrots intake and cardiovascular disease mortality (highest vs. lowest level of intake). All results are presented as relative risk (RR) with 95% confidence intervals (95% CI). Pooled risk estimate is represented by the black diamond using (A) fixed effects and (B) random effects models. Inter-study heterogeneity was assessed using the Cochran Q statistic (χ^2) at a significance level of $p < 0.10$, and quantified by I^2 , with values $\geq 50\%$ indicating substantial heterogeneity.

CELERY AND CARDIOVASCULAR DISEASE MORTALITY

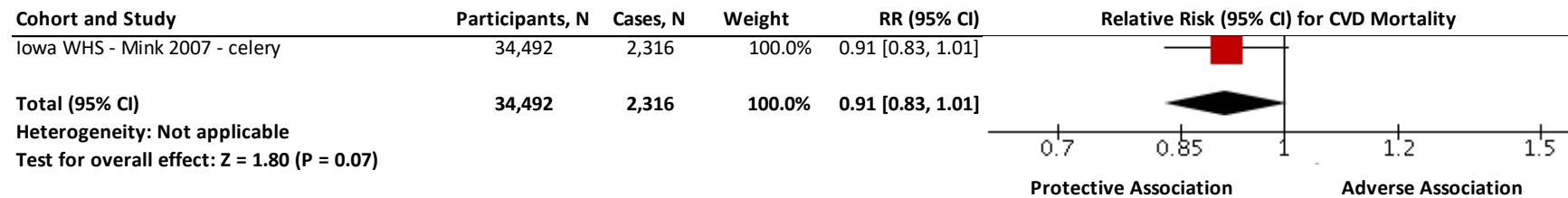
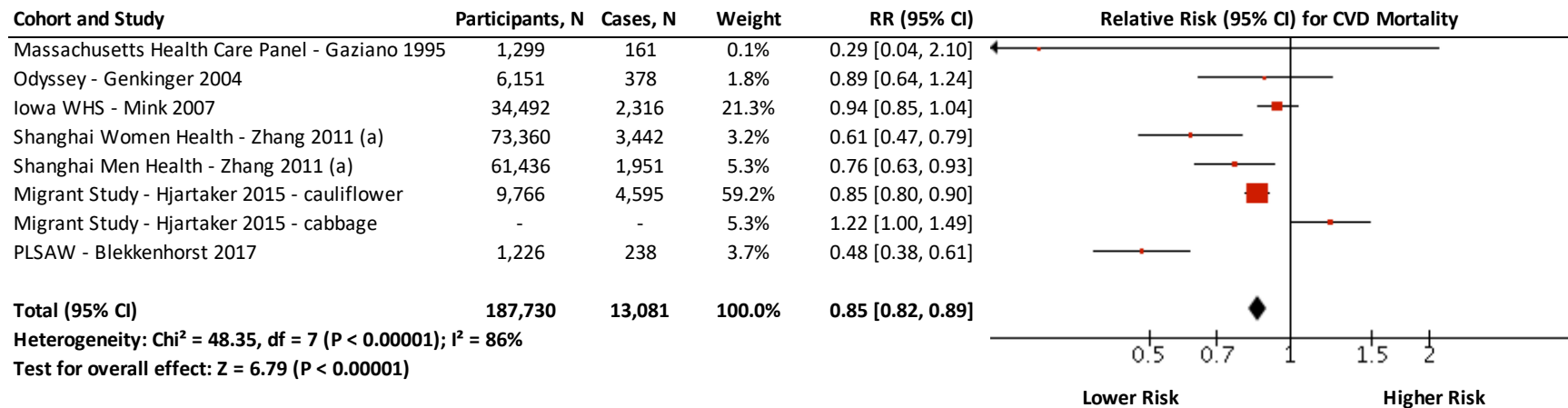


Figure S27. Relation between celery intake and cardiovascular disease mortality (highest vs. lowest level of intake). All results are presented as relative risk (RR) with 95% confidence intervals (95% CI). Pooled risk estimate is represented by the black diamond using (A) fixed effects and (B) random effects models. Inter-study heterogeneity was assessed using the Cochran Q statistic (χ^2) at a significance level of $p < 0.10$, and quantified by I^2 , with values $\geq 50\%$ indicating substantial heterogeneity.

CRUCIFEROUS VEGETABLES AND CARDIOVASCULAR DISEASE MORTALITY

A. Fixed Effects



B. Random Effects

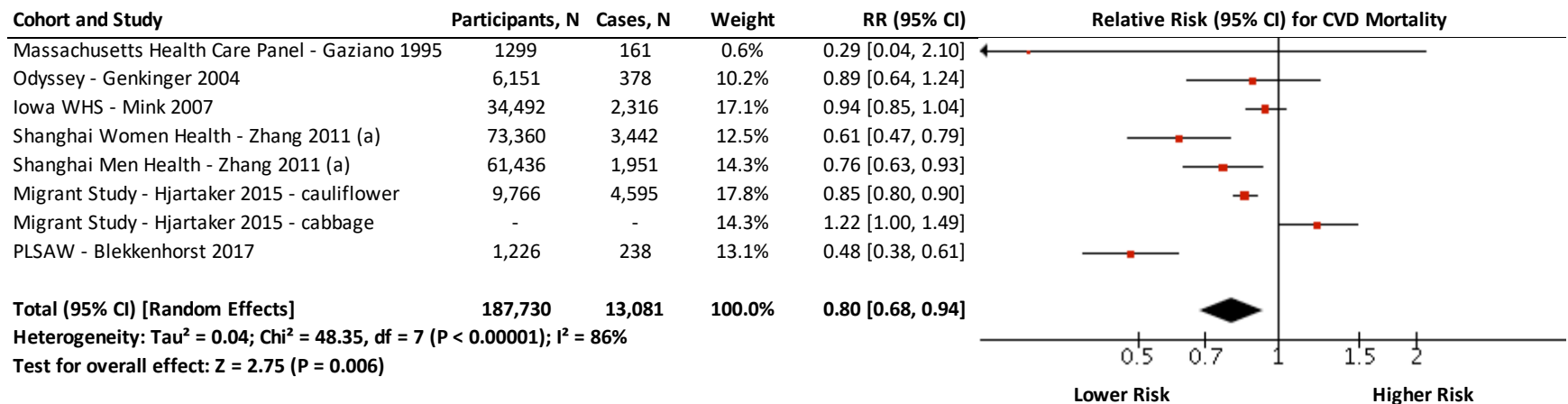
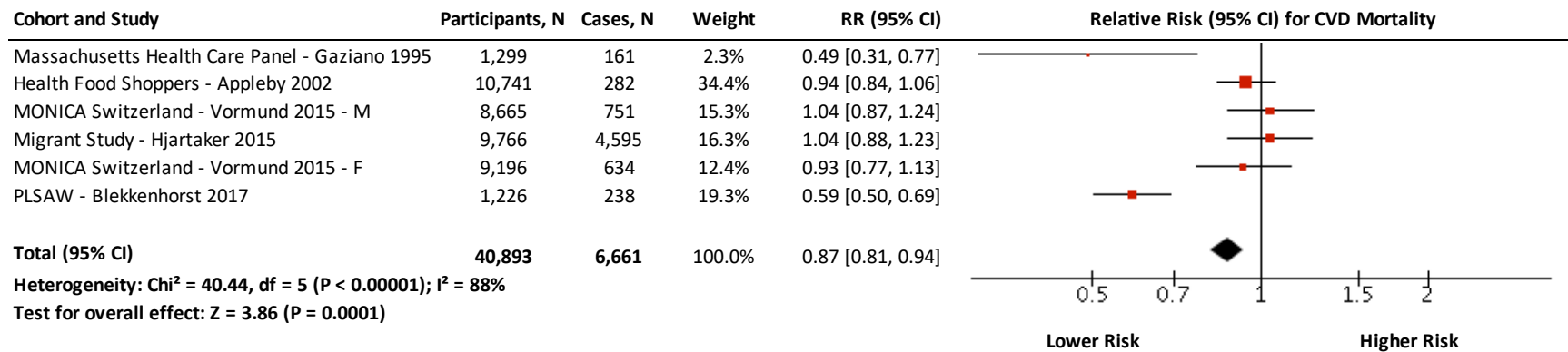


Figure S28. Relation between intake of cruciferous vegetables and cardiovascular disease mortality (highest vs. lowest level of intake). All results are presented as relative risk (RR) with 95% confidence intervals (95% CI). Pooled risk estimate is represented by the black diamond using (A) fixed effects and (B) random effects models. Inter-study heterogeneity was assessed using the Cochran Q statistic (χ^2) at a significance level of $p < 0.10$, and quantified by I^2 , with values $\geq 50\%$ indicating substantial heterogeneity.

GREEN LEAFY VEGETABLES AND CARDIOVASCULAR DISEASE MORTALITY

A. Fixed Effects



B. Random Effects

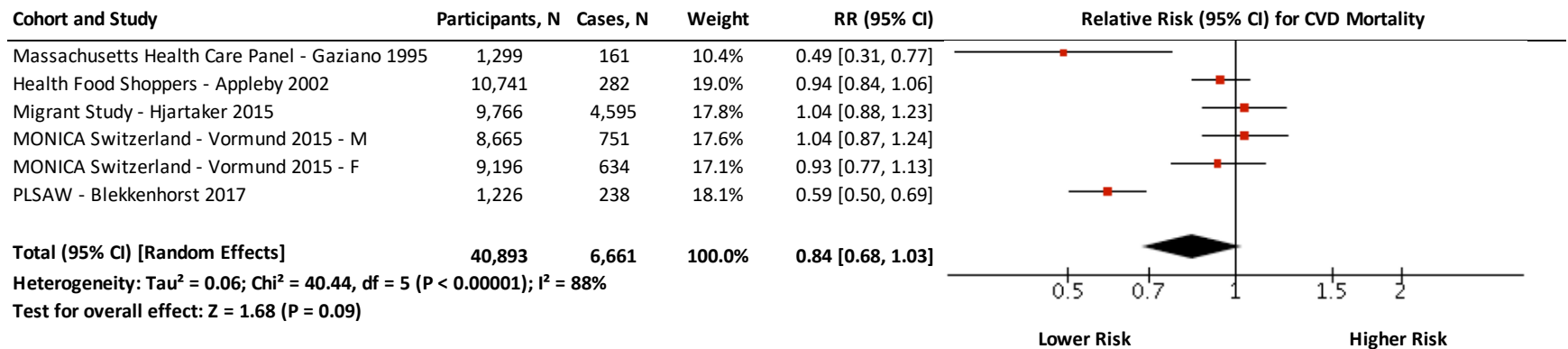
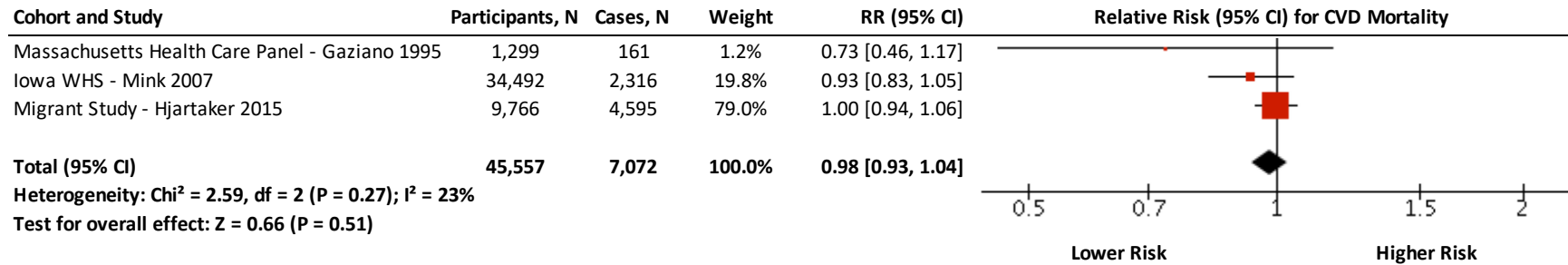


Figure S29. Relation between intake of green leafy vegetables and cardiovascular disease mortality (highest vs. lowest level of intake). All results are presented as relative risk (RR) with 95% confidence intervals (95% CI). Pooled risk estimate is represented by the black diamond using (A) fixed effects and (B) random effects models. Inter-study heterogeneity was assessed using the Cochran Q statistic (χ^2) at a significance level of $p < 0.10$, and quantified by I^2 , with values $\geq 50\%$ indicating substantial heterogeneity.

TOMATOES AND CARDIOVASCULAR DISEASE MORTALITY

A. Fixed Effects



B. Random Effects

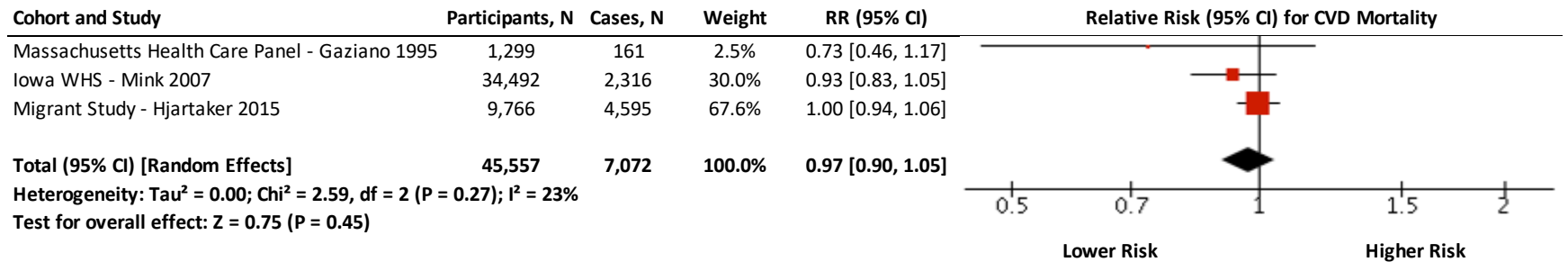
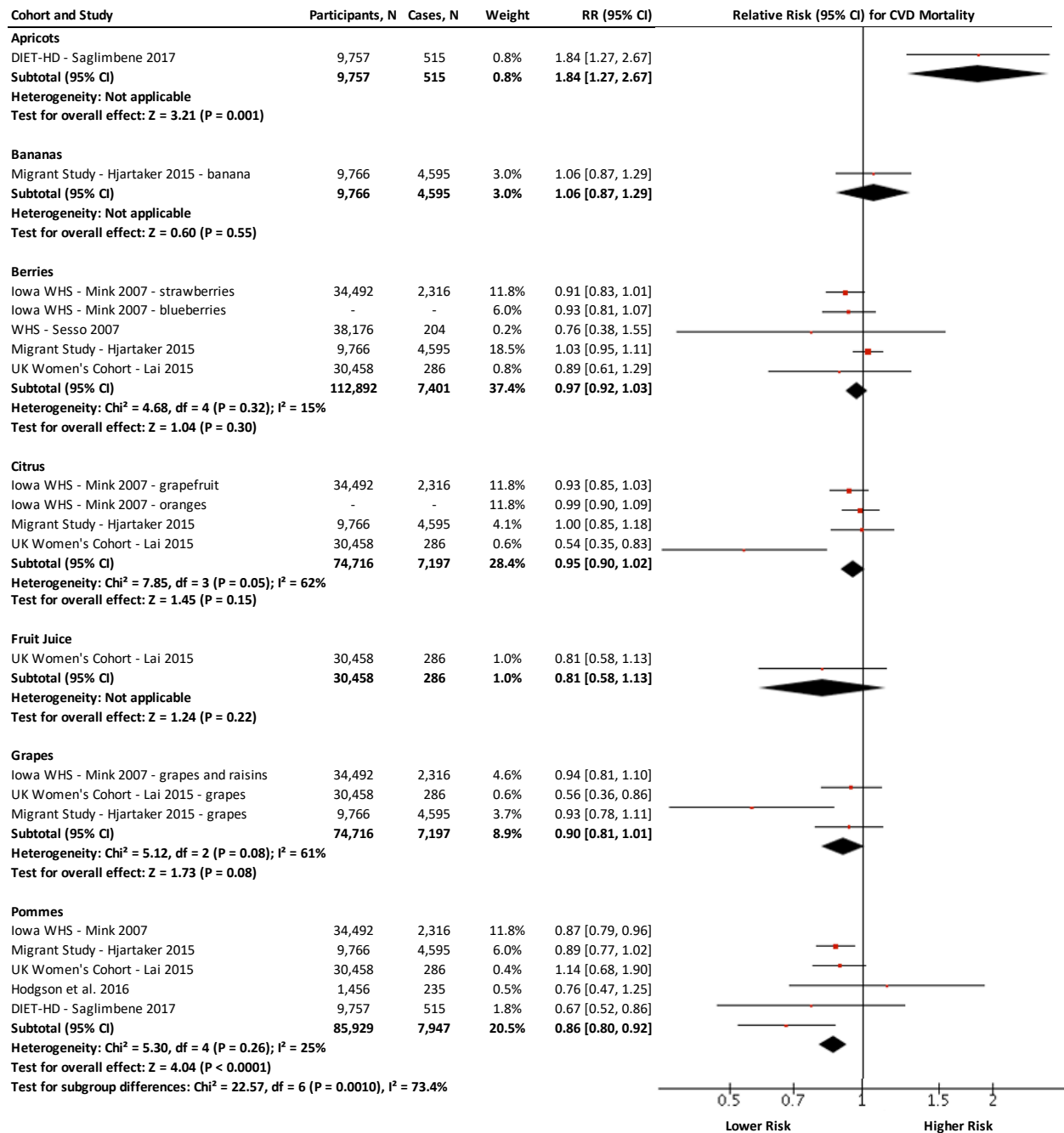


Figure S30. Relation between tomato intake and cardiovascular disease mortality (highest vs. lowest level of intake). All results are presented as relative risk (RR) with 95% confidence intervals (95% CI). Pooled risk estimate is represented by the black diamond using (A) fixed effects and (B) random effects models. Inter-study heterogeneity was assessed using the Cochran Q statistic (χ^2) at a significance level of $p < 0.10$, and quantified by I^2 , with values $\geq 50\%$ indicating substantial heterogeneity.

A. Fixed Effects



B. Random Effects

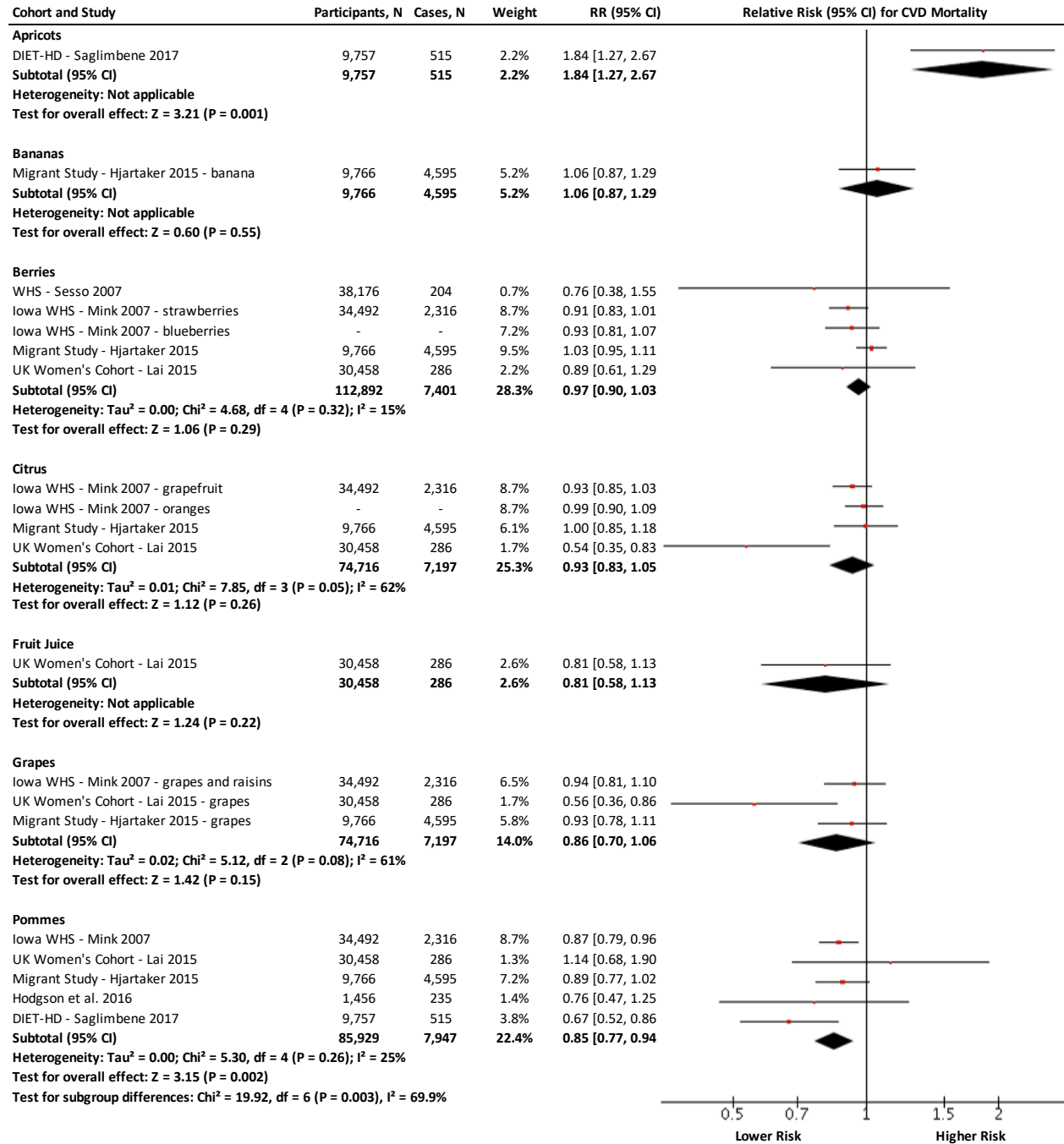
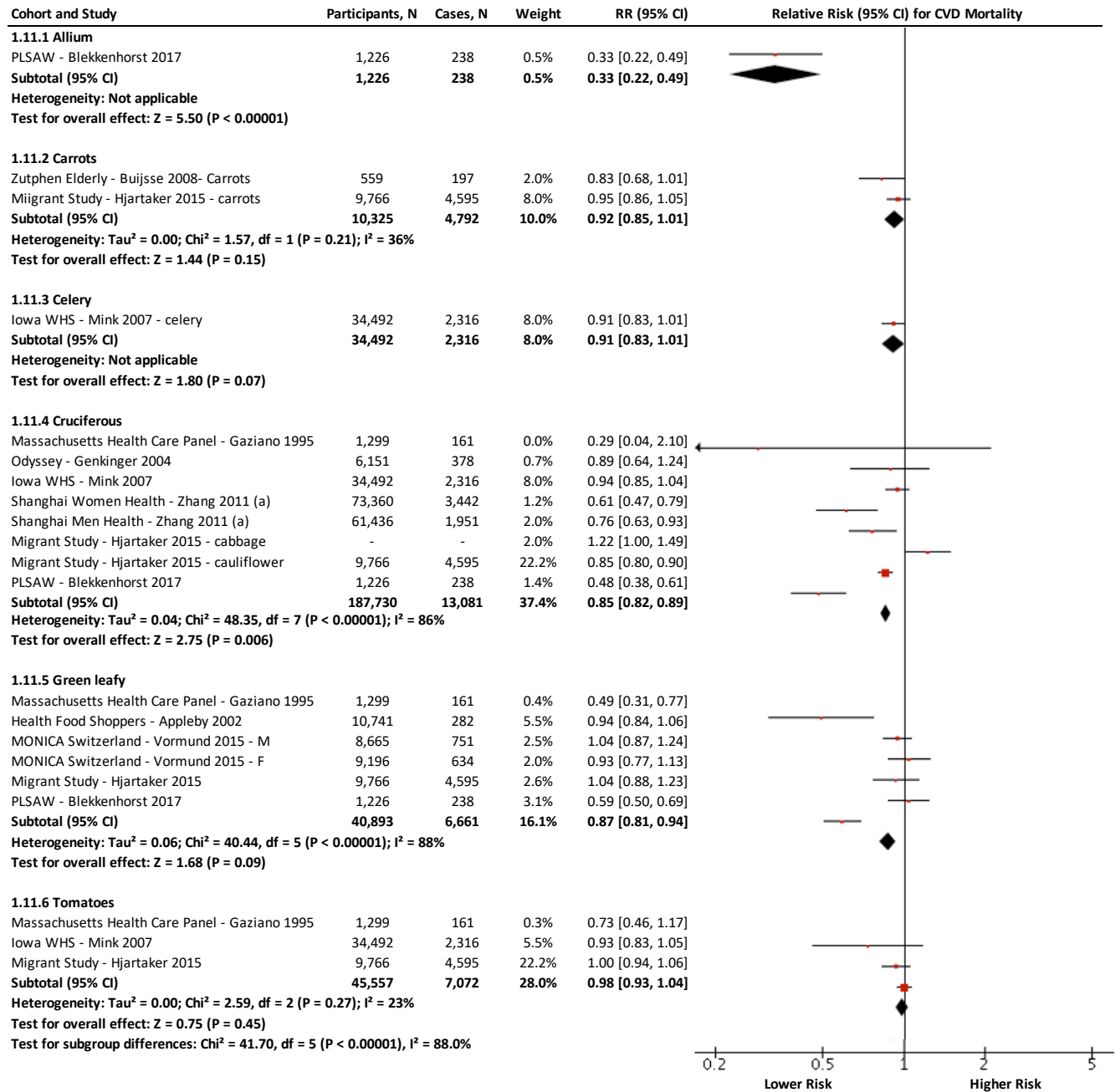


Figure S31. Relation between sources of fruit and CVD mortality (highest vs. lowest level of intake). All results are presented as relative risk (RR) with 95% confidence intervals (95% CI). Pooled risk estimate is represented by the black diamond using (A) fixed effects and (B) random effects models. Inter-study heterogeneity was assessed using the Cochran Q statistic (Chi²) at a significance level of p<0.10, and quantified by I², with values ≥ 50% indicating substantial heterogeneity.

A. Fixed Effects



B. Random Effects

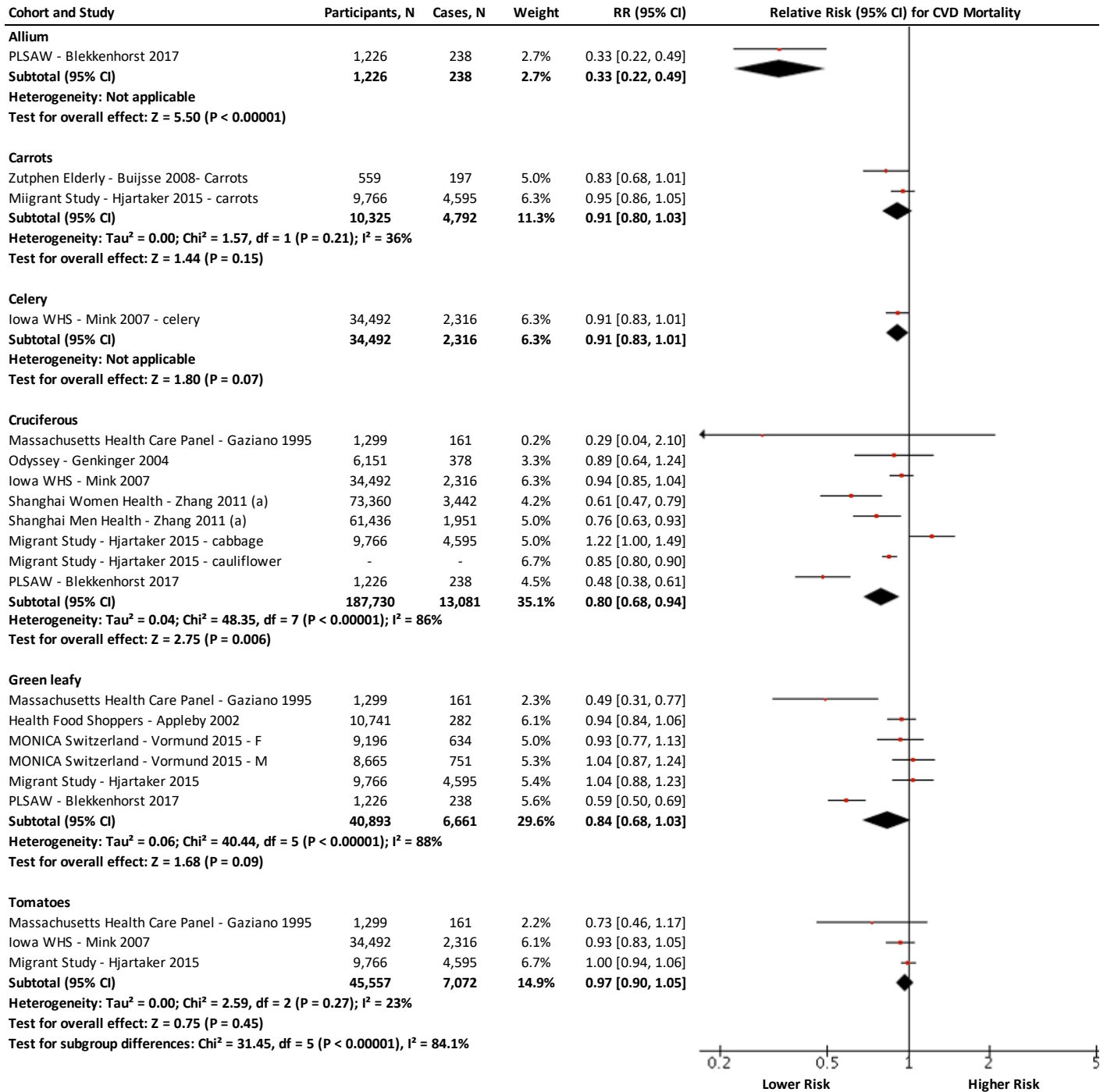


Figure S32. Relation between sources of vegetables and CVD mortality (highest vs. lowest level of intake). All results are presented as relative risk (RR) with 95% confidence intervals (95% CI). Pooled risk estimate is represented by the black diamond using (A) fixed effects and (B) random effects models. Inter-study heterogeneity was assessed using the Cochran Q statistic (Chi²) at a significance level of p<0.10, and quantified by I², with values ≥ 50% indicating substantial heterogeneity.

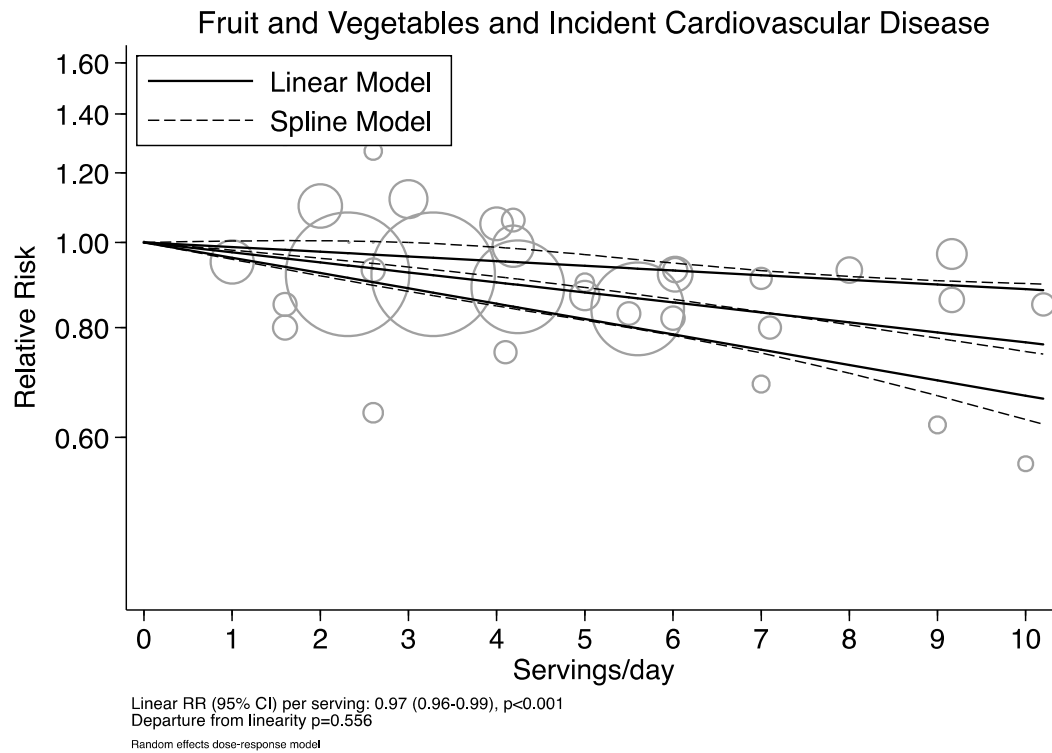


Figure S33. Linear and cubic-spline dose-response relation between increasing fruit and vegetable intake and incidence of cardiovascular disease. Linear dose-response data was modeled using the Greenland and Longnecker method to estimate the covariances of multivariable-adjusted relative risk. Cubic spline data were modeled with fixed-effects restricted cubic spline with 3 knots and using the Greenland and Longnecker method to estimate the covariances of multivariable-adjusted relative risk. All data was kept on the original dose scale. The fitted trend for each model is represented by a central line (solid lines for linear model; dashed lines for cubic spline model) with 95% confidence intervals represented by the outer lines. Individual observations are represented by the circles, with the weight of the study in the overall analysis represented by the size of the circles.

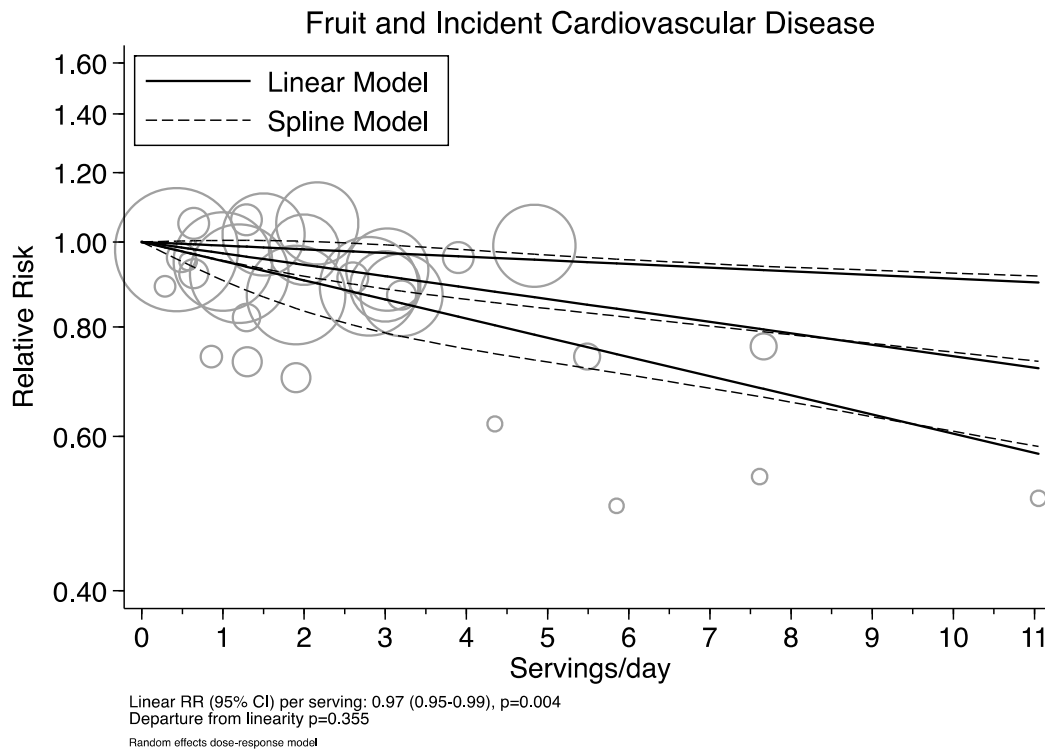


Figure S34. Linear and cubic-spline dose-response relation between increasing fruit intake and incidence of cardiovascular disease. Linear dose-response data was modeled using the Greenland and Longnecker²³ method to estimate the covariances of multivariable-adjusted relative risk. Cubic spline data were modeled with fixed-effects restricted cubic spline with 3 knots and using the Greenland and Longnecker²³ method to estimate the covariances of multivariable-adjusted relative risk. All data was kept on the original dose scale. The fitted trend for each model is represented by a central line (solid lines for linear model; dashed lines for cubic spline model) with 95% confidence intervals represented by the outer lines. Individual observations are represented by the circles, with the weight of the study in the overall analysis represented by the size of the circles.

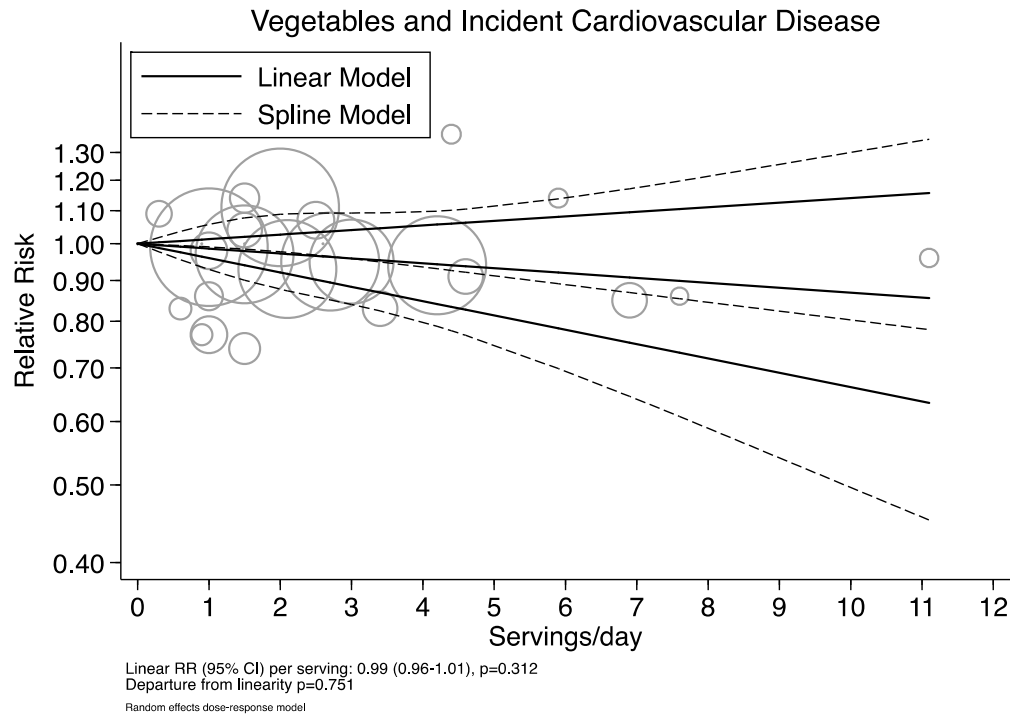


Figure S35. Linear and cubic-spline dose-response relation between increasing intake of vegetables and incidence of cardiovascular disease. Linear dose-response data was modeled using the Greenland and Longnecker²³ method to estimate the covariances of multivariable-adjusted relative risk. Cubic spline data were modeled with fixed-effects restricted cubic spline with 3 knots and using the Greenland and Longnecker²³ method to estimate the covariances of multivariable-adjusted relative risk. All data was kept on the original dose scale. The fitted trend for each model is represented by a central line (solid lines for linear model; dashed lines for cubic spline model) with 95% confidence intervals represented by the outer lines. Individual observations are represented by the circles, with the weight of the study in the overall analysis represented by the size of the circles.

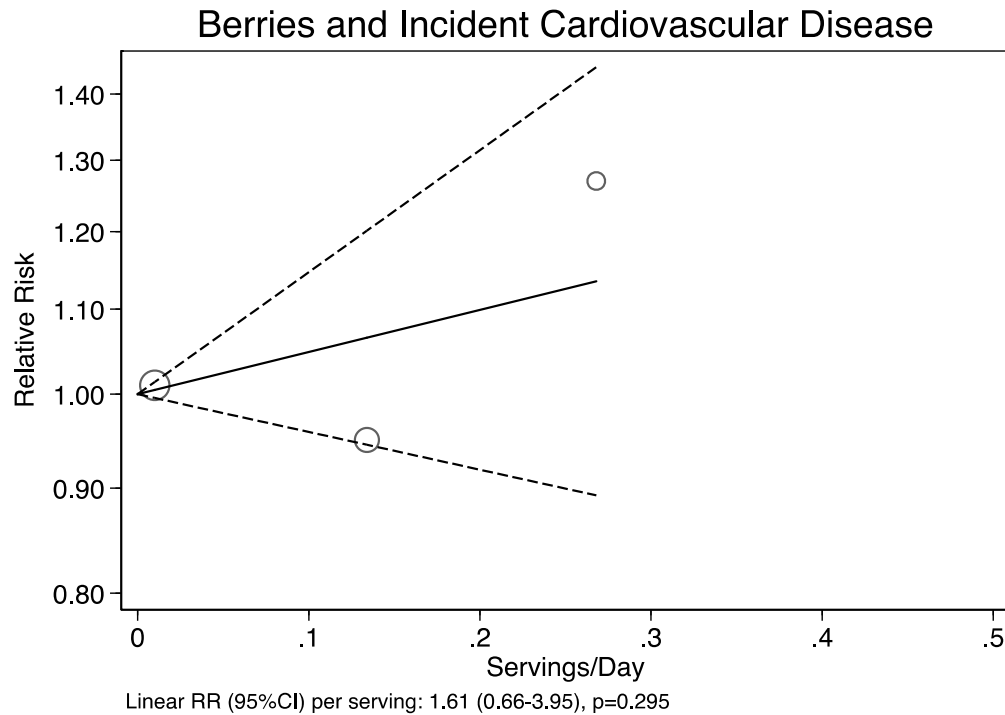


Figure S36. Linear dose-response relation between increasing berries intake and incidence of cardiovascular disease. Linear dose-response data was modeled using the Greenland and Longnecker²³ method to estimate the covariances of multivariable-adjusted relative risk, with kept on the original dose scale. Dashed lines represent the pointwise 95% confidence intervals for the fitted linear trend represented by a solid line. Individual observations are represented by the circles, with the weight of the study in the overall analysis represented by the size of the circles.

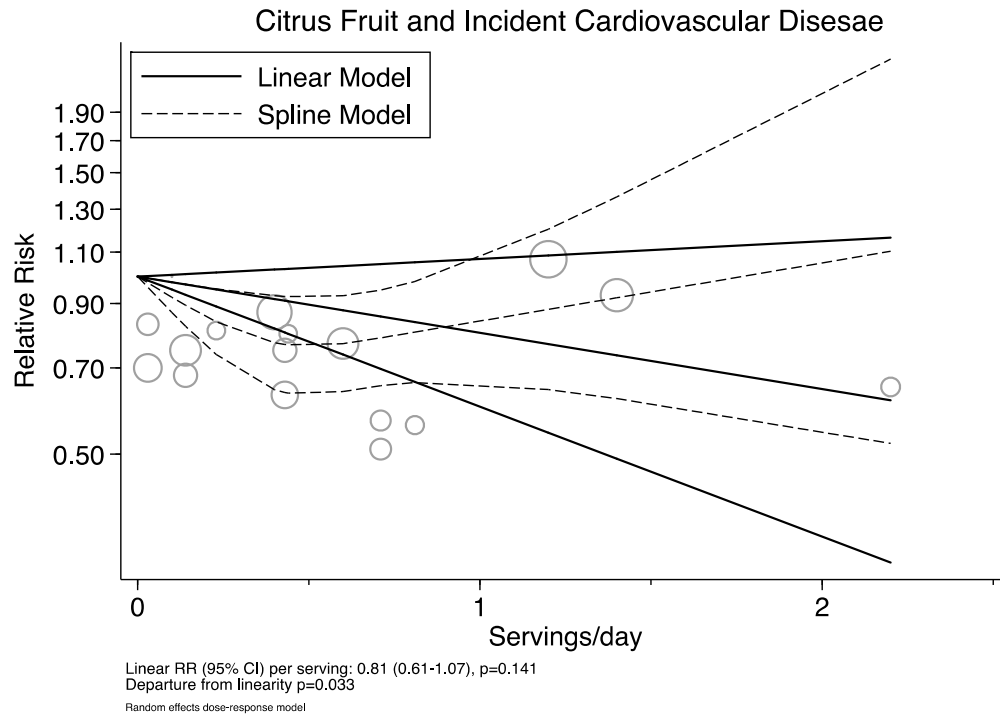


Figure S37. Linear and cubic-spline dose-response relation between increasing citrus fruit intake and incidence of cardiovascular disease. Linear dose-response data was modeled using the Greenland and Longnecker²³ method to estimate the covariances of multivariable-adjusted relative risk. Cubic spline data were modeled with fixed-effects restricted cubic spline with 3 knots and using the Greenland and Longnecker²³ method to estimate the covariances of multivariable-adjusted relative risk. All data was kept on the original dose scale. The fitted trend for each model is represented by a central line (solid lines for linear model; dashed lines for cubic spline model) with 95% confidence intervals represented by the outer lines. Individual observations are represented by the circles, with the weight of the study in the overall analysis represented by the size of the circles.

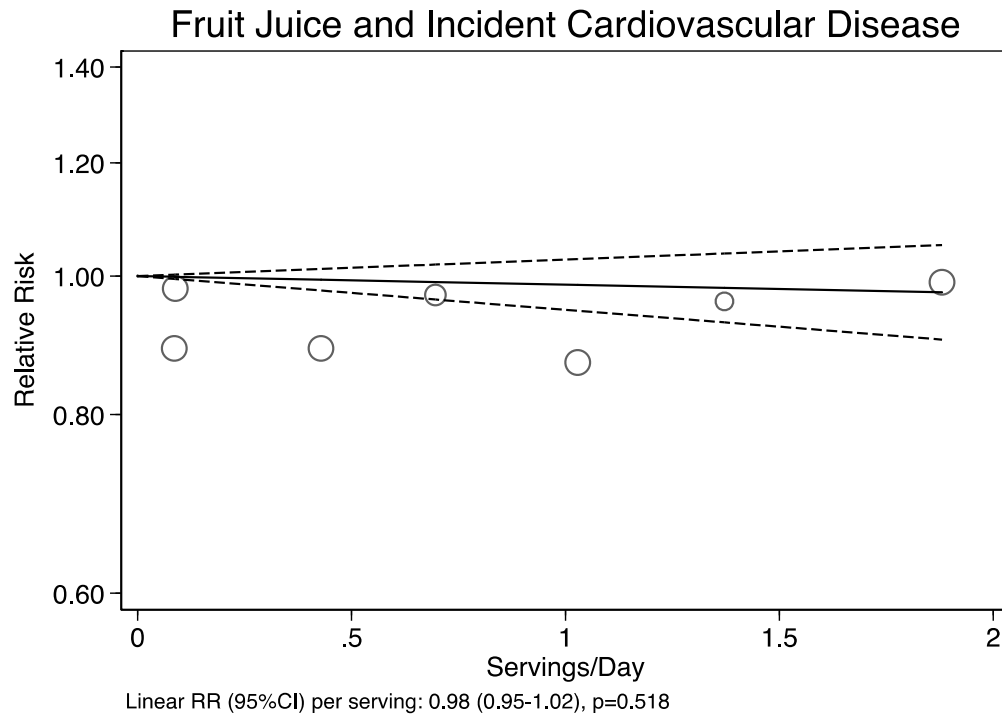


Figure S38. Linear and cubic-spline dose-response relation between increasing fruit juice intake and incidence of cardiovascular disease. Linear dose-response data was modeled using the Greenland and Longnecker²³ method to estimate the covariances of multivariable-adjusted relative risk. Cubic spline data were modeled with fixed-effects restricted cubic spline with 3 knots and using the Greenland and Longnecker²³ method to estimate the covariances of multivariable-adjusted relative risk. All data was kept on the original dose scale. The fitted trend for each model is represented by a central line (solid lines for linear model; dashed lines for cubic spline model) with 95% confidence intervals represented by the outer lines. Individual observations are represented by the circles, with the weight of the study in the overall analysis represented by the size of the circles.

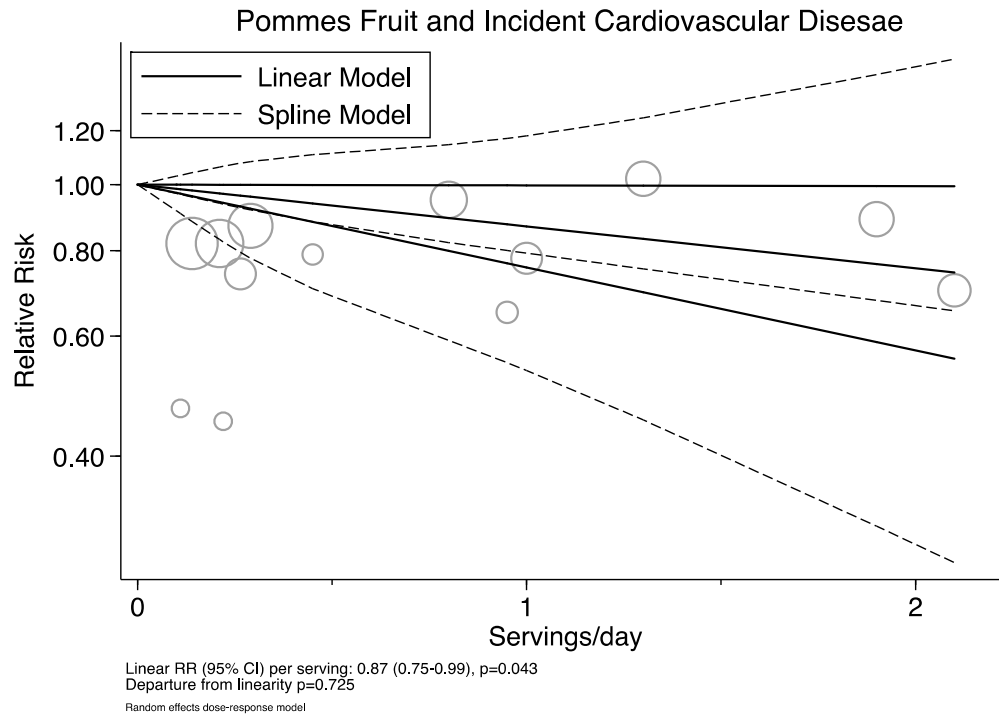


Figure S39. Linear dose-response relation between increasing pommes intake and incidence of cardiovascular disease. Linear dose-response data was modeled using the Greenland and Longnecker²³ method to estimate the covariances of multivariable-adjusted relative risk, with kept on the original dose scale. Dashed lines represent the pointwise 95% confidence intervals for the fitted linear trend represented by a solid line. Individual observations are represented by the circles, with the weight of the study in the overall analysis represented by the size of the circles.

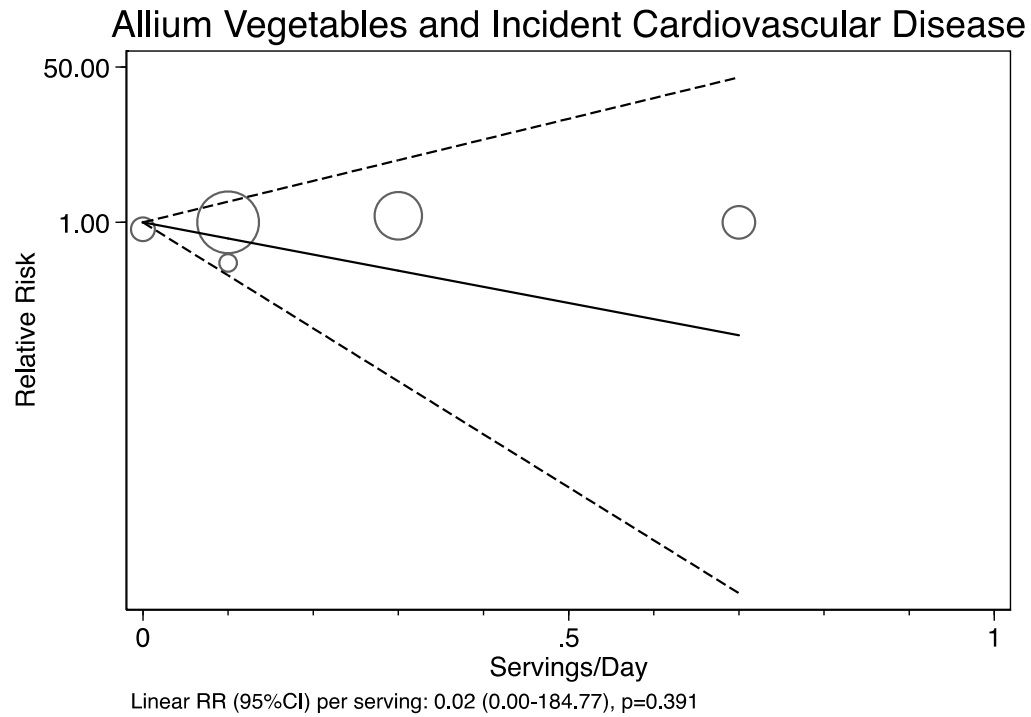


Figure S40. Linear dose-response relation between increasing intake of allium vegetables and incidence of cardiovascular disease. Linear dose-response data was modeled using the Greenland and Longnecker²³ method to estimate the covariances of multivariable-adjusted relative risk, with kept on the original dose scale. Dashed lines represent the pointwise 95% confidence intervals for the fitted linear trend represented by a solid line. Individual observations are represented by the circles, with the weight of the study in the overall analysis represented by the size of the circles.

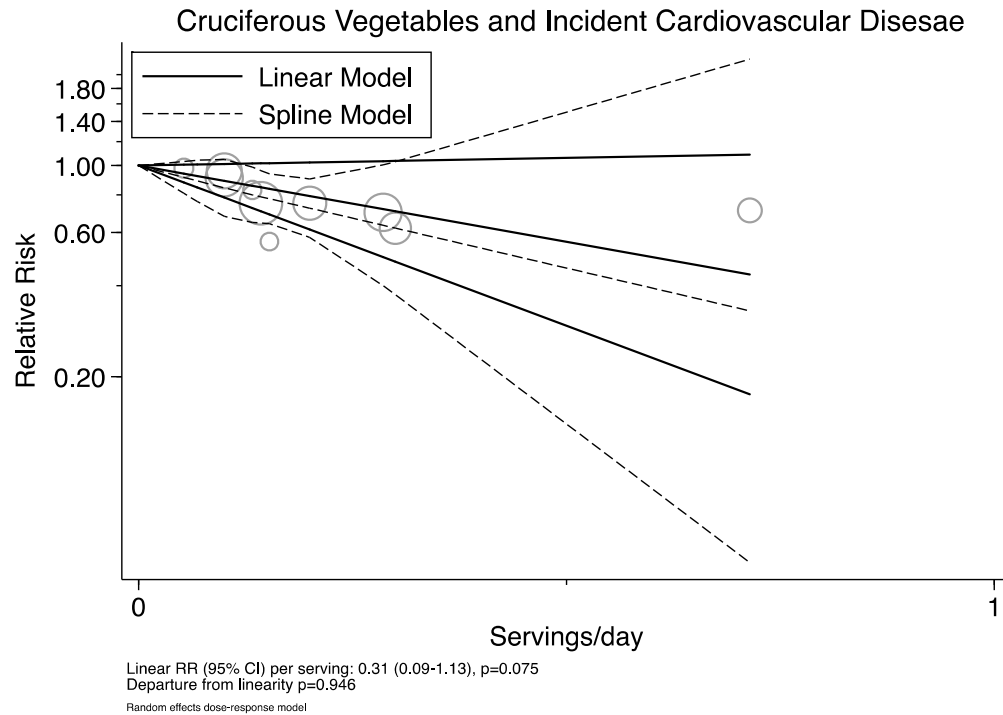


Figure S41. Linear dose-response relation between increasing intake of cruciferous vegetables and incidence of cardiovascular disease y. Linear dose-response data was modeled using the Greenland and Longnecker²³ method to estimate the covariances of multivariable-adjusted relative risk, with kept on the original dose scale. Dashed lines represent the pointwise 95% confidence intervals for the fitted linear trend represented by a solid line. Individual observations are represented by the circles, with the weight of the study in the overall analysis represented by the size of the circles.

Green Leafy Vegetables and Incident Cardiovascular Diseases

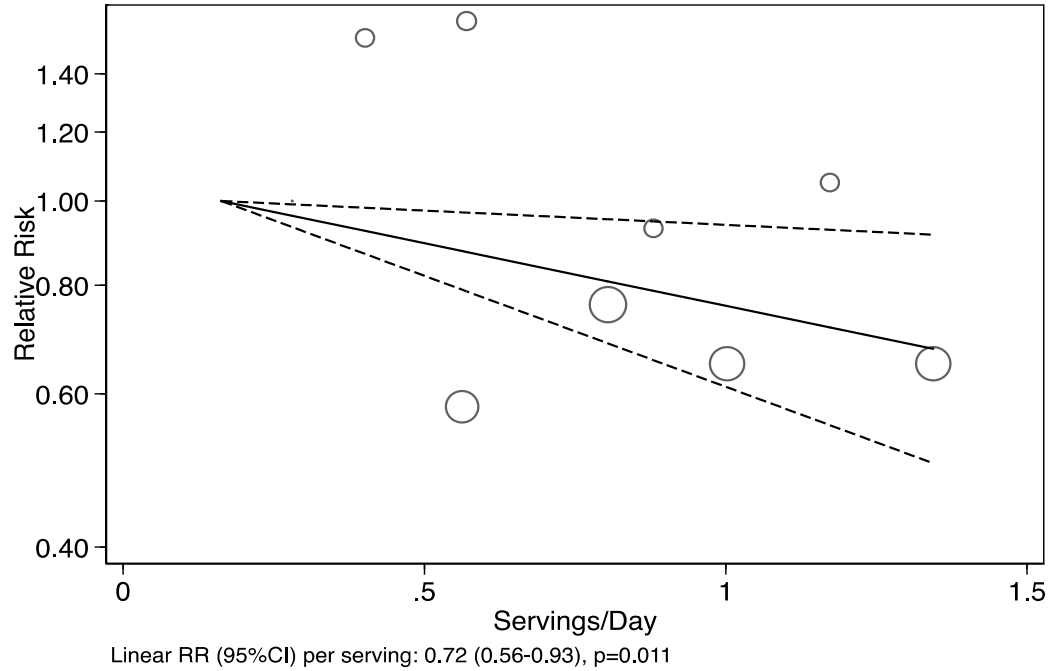


Figure S42. Linear dose-response relation between increasing intake of green leafy vegetables and incidence of cardiovascular disease. Linear dose-response data was modeled using the Greenland and Longnecker²³ method to estimate the covariances of multivariable-adjusted relative risk, with kept on the original dose scale. Dashed lines represent the pointwise 95% confidence intervals for the fitted linear trend represented by a solid line. Individual observations are represented by the circles, with the weight of the study in the overall analysis represented by the size of the circles.

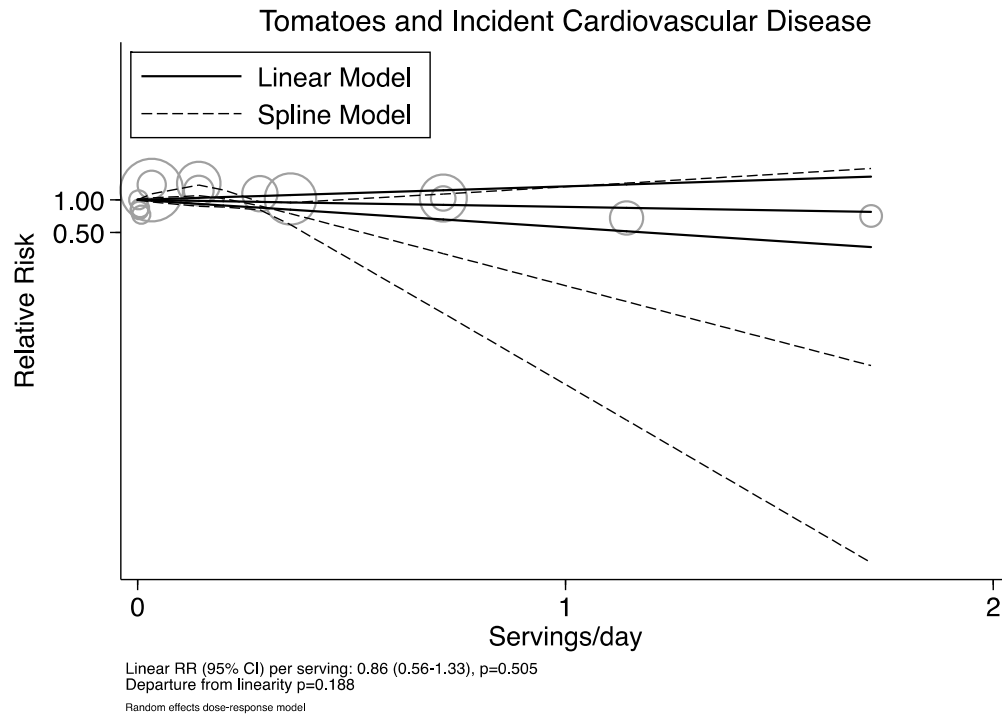


Figure S43. Linear and cubic-spline dose-response relation between increasing tomato intake and incidence of cardiovascular disease. Linear dose-response data was modeled using the Greenland and Longnecker²³ method to estimate the covariances of multivariable-adjusted relative risk. Cubic spline data were modeled with fixed-effects restricted cubic spline with 3 knots and using the Greenland and Longnecker²³ method to estimate the covariances of multivariable-adjusted relative risk. All data was kept on the original dose scale. The fitted trend for each model is represented by a central line (solid lines for linear model; dashed lines for cubic spline model) with 95% confidence intervals represented by the outer lines. Individual observations are represented by the circles, with the weight of the study in the overall analysis represented by the size of the circles.

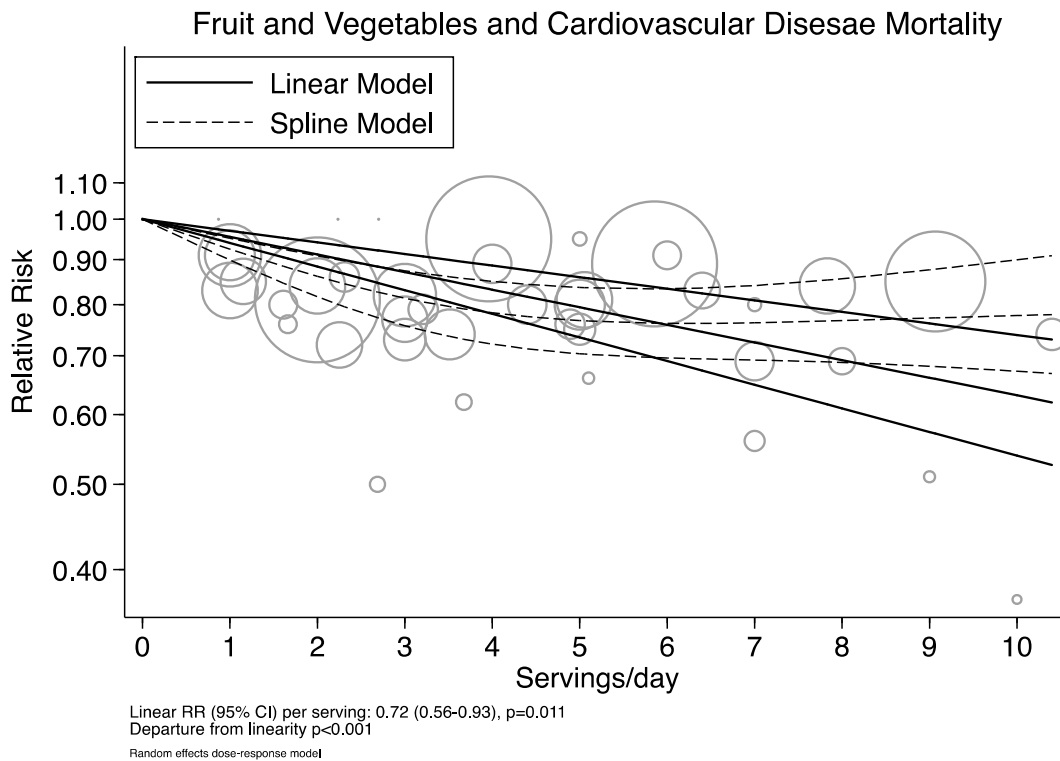


Figure S44. Linear and cubic-spline dose-response relation between increasing fruit and vegetable intake and cardiovascular disease mortality. Linear dose-response data was modeled using the Greenland and Longnecker²³ method to estimate the covariances of multivariable-adjusted relative risk. Cubic spline data were modeled with fixed-effects restricted cubic spline with 3 knots and using the Greenland and Longnecker²³ method to estimate the covariances of multivariable-adjusted relative risk. All data was kept on the original dose scale. The fitted trend for each model is represented by a central line (solid lines for linear model; dashed lines for cubic spline model) with 95% confidence intervals represented by the outer lines. Individual observations are represented by the circles, with the weight of the study in the overall analysis represented by the size of the circles.

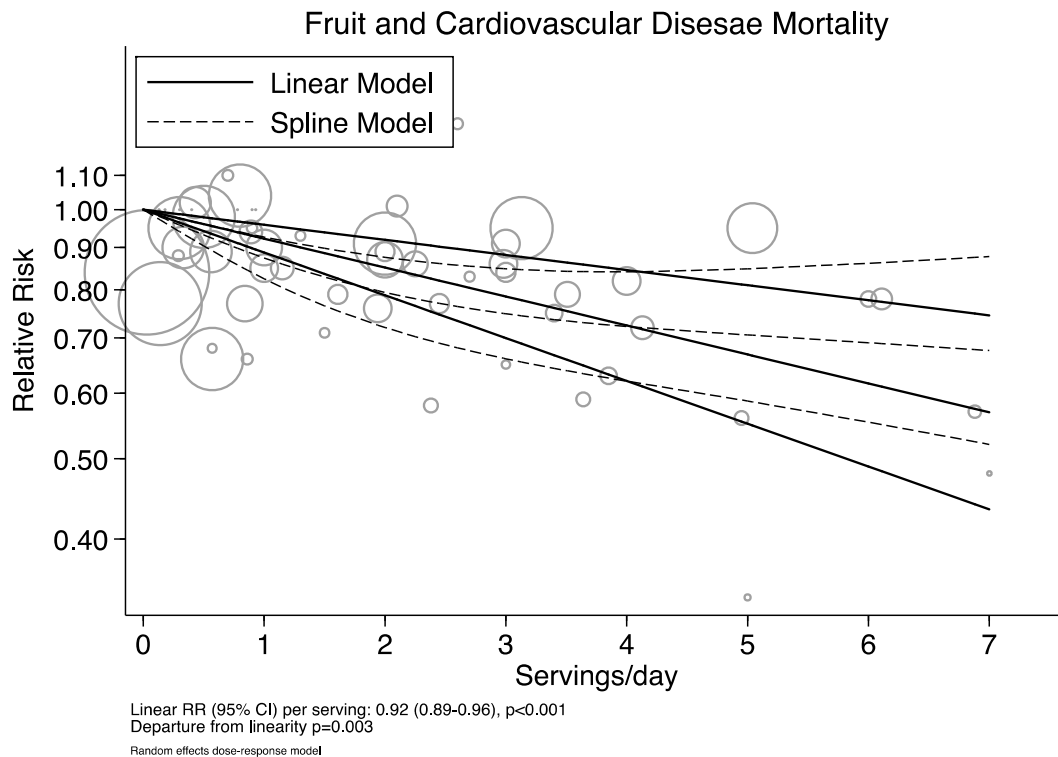


Figure S45. Linear and cubic-spline dose-response relation between increasing fruit intake and cardiovascular disease mortality. Linear dose-response data was modeled using the Greenland and Longnecker²³ method to estimate the covariances of multivariable-adjusted relative risk. Cubic spline data were modeled with fixed-effects restricted cubic spline with 3 knots and using the Greenland and Longnecker²³ method to estimate the covariances of multivariable-adjusted relative risk. All data was kept on the original dose scale. The fitted trend for each model is represented by a central line (solid lines for linear model; dashed lines for cubic spline model) with 95% confidence intervals represented by the outer lines. Individual observations are represented by the circles, with the weight of the study in the overall analysis represented by the size of the circles.

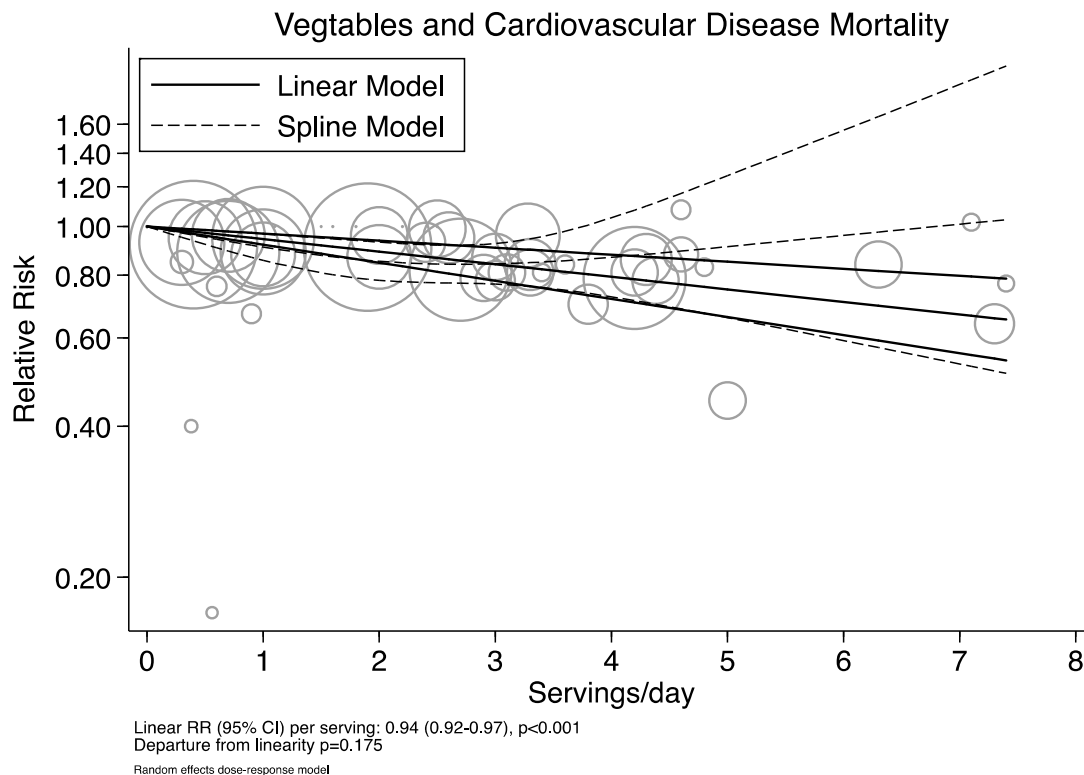


Figure S46. Linear and cubic-spline dose-response relation between increasing intake of vegetables and cardiovascular disease mortality. Linear dose-response data was modeled using the Greenland and Longnecker²³ method to estimate the covariances of multivariable-adjusted relative risk. Cubic spline data were modeled with fixed-effects restricted cubic spline with 3 knots and using the Greenland and Longnecker²³ method to estimate the covariances of multivariable-adjusted relative risk. All data was kept on the original dose scale. The fitted trend for each model is represented by a central line (solid lines for linear model; dashed lines for cubic spline model) with 95% confidence intervals represented by the outer lines. Individual observations are represented by the circles, with the weight of the study in the overall analysis represented by the size of the circles.

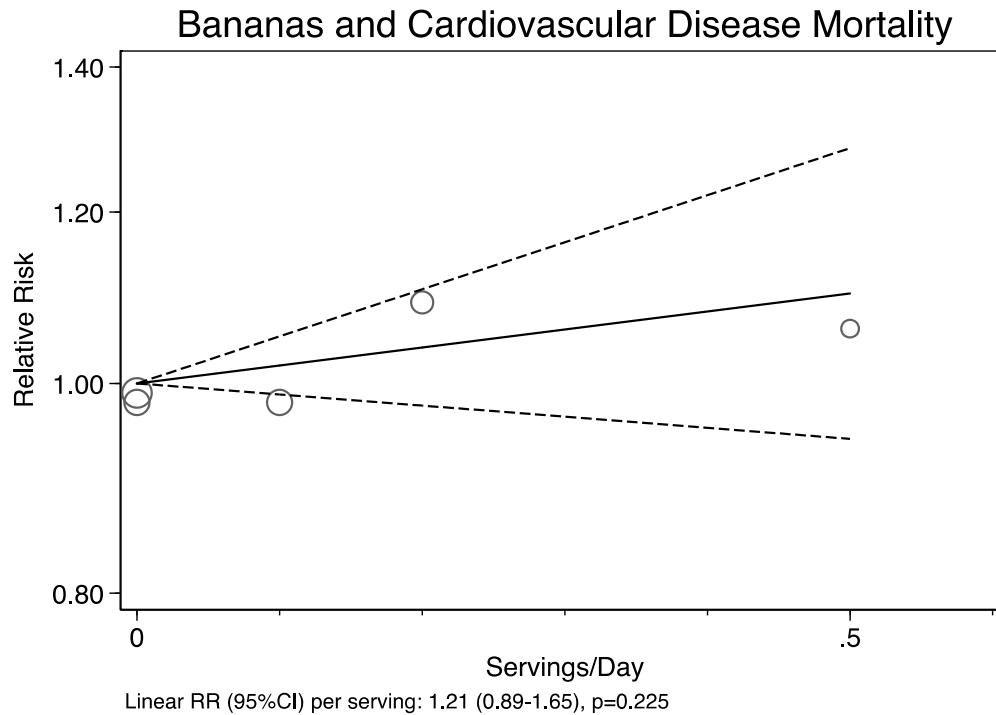


Figure S47. Linear dose-response relation between increasing banana intake and cardiovascular disease mortality. Linear dose-response data was modeled using the Greenland and Longnecker²³ method to estimate the covariances of multivariable-adjusted relative risk, with kept on the original dose scale. Dashed lines represent the pointwise 95% confidence intervals for the fitted linear trend represented by a solid line. Individual observations are represented by the circles, with the weight of the study in the overall analysis represented by the size of the circles.

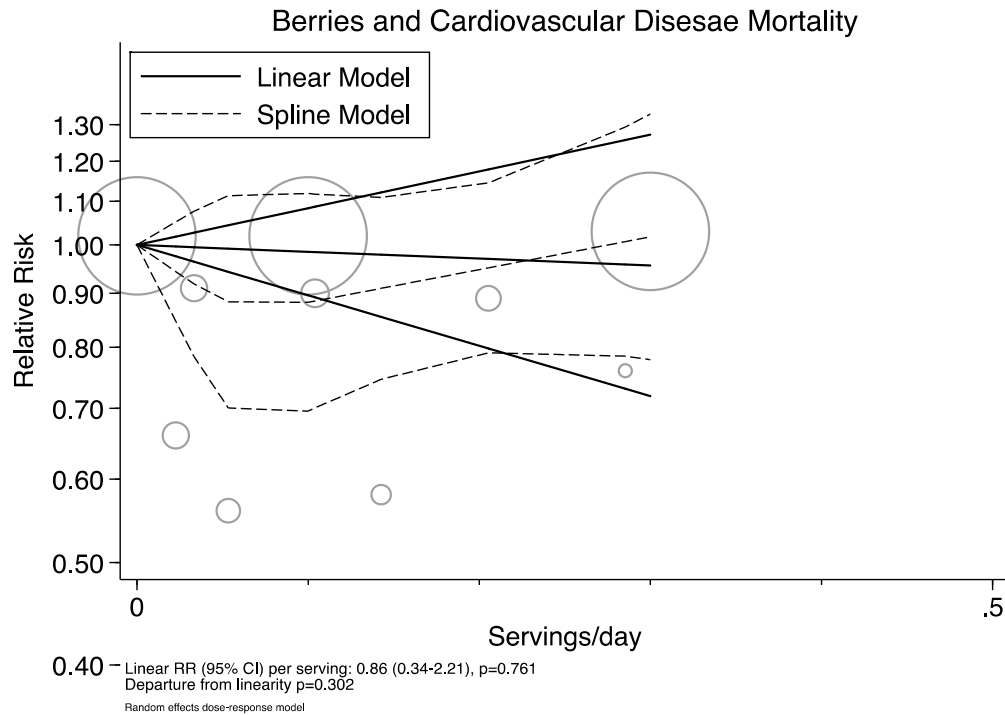


Figure S48. Linear and cubic-spline dose-response relation between increasing berry fruit intake and cardiovascular disease mortality. Linear dose-response data was modeled using the Greenland and Longnecker²³ method to estimate the covariances of multivariable-adjusted relative risk. Cubic spline data were modeled with fixed-effects restricted cubic spline with 3 knots and using the Greenland and Longnecker²³ method to estimate the covariances of multivariable-adjusted relative risk. All data was kept on the original dose scale. The fitted trend for each model is represented by a central line (solid lines for linear model; dashed lines for cubic spline model) with 95% confidence intervals represented by the outer lines. Individual observations are represented by the circles, with the weight of the study in the overall analysis represented by the size of the circles.

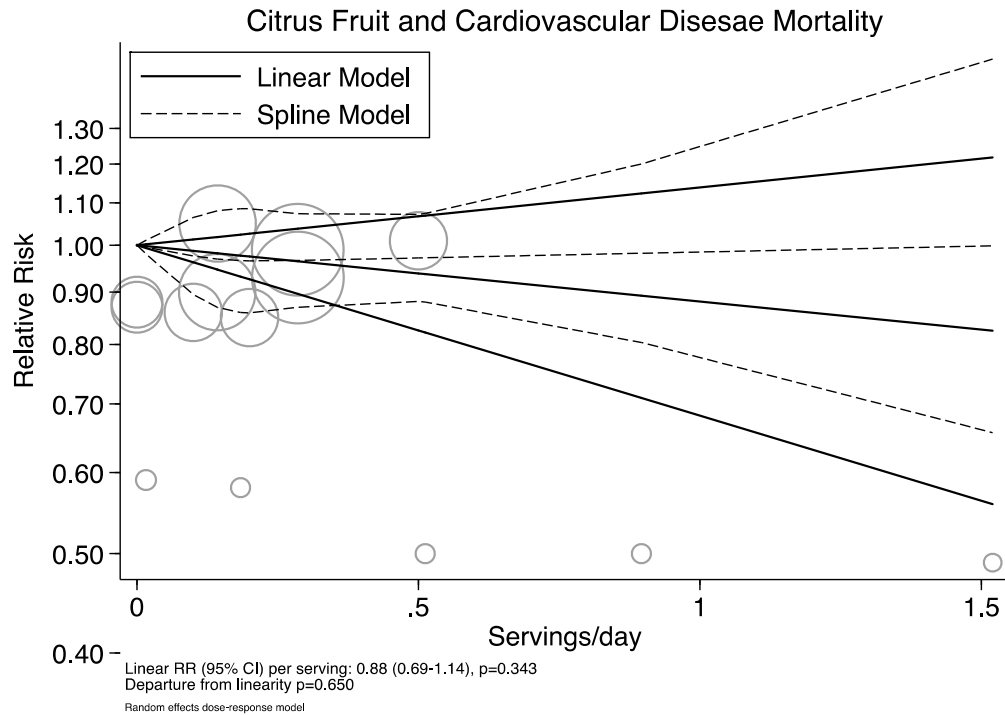


Figure S49. Linear and cubic-spline dose-response relation between increasing citrus fruit intake and cardiovascular disease mortality. Linear dose-response data was modeled using the Greenland and Longnecker²³ method to estimate the covariances of multivariable-adjusted relative risk. Cubic spline data were modeled with fixed-effects restricted cubic spline with 3 knots and using the Greenland and Longnecker²³ method to estimate the covariances of multivariable-adjusted relative risk. All data was kept on the original dose scale. The fitted trend for each model is represented by a central line (solid lines for linear model; dashed lines for cubic spline model) with 95% confidence intervals represented by the outer lines. Individual observations are represented by the circles, with the weight of the study in the overall analysis represented by the size of the circles.

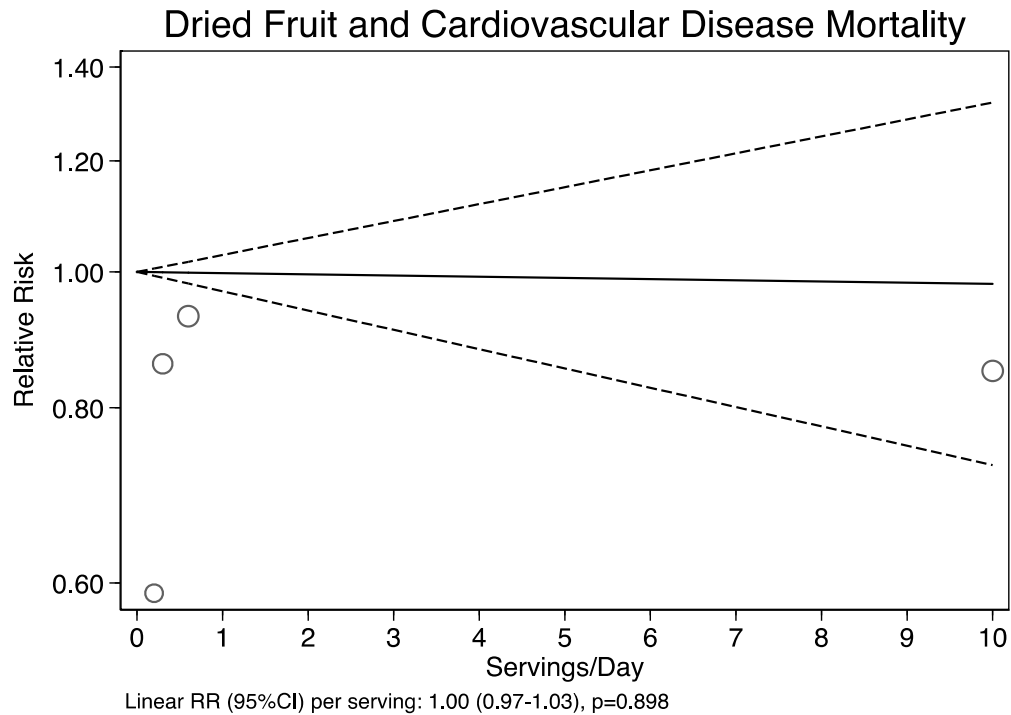


Figure S50. Linear and cubic-spline dose-response relation between increasing dried fruit intake and cardiovascular disease mortality. Linear dose-response data was modeled using the Greenland and Longnecker²³ method to estimate the covariances of multivariable-adjusted relative risk. Cubic spline data were modeled with fixed-effects restricted cubic spline with 3 knots and using the Greenland and Longnecker²³ method to estimate the covariances of multivariable-adjusted relative risk. All data was kept on the original dose scale. The fitted trend for each model is represented by a central line (solid lines for linear model; dashed lines for cubic spline model) with 95% confidence intervals represented by the outer lines. Individual observations are represented by the circles, with the weight of the study in the overall analysis represented by the size of the circles.

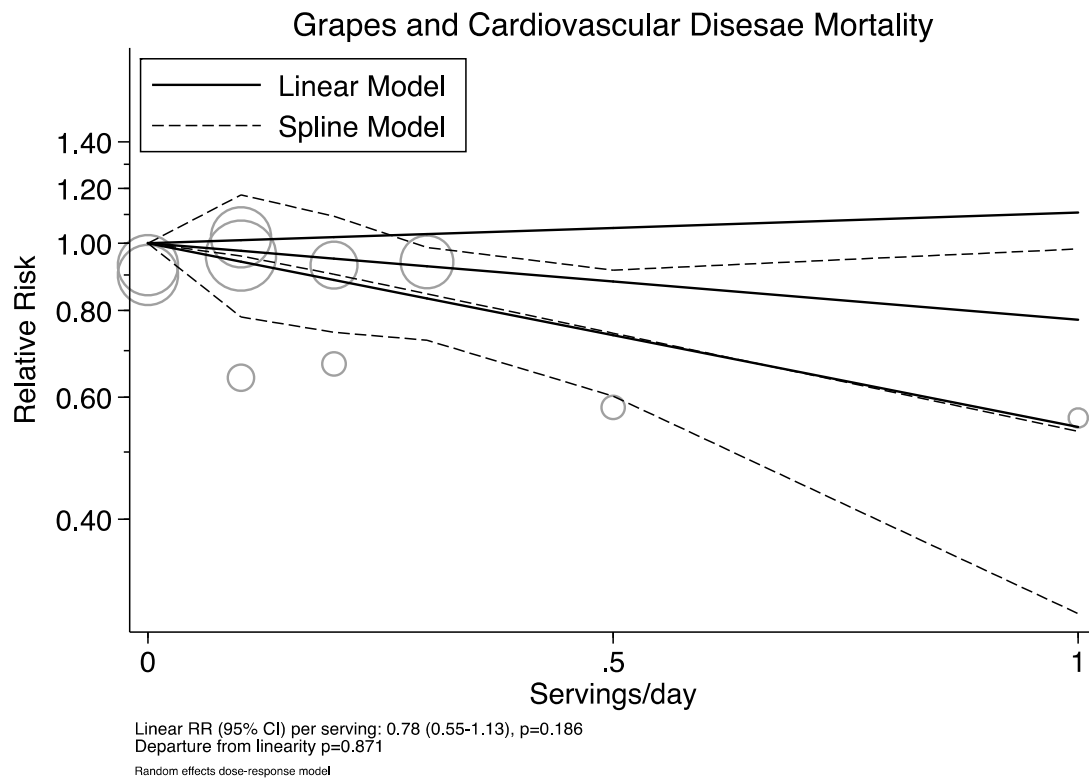


Figure S51. Linear and cubic-spline dose-response relation between increasing grapes intake and cardiovascular disease mortality. Linear dose-response data was modeled using the Greenland and Longnecker²³ method to estimate the covariances of multivariable-adjusted relative risk. Cubic spline data were modeled with fixed-effects restricted cubic spline with 3 knots and using the Greenland and Longnecker²³ method to estimate the covariances of multivariable-adjusted relative risk. All data was kept on the original dose scale. The fitted trend for each model is represented by a central line (solid lines for linear model; dashed lines for cubic spline model) with 95% confidence intervals represented by the outer lines. Individual observations are represented by the circles, with the weight of the study in the overall analysis represented by the size of the circles.

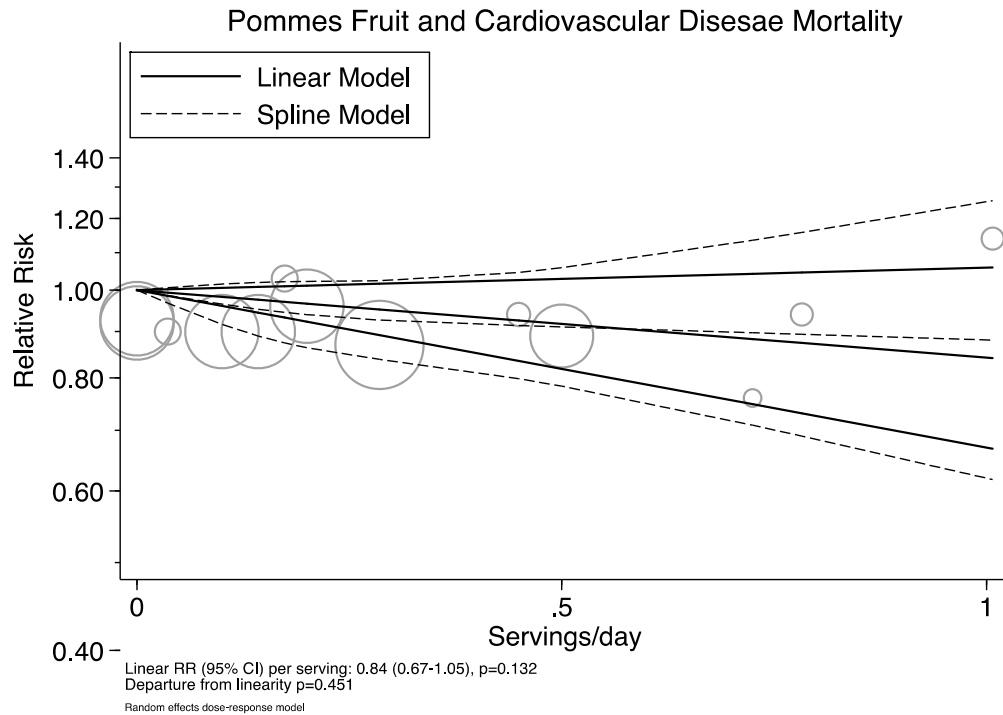


Figure S52. Linear and cubic-spline dose-response relation between increasing pommes intake and cardiovascular disease mortality. Linear dose-response data was modeled using the Greenland and Longnecker²³ method to estimate the covariances of multivariable-adjusted relative risk. Cubic spline data were modeled with fixed-effects restricted cubic spline with 3 knots and using the Greenland and Longnecker²³ method to estimate the covariances of multivariable-adjusted relative risk. All data was kept on the original dose scale. The fitted trend for each model is represented by a central line (solid lines for linear model; dashed lines for cubic spline model) with 95% confidence intervals represented by the outer lines. Individual observations are represented by the circles, with the weight of the study in the overall analysis represented by the size of the circles.

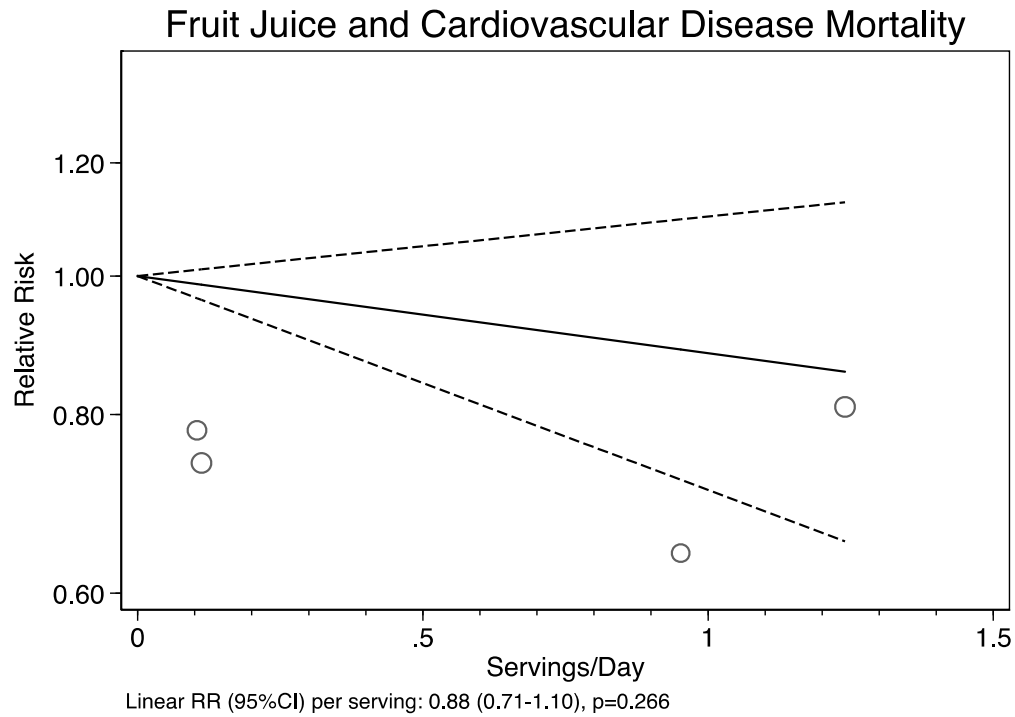


Figure S53. Linear dose-response relation between increasing fruit juice intake and cardiovascular disease mortality. Linear dose-response data was modeled using the Greenland and Longnecker²³ method to estimate the covariances of multivariable-adjusted relative risk, with kept on the original dose scale. Dashed lines represent the pointwise 95% confidence intervals for the fitted linear trend represented by a solid line. Individual observations are represented by the circles, with the weight of the study in the overall analysis represented by the size of the circles.

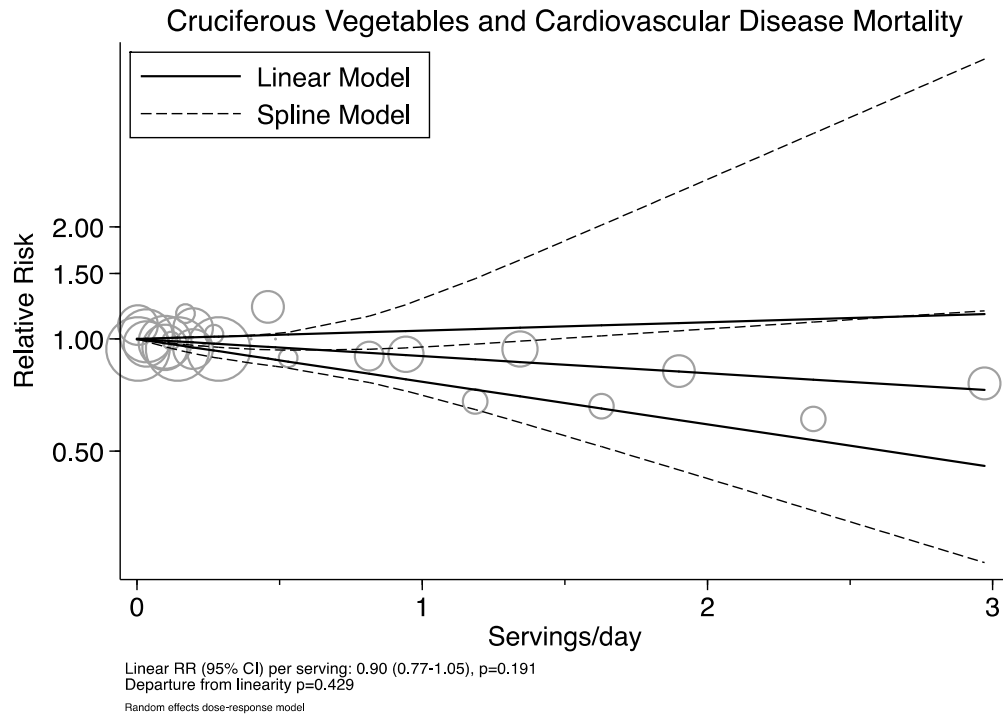


Figure S54. Linear and cubic-spline dose-response relation between increasing intake of cruciferous vegetables and cardiovascular disease mortality. Linear dose-response data was modeled using the Greenland and Longnecker²³ method to estimate the covariances of multivariable-adjusted relative risk. Cubic spline data were modeled with fixed-effects restricted cubic spline with 3 knots and using the Greenland and Longnecker²³ method to estimate the covariances of multivariable-adjusted relative risk. All data was kept on the original dose scale. The fitted trend for each model is represented by a central line (solid lines for linear model; dashed lines for cubic spline model) with 95% confidence intervals represented by the outer lines. Individual observations are represented by the circles, with the weight of the study in the overall analysis represented by the size of the circles.

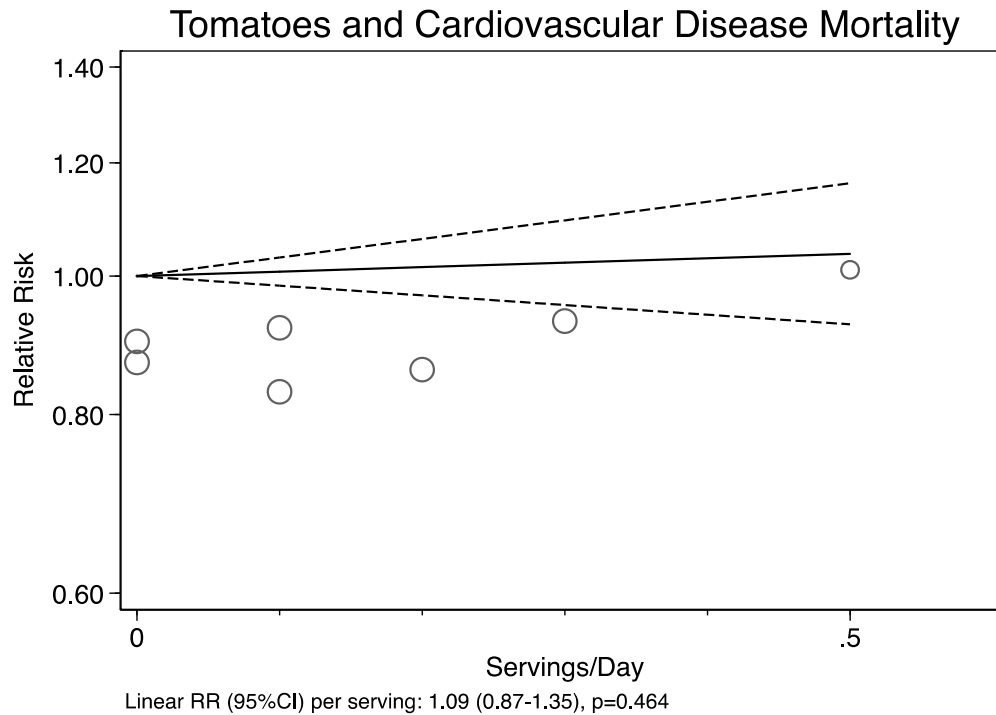
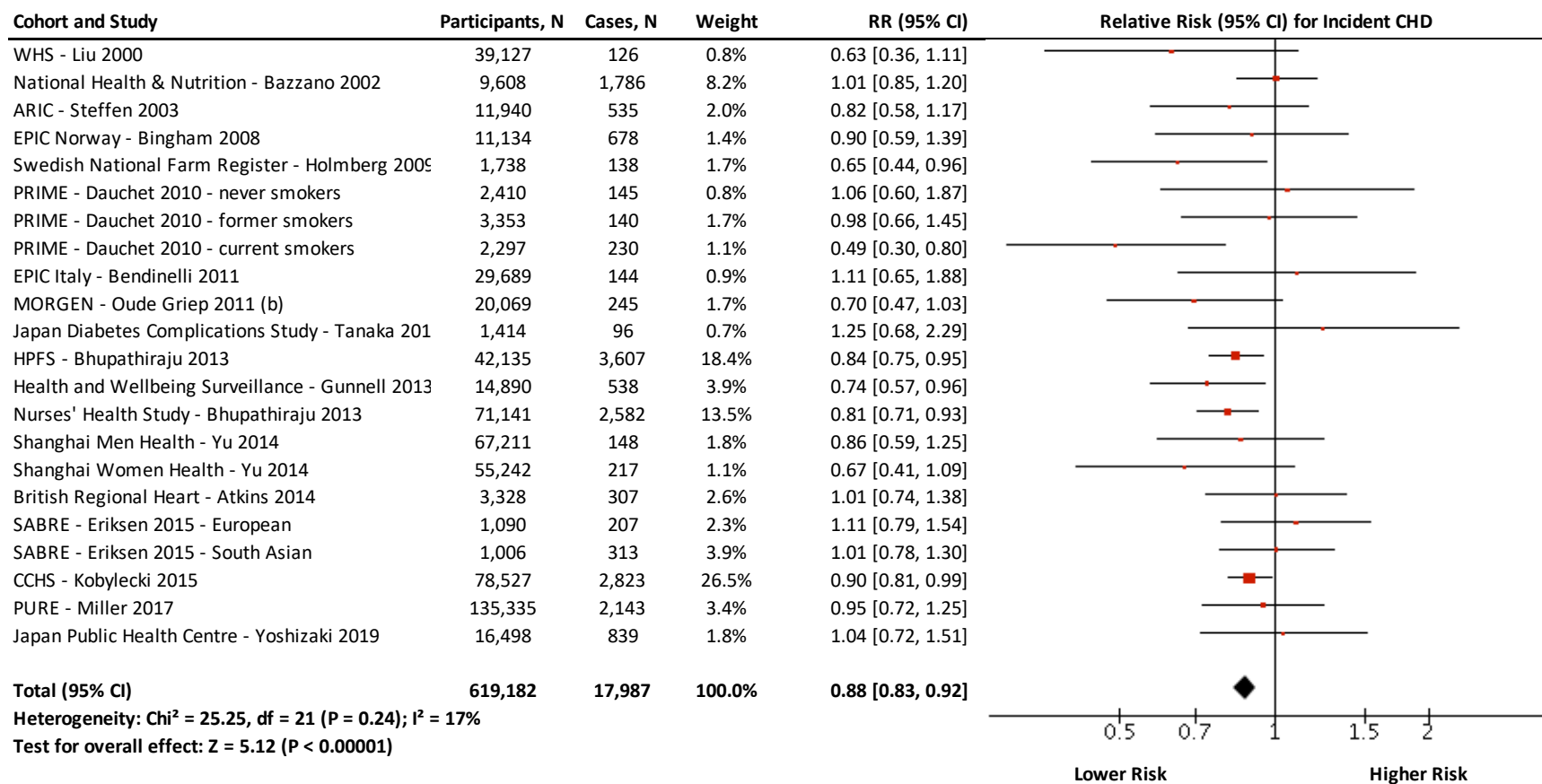


Figure S55. Linear dose-response relation between increasing tomato intake and cardiovascular disease mortality. Linear dose-response data was modeled using the Greenland and Longnecker²³ method to estimate the covariances of multivariable-adjusted relative risk, with kept on the original dose scale. Dashed lines represent the pointwise 95% confidence intervals for the fitted linear trend represented by a solid line. Individual observations are represented by the circles, with the weight of the study in the overall analysis represented by the size of the circles.

TOTAL FRUIT AND VEGETABLES AND CORONARY HEART DISEASE INCIDENCE

A. Fixed Effects



B. Random Effects

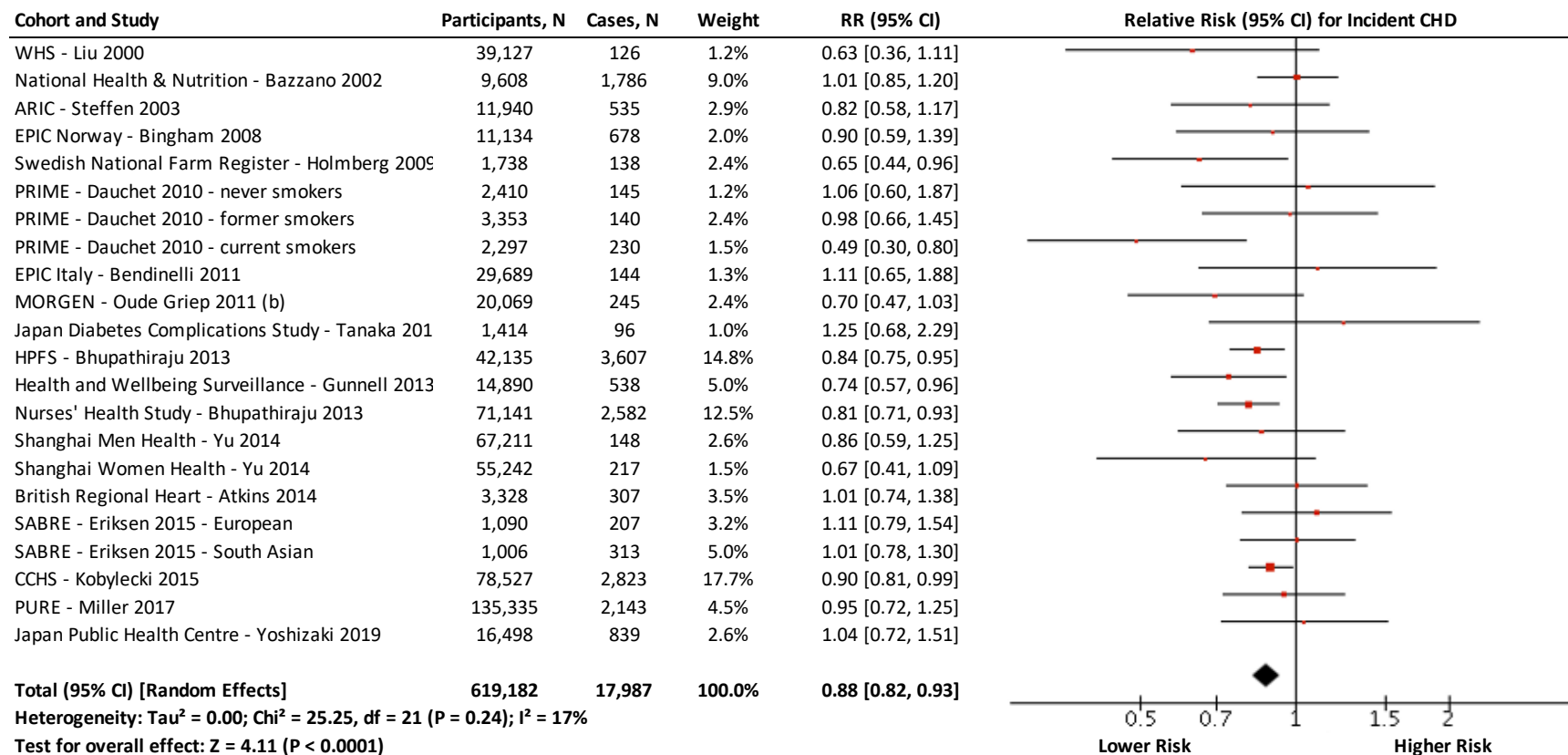
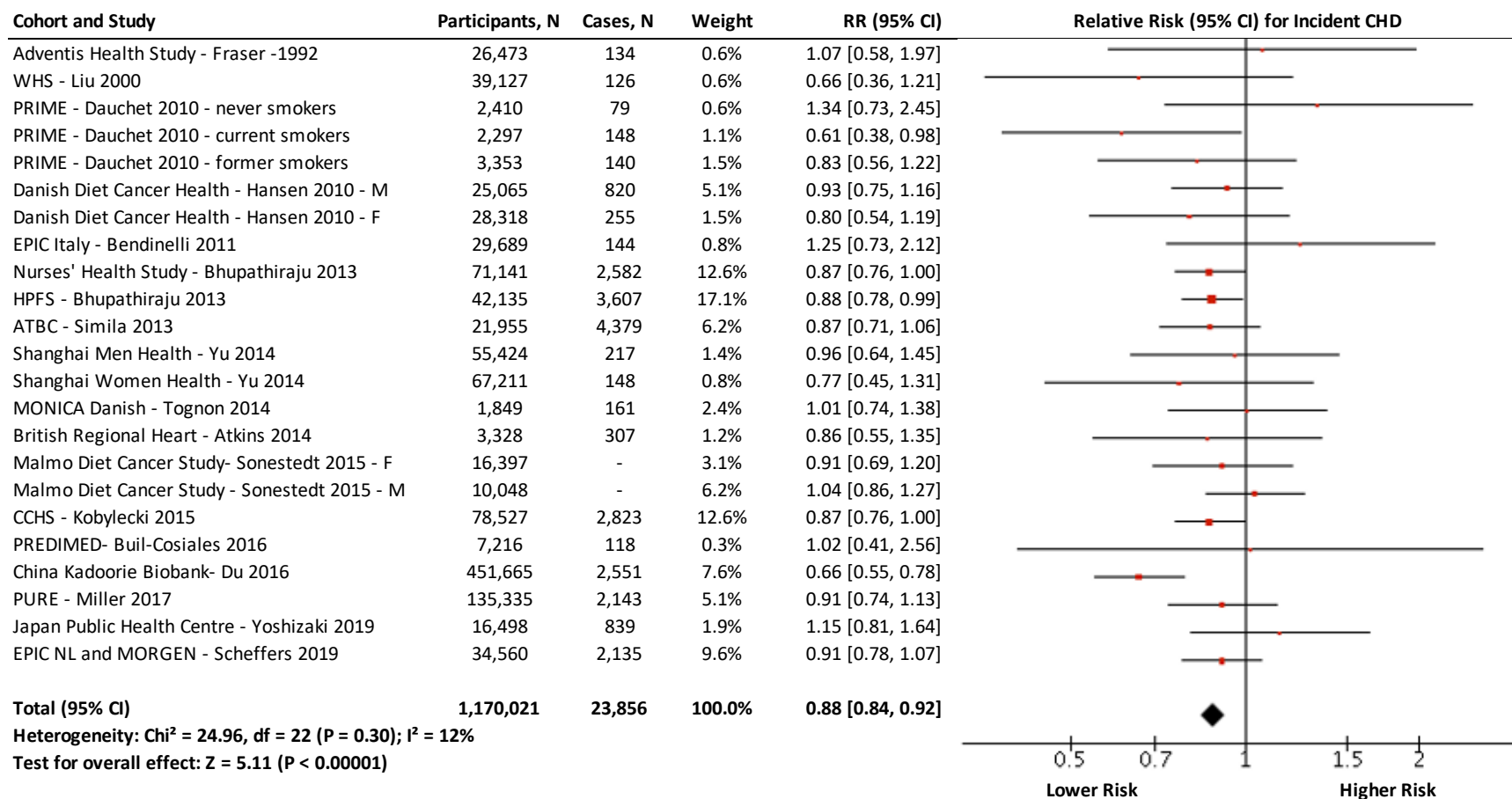


Figure S56. Relation between total fruit and vegetables intake and coronary heart disease incidence (highest vs. lowest level of intake). All results are presented as relative risk (RR) with 95% confidence intervals (95% CI). Pooled risk estimate is represented by the black diamond using (A) fixed effects and (B) random effects models. Inter-study heterogeneity was assessed using the Cochran Q statistic (χ^2) at a significance level of $p < 0.10$, and quantified by I^2 , with values $\geq 50\%$ indicating substantial heterogeneity.

FRUIT AND CORONARY HEART DISEASE INCIDENCE

A. Fixed Effects



B. Random Effects

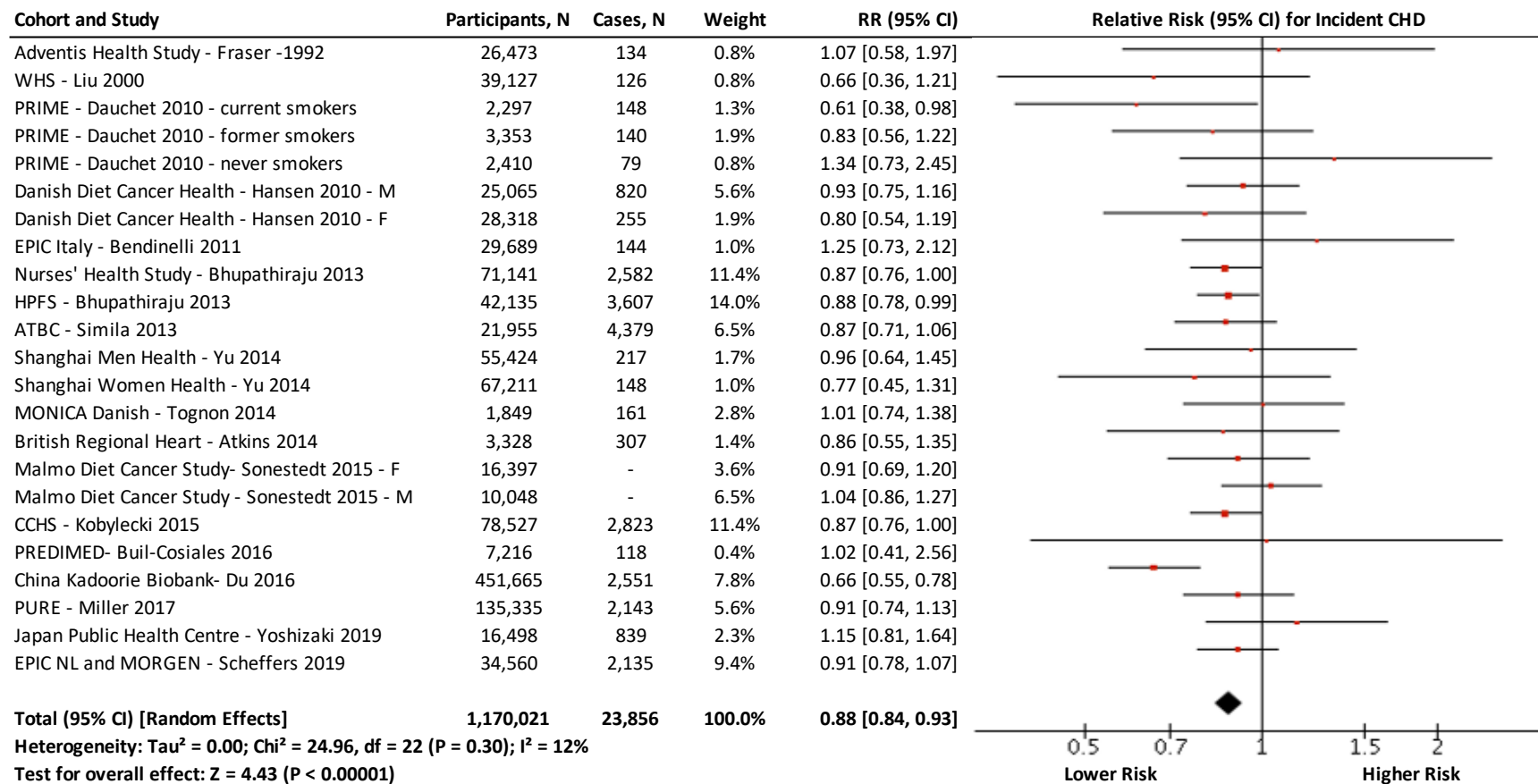
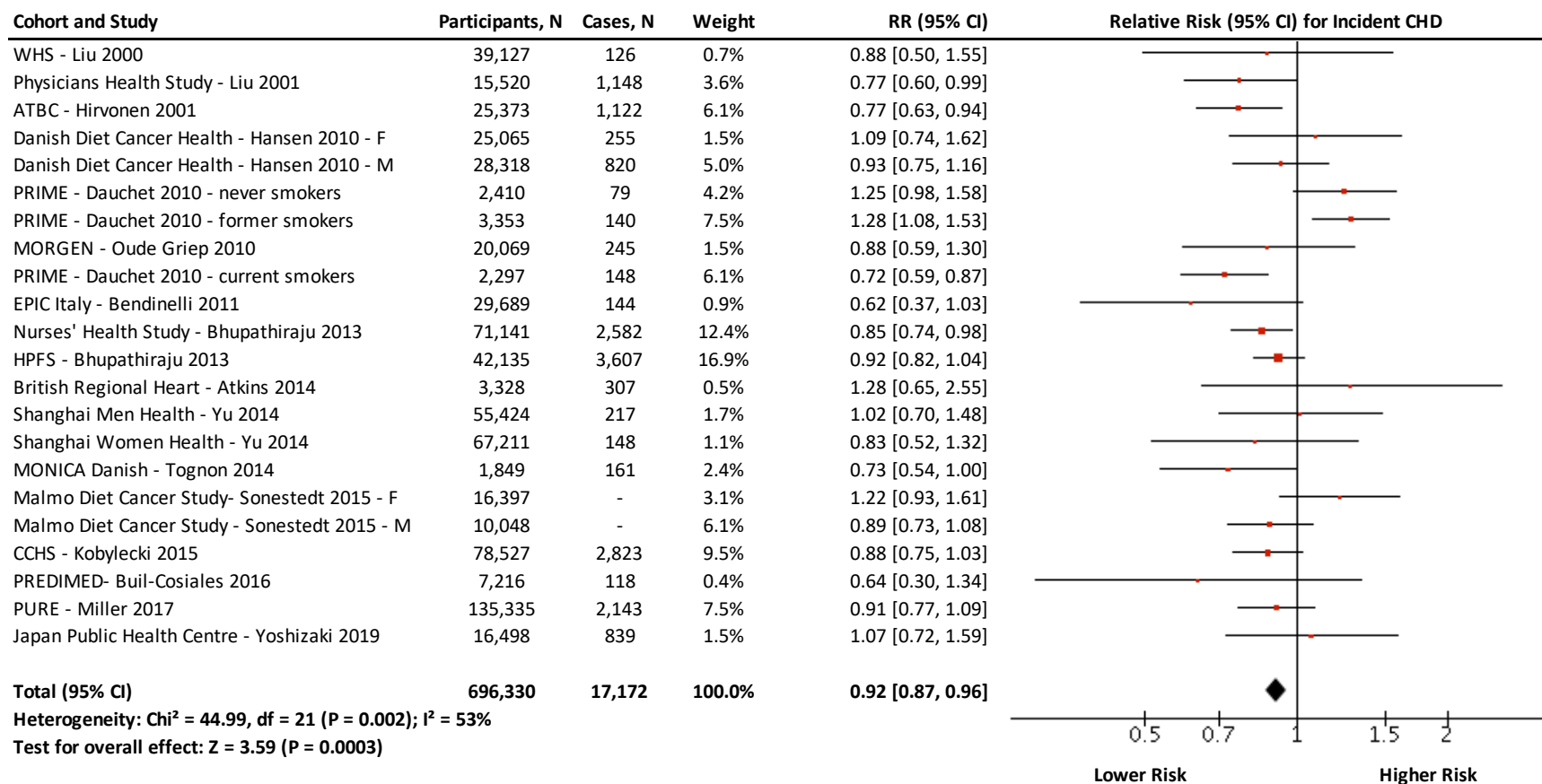


Figure S57. Relation between fruit intake and coronary heart disease incidence (highest vs. lowest level of intake). All results are presented as relative risk (RR) with 95% confidence intervals (95% CI). Pooled risk estimate is represented by the black diamond using (A) fixed effects and (B) random effects models. Inter-study heterogeneity was assessed using the Cochran Q statistic (Chi²) at a significance level of p<0.10, and quantified by I², with values ≥ 50% indicating substantial heterogeneity.

VEGETABLES AND CORONARY HEART DISEASE INCIDENCE

A. Fixed Effects



B. Random Effects

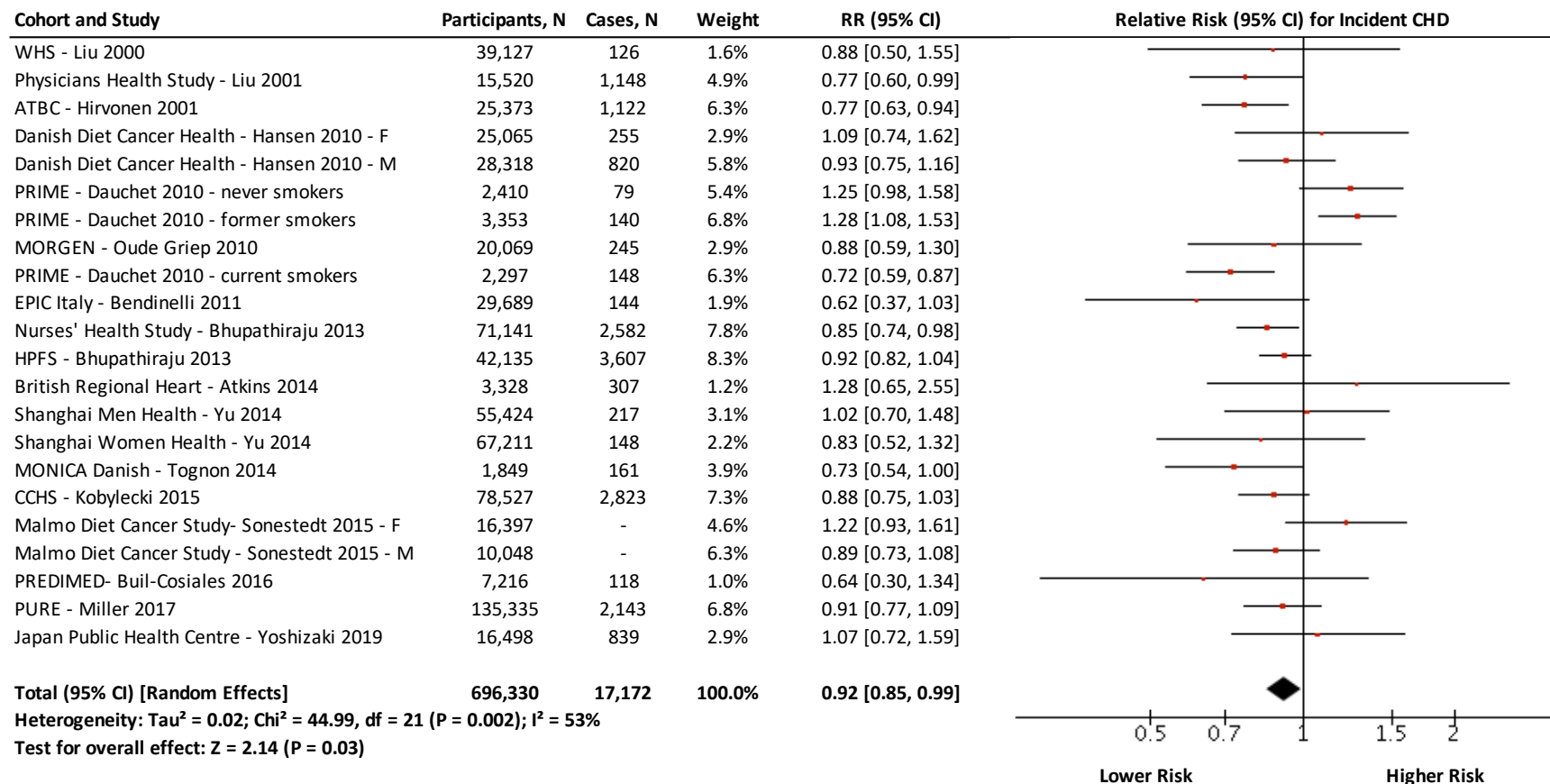
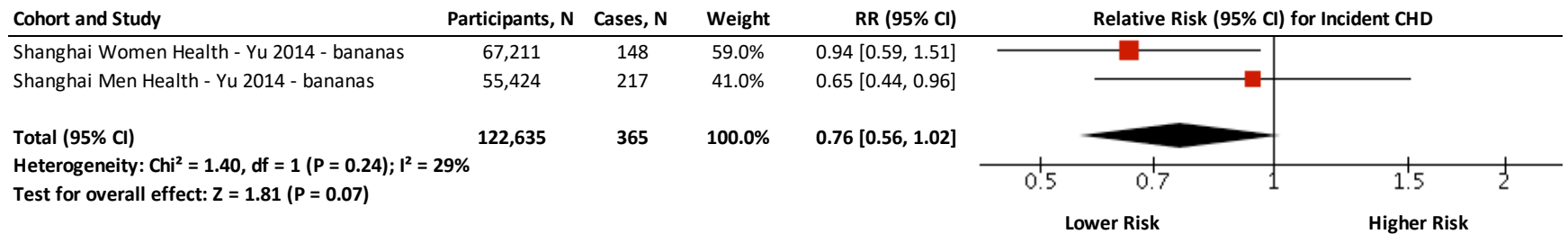


Figure S58. Relation between intake of vegetables and coronary heart disease incidence (highest vs. lowest level of intake). All results are presented as relative risk (RR) with 95% confidence intervals (95% CI). Pooled risk estimate is represented by the black diamond using (A) fixed effects and (B) random effects models. Inter-study heterogeneity was assessed using the Cochran Q statistic (Chi²) at a significance level of $p < 0.10$, and quantified by I², with values $\geq 50\%$ indicating substantial heterogeneity.

BANANAS AND CORONARY HEART DISEASE INCIDENCE

A. Fixed Effects



B. Random Effects

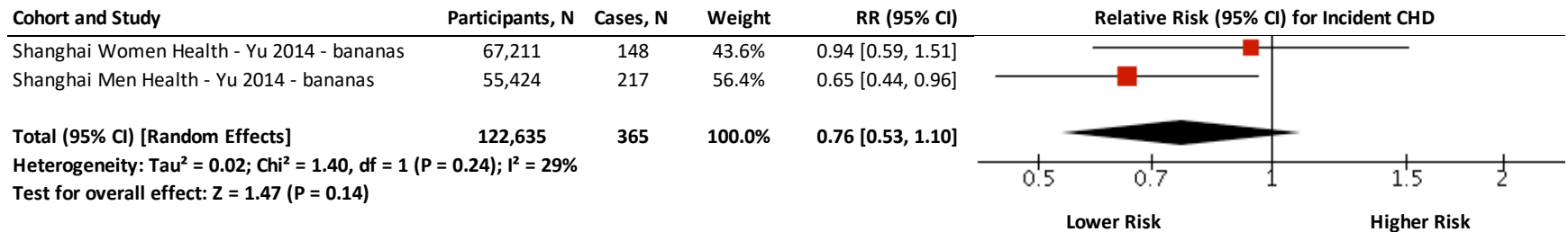
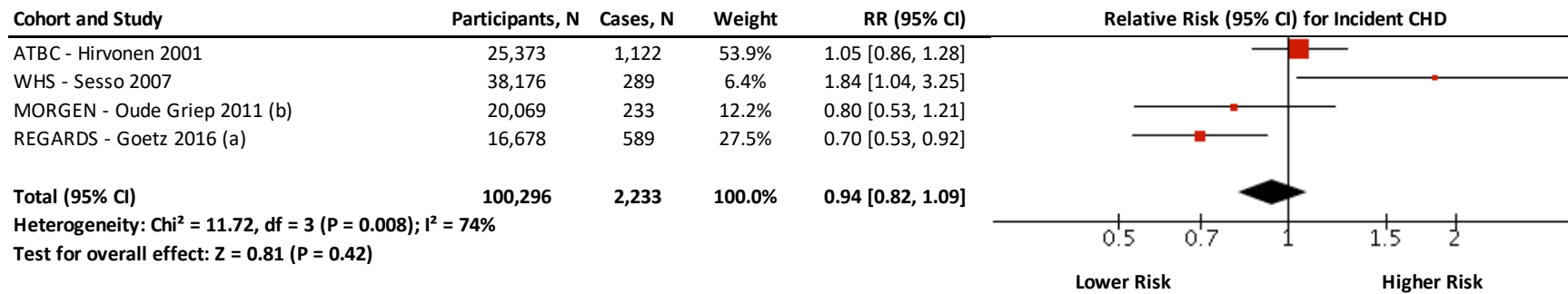


Figure S59. Relation between intake of bananas and coronary heart disease incidence (highest vs. lowest level of intake). All results are presented as relative risk (RR) with 95% confidence intervals (95% CI). Pooled risk estimate is represented by the black diamond using (A) fixed effects and (B) random effects models. Inter-study heterogeneity was assessed using the Cochran Q statistic (Chi^2) at a significance level of $p < 0.10$, and quantified by I^2 , with values $\geq 50\%$ indicating substantial heterogeneity.

BERRIES AND CORONARY HEART DISEASE INCIDENCE

A. Fixed Effects



B. Random Effects

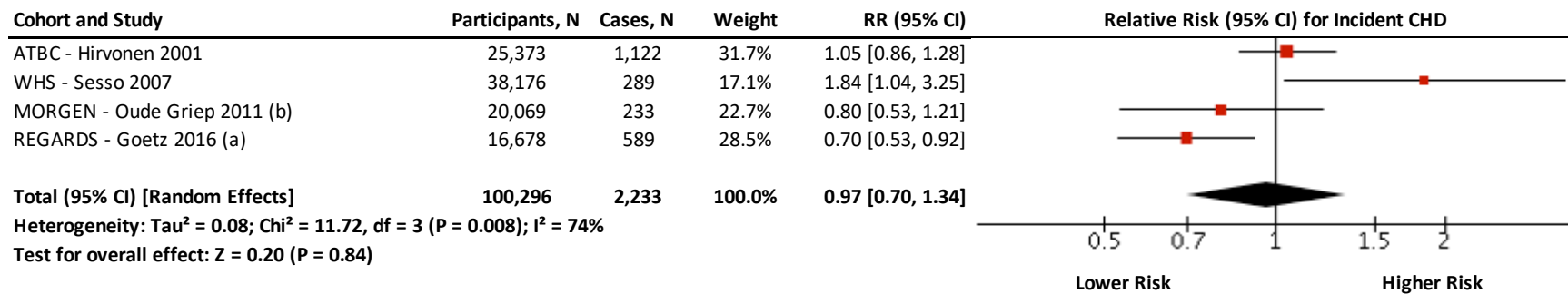
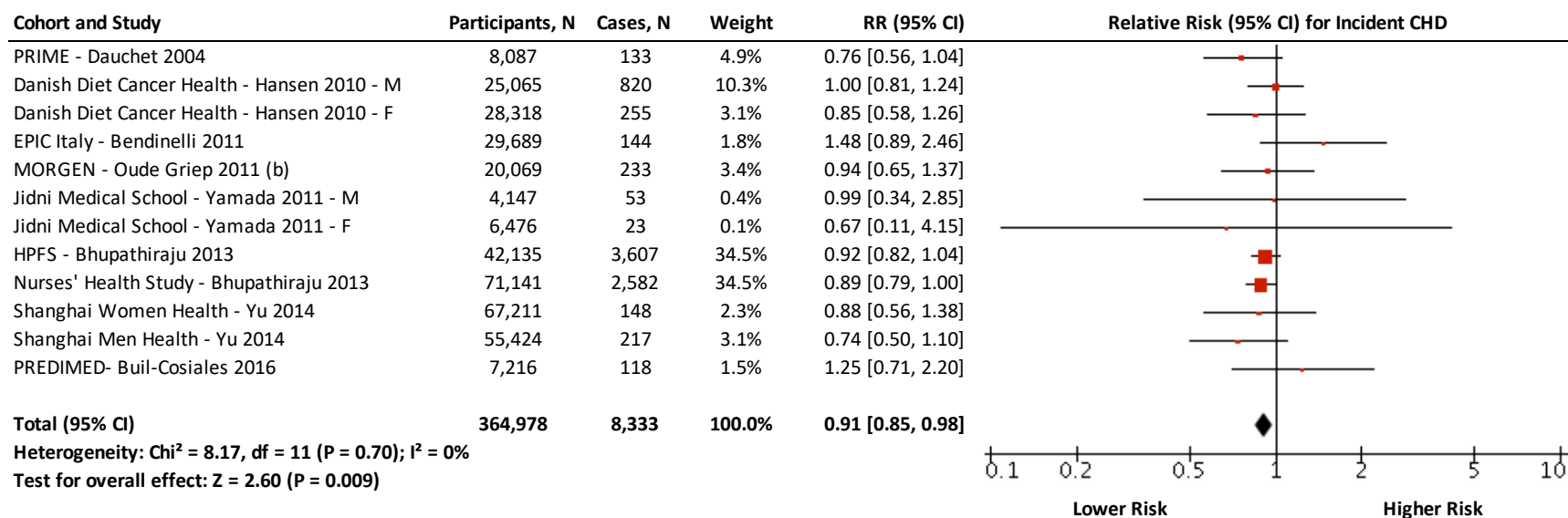


Figure S60. Relation between intake of berries and coronary heart disease incidence (highest vs. lowest level of intake). All results are presented as relative risk (RR) with 95% confidence intervals (95% CI). Pooled risk estimate is represented by the black diamond using (A) fixed effects and (B) random effects models. Inter-study heterogeneity was assessed using the Cochran Q statistic (χ^2) at a significance level of $p < 0.10$, and quantified by I^2 , with values $\geq 50\%$ indicating substantial heterogeneity.

CITRUS FRUIT AND CORONARY HEART DISEASE INCIDENCE

A. Fixed Effects



B. Random Effects

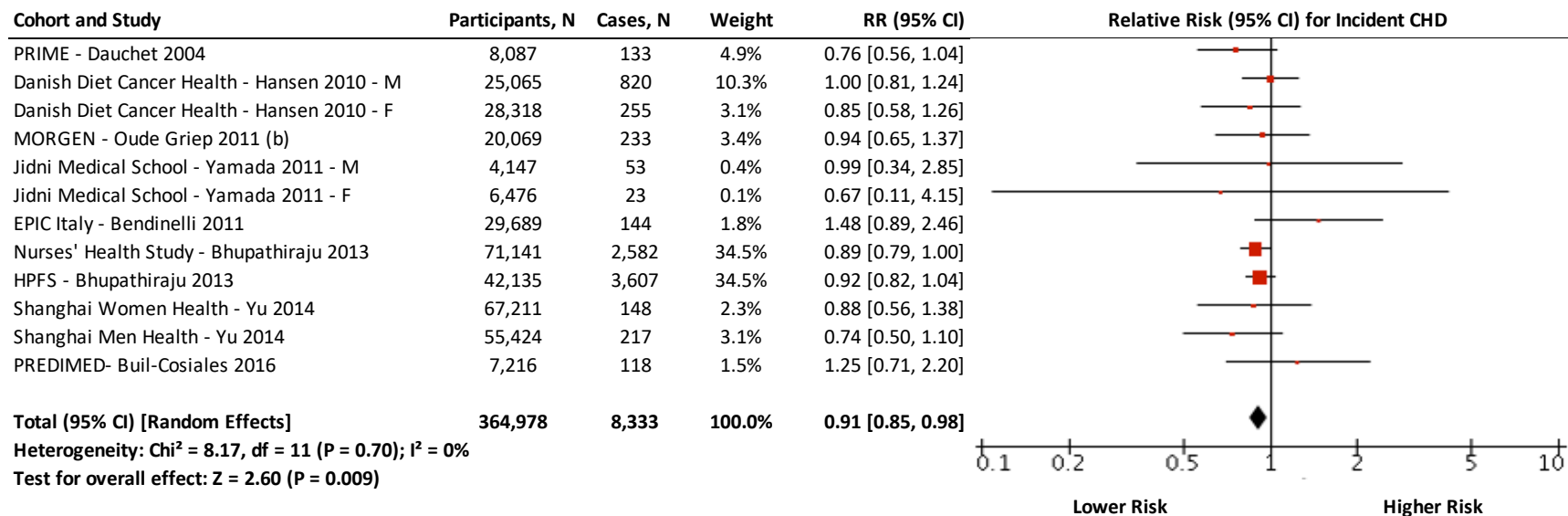
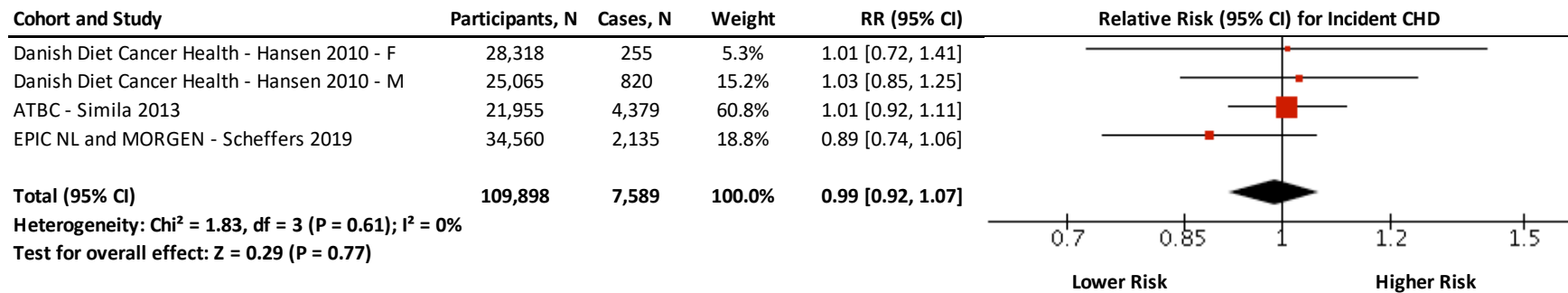


Figure S61. Relation between citrus fruit intake and coronary heart disease incidence (highest vs. lowest level of intake). All results are presented as relative risk (RR) with 95% confidence intervals (95% CI). Pooled risk estimate is represented by the black diamond using (A) fixed effects and (B) random effects models. Inter-study heterogeneity was assessed using the Cochran Q statistic (χ^2) at a significance level of $p < 0.10$, and quantified by I^2 , with values $\geq 50\%$ indicating substantial heterogeneity.

FRUIT JUICE AND CORONARY HEART DISEASE INCIDENCE

A. Fixed Effects



B. Random Effects

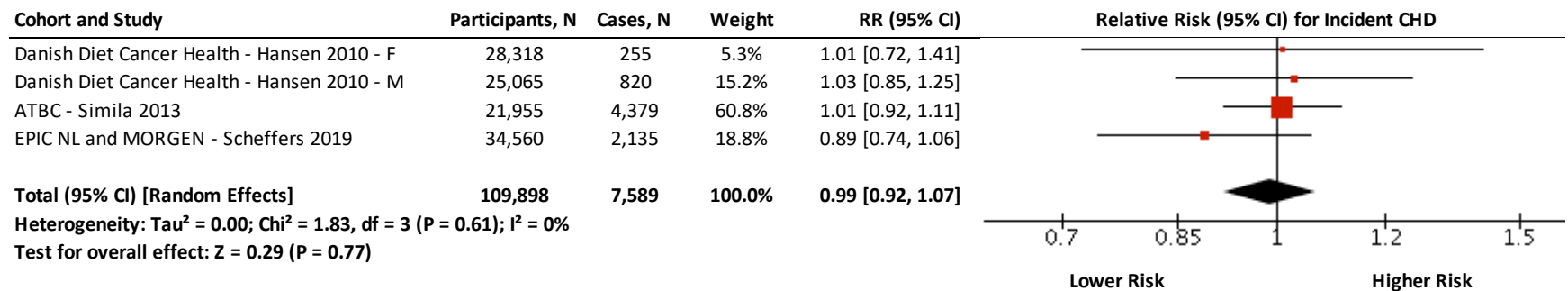


Figure S62. Relation between intake of fruit juice and coronary heart disease incidence (highest vs. lowest level of intake). All results are presented as relative risk (RR) with 95% confidence intervals (95% CI). Pooled risk estimate is represented by the black diamond using (A) fixed effects and (B) random effects models. Inter-study heterogeneity was assessed using the Cochran Q statistic (χ^2) at a significance level of $p < 0.10$, and quantified by I^2 , with values $\geq 50\%$ indicating substantial heterogeneity.

GRAPES AND CORONARY HEART DISEASE INCIDENCE

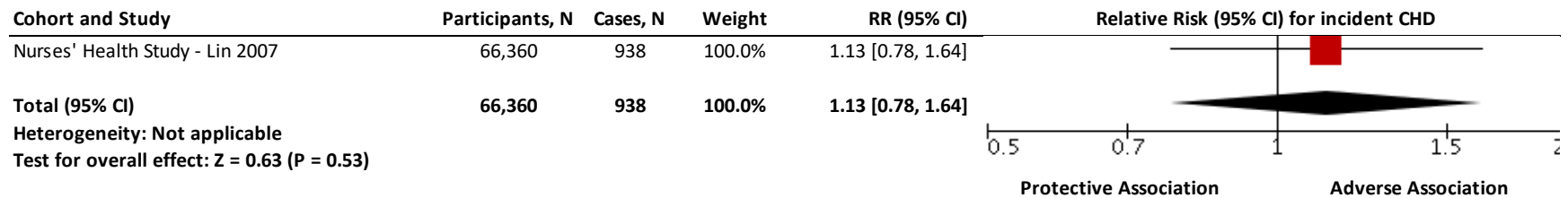
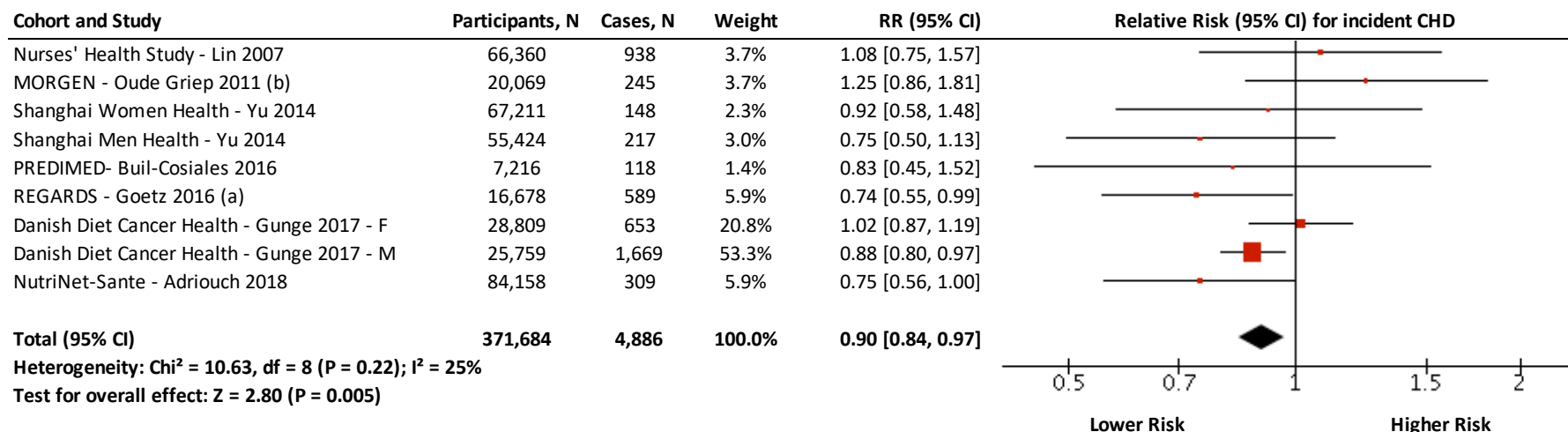


Figure S63. Relation between intake of grapes and coronary heart disease incidence (highest vs. lowest level of intake). All results are presented as relative risk (RR) with 95% confidence intervals (95% CI). Pooled risk estimate is represented by the black diamond. Inter-study heterogeneity was assessed using the Cochran Q statistic (χ^2) at a significance level of $p < 0.10$, and quantified by I^2 , with values $\geq 50\%$ indicating substantial heterogeneity.

POMMES AND CORONARY HEART DISEASE INCIDENCE

A. Fixed Effects



B. Random Effects

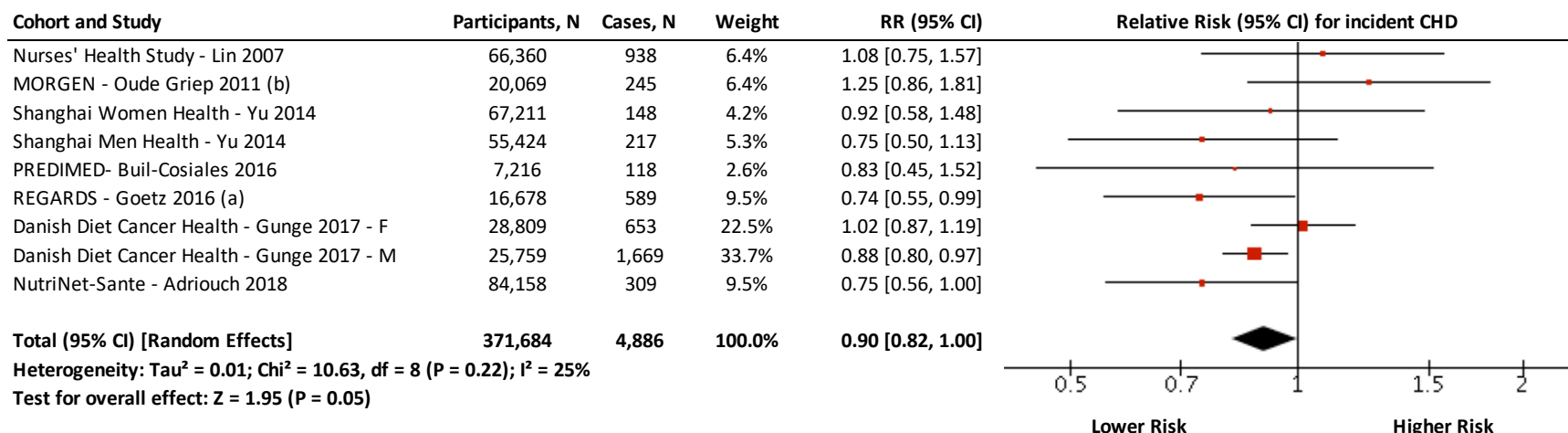
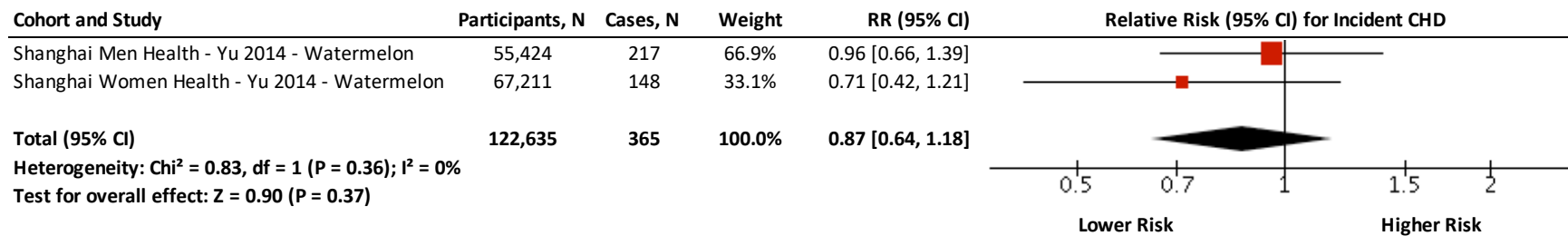


Figure S64. Relation between intake of pomes fruit and coronary heart disease incidence (highest vs. lowest level of intake). All results are presented as relative risk (RR) with 95% confidence intervals (95% CI). Pooled risk estimate is represented by the black diamond using (A) fixed effects and (B) random effects models. Inter-study heterogeneity was assessed using the Cochran Q statistic (Chi²) at a significance level of p<0.10, and quantified by I², with values ≥ 50% indicating substantial heterogeneity.

WATERMELON AND CORONARY HEART DISEASE INCIDENCE

A. Fixed Effects



B. Random Effects

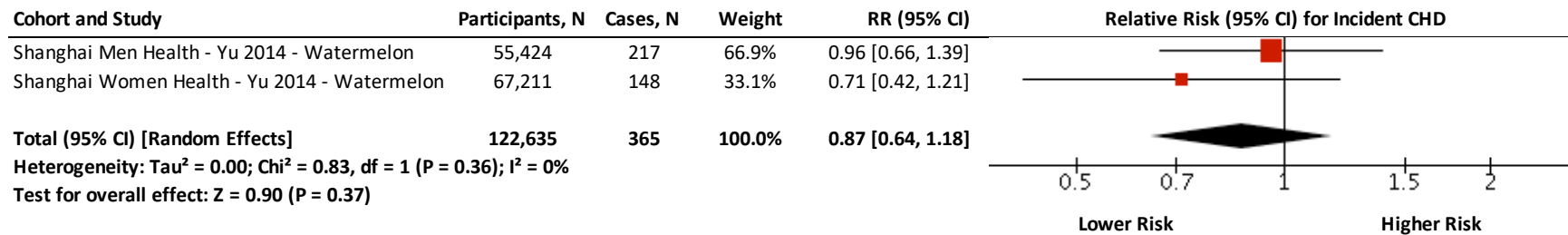
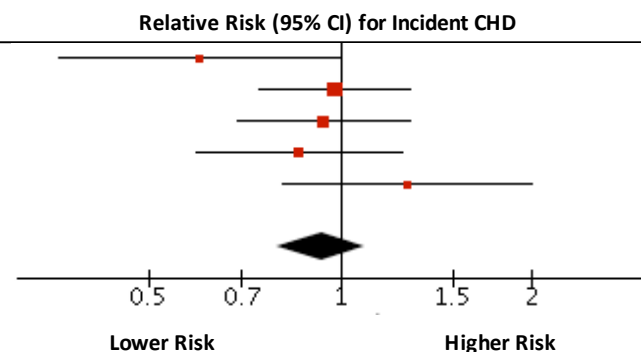


Figure S65. Relation between watermelon intake and coronary heart disease incidence (highest vs. lowest level of intake). All results are presented as relative risk (RR) with 95% confidence intervals (95% CI). Pooled risk estimate is represented by the black diamond using (A) fixed effects and (B) random effects models. Inter-study heterogeneity was assessed using the Cochran Q statistic (χ^2) at a significance level of $p < 0.10$, and quantified by I^2 , with values $\geq 50\%$ indicating substantial heterogeneity.

ALLIUM VEGETABLES AND CORONARY HEART DISEASE INCIDENCE

A. Fixed Effects

Cohort and Study	Participants, N	Cases, N	Weight	RR (95% CI)
Caerphilly Prospective Study - Hertog 1997	1,900	186	9.8%	0.60 [0.36, 1.00]
Nurses' Health Study - Lin 2007	66,360	938	33.7%	0.98 [0.74, 1.29]
MORGEN - Oude Griep 2011 (b)	20,069	245	25.8%	0.94 [0.69, 1.29]
Shanghai Men Health - Yu 2014	55,424	217	18.3%	0.86 [0.59, 1.25]
Shanghai Women Health - Yu 2014	67,211	148	12.5%	1.27 [0.81, 2.00]
Total (95% CI)	210,964	1,734	100.0%	0.93 [0.80, 1.09]
Heterogeneity: $\chi^2 = 4.99$, $df = 4$ ($P = 0.29$); $I^2 = 20\%$				
Test for overall effect: $Z = 0.86$ ($P = 0.39$)				



B. Random Effects

Cohort and Study	Participants, N	Cases, N	Weight	RR (95% CI)
Caerphilly Prospective Study - Hertog 1997	1,900	186	11.3%	0.60 [0.36, 1.00]
Nurses' Health Study - Lin 2007	66,360	938	30.5%	0.98 [0.74, 1.29]
MORGEN - Oude Griep 2011 (b)	20,069	245	25.1%	0.94 [0.69, 1.29]
Shanghai Women Health - Yu 2014	67,211	148	14.0%	1.27 [0.81, 2.00]
Shanghai Men Health - Yu 2014	55,424	217	19.2%	0.86 [0.59, 1.25]
Total (95% CI) [Random Effects]	210,964	1,734	100.0%	0.93 [0.77, 1.11]
Heterogeneity: $\tau^2 = 0.01$; $\chi^2 = 4.99$, $df = 4$ ($P = 0.29$); $I^2 = 20\%$				
Test for overall effect: $Z = 0.80$ ($P = 0.42$)				

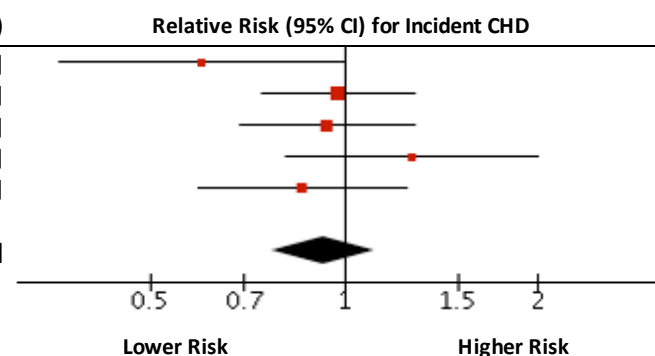


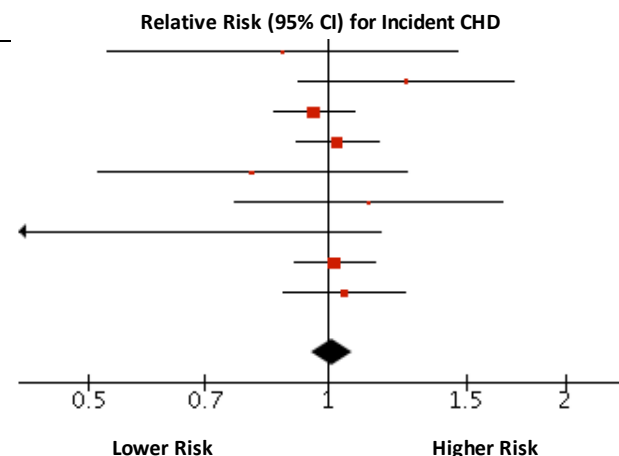
Figure S66. Relation between intake of allium vegetables and coronary heart disease incidence (highest vs. lowest level of intake). All results are presented as relative risk (RR) with 95% confidence intervals (95% CI). Pooled risk estimate is represented by the black diamond using (A) fixed effects and (B) random effects models. Inter-study heterogeneity was assessed using the Cochran Q statistic (χ^2) at a significance level of $p < 0.10$, and quantified by I^2 , with values $\geq 50\%$ indicating substantial heterogeneity.

CRUCIFEROUS VEGETABLES AND CORONARY HEART DISEASE INCIDENCE

A. Fixed Effects

Cohort and Study	Participants, N	Cases, N	Weight	RR (95% CI)
EPIC Italy - Bendinelli 2011	29,689	144	1.4%	0.88 [0.53, 1.46]
MORGEN - Oude Griep 2011(b)-green cabbage ve	20,069	245	3.7%	1.26 [0.92, 1.72]
HPFS - Bhupathiraju 2013	42,135	3,607	26.3%	0.96 [0.85, 1.08]
Nurses' Health Study - Bhupathiraju 2013	71,141	2,582	26.3%	1.03 [0.92, 1.16]
Shanghai Women Health - Yu 2014	67,211	148	1.8%	0.80 [0.51, 1.26]
Shanghai Men Health - Yu 2014	55,424	217	2.4%	1.13 [0.76, 1.67]
PREDIMED- Buil-Cosiales 2016	7,216	118	0.2%	0.32 [0.09, 1.17]
Danish Diet Cancer Health - Gunge 2017 - M	25,759	1,669	26.3%	1.02 [0.91, 1.15]
Danish Diet Cancer Health - Gunge 2017 - F	28,809	653	11.7%	1.05 [0.88, 1.25]
Total (95% CI)	347,453	9,383	100.0%	1.01 [0.95, 1.07]

Heterogeneity: $\text{Chi}^2 = 7.55$, $\text{df} = 8$ ($P = 0.48$); $I^2 = 0\%$
 Test for overall effect: $Z = 0.38$ ($P = 0.71$)



B. Random Effects

Cohort and Study	Participants, N	Cases, N	Weight	RR (95% CI)
MORGEN - Oude Griep 2011(b)-green cabbage ve	20,069	245	3.7%	1.26 [0.92, 1.72]
EPIC Italy - Bendinelli 2011	29,689	144	1.4%	0.88 [0.53, 1.46]
Nurses' Health Study - Bhupathiraju 2013	71,141	2,582	26.3%	1.03 [0.92, 1.16]
HPFS - Bhupathiraju 2013	42,135	3,607	26.3%	0.96 [0.85, 1.08]
Shanghai Men Health - Yu 2014	55,424	217	2.4%	1.13 [0.76, 1.67]
Shanghai Women Health - Yu 2014	67,211	148	1.8%	0.80 [0.51, 1.26]
PREDIMED- Buil-Cosiales 2016	7,216	118	0.2%	0.32 [0.09, 1.17]
Danish Diet Cancer Health - Gunge 2017 - F	28,809	653	11.7%	1.05 [0.88, 1.25]
Danish Diet Cancer Health - Gunge 2017 - M	25,759	1,669	26.3%	1.02 [0.91, 1.15]
Total (95% CI) [Random Effects]	347,453	9,383	100.0%	1.01 [0.95, 1.07]

Heterogeneity: $\text{Tau}^2 = 0.00$; $\text{Chi}^2 = 7.55$, $\text{df} = 8$ ($P = 0.48$); $I^2 = 0\%$
 Test for overall effect: $Z = 0.38$ ($P = 0.71$)

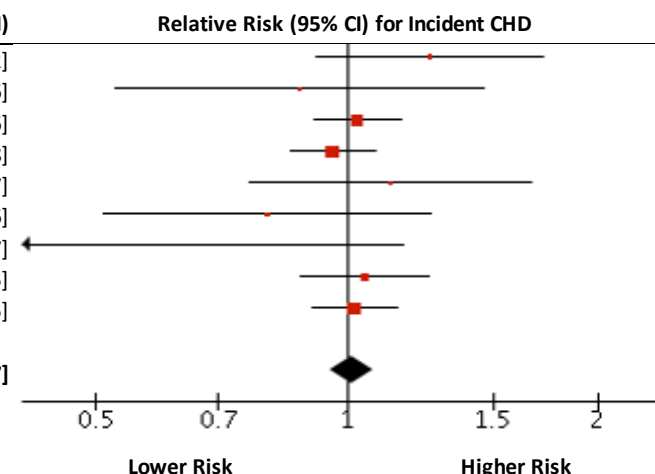
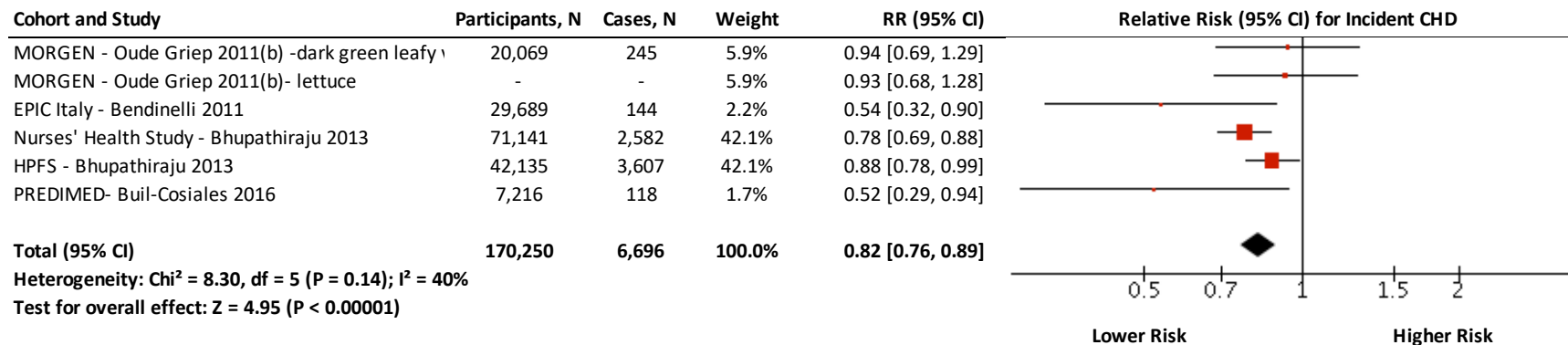


Figure S67. Relation between intake of cruciferous vegetables and coronary heart disease incidence (highest vs. lowest level of intake). All results are presented as relative risk (RR) with 95% confidence intervals (95% CI). Pooled risk estimate is represented by the black diamond using (A) fixed effects and (B) random effects models. Inter-study heterogeneity was assessed using the Cochran Q statistic (Chi^2) at a significance level of $p < 0.10$, and quantified by I^2 , with values $\geq 50\%$ indicating substantial heterogeneity.

GREEN LEAFY VEGETABLES AND CORONARY HEART DISEASE INCIDENCE

A. Fixed Effects



B. Random Effects

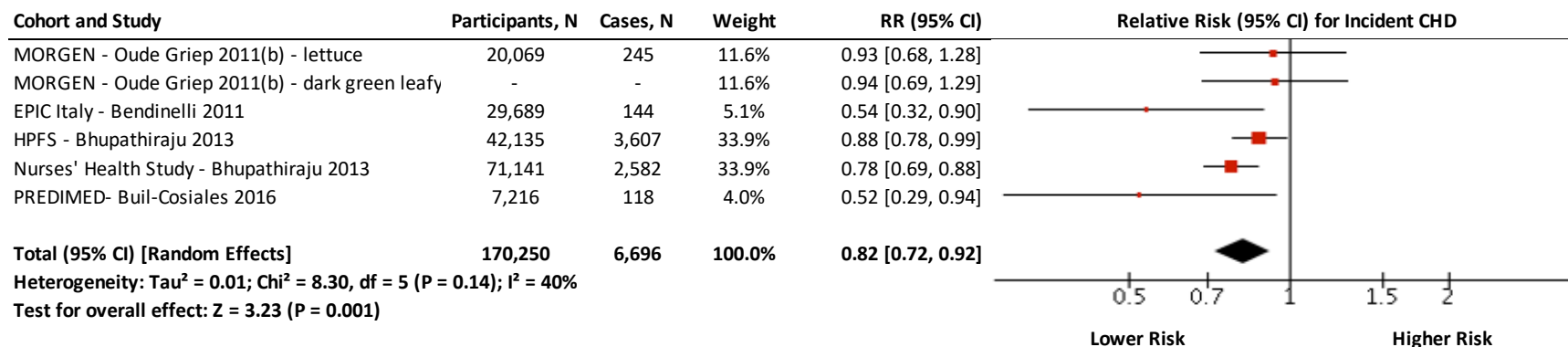
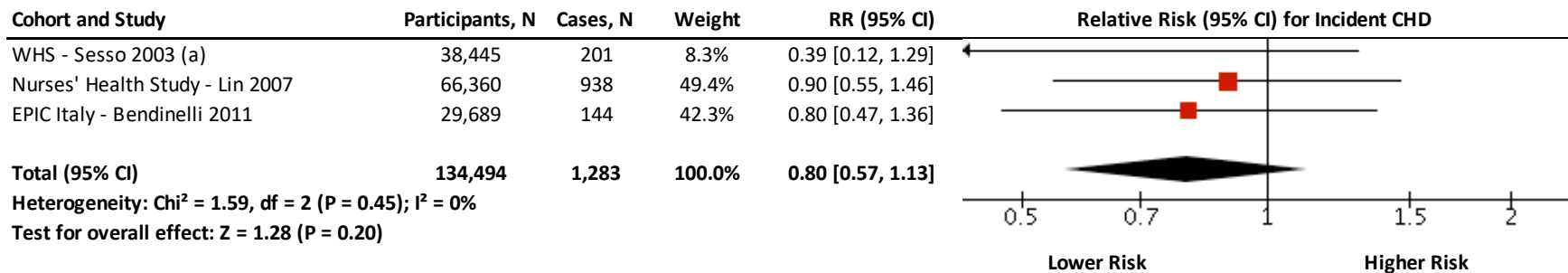


Figure S68. Relation between intake of green leafy vegetables and coronary heart disease incidence (highest vs. lowest level of intake). All results are presented as relative risk (RR) with 95% confidence intervals (95% CI). Pooled risk estimate is represented by the black diamond using (A) fixed effects and (B) random effects models. Inter-study heterogeneity was assessed using the Cochran Q statistic (χ^2) at a significance level of $p < 0.10$, and quantified by I^2 , with values $\geq 50\%$ indicating substantial heterogeneity.

TOMATOES AND CORONARY HEART DISEASE INCIDENCE

A. Fixed Effects



B. Random Effects

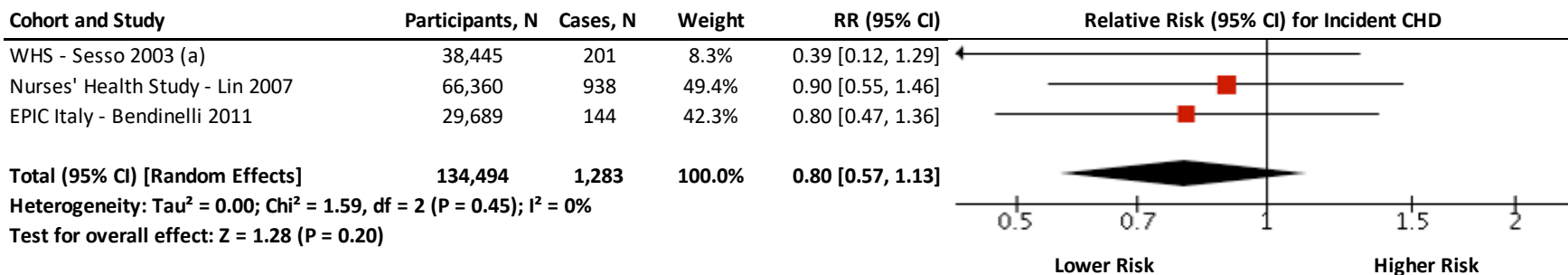
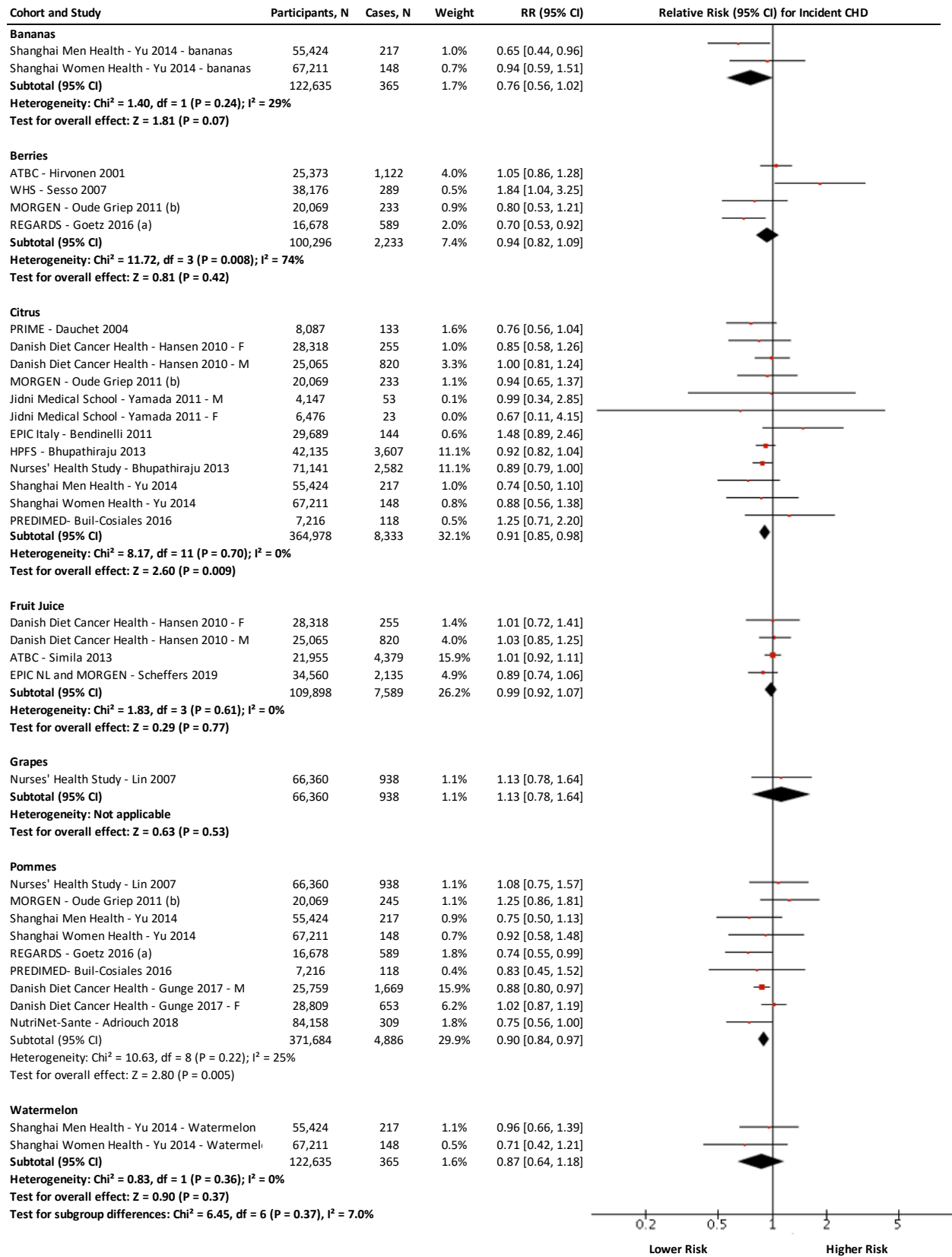


Figure S69. Relation between intake of tomatoes and coronary heart disease incidence (highest vs. lowest level of intake). All results are presented as relative risk (RR) with 95% confidence intervals (95% CI). Pooled risk estimate is represented by the black diamond using (A) fixed effects and (B) random effects models. Inter-study heterogeneity was assessed using the Cochran Q statistic (χ^2) at a significance level of $p < 0.10$, and quantified by I^2 , with values $\geq 50\%$ indicating substantial heterogeneity.

A. Fixed Effects



B. Random Effects

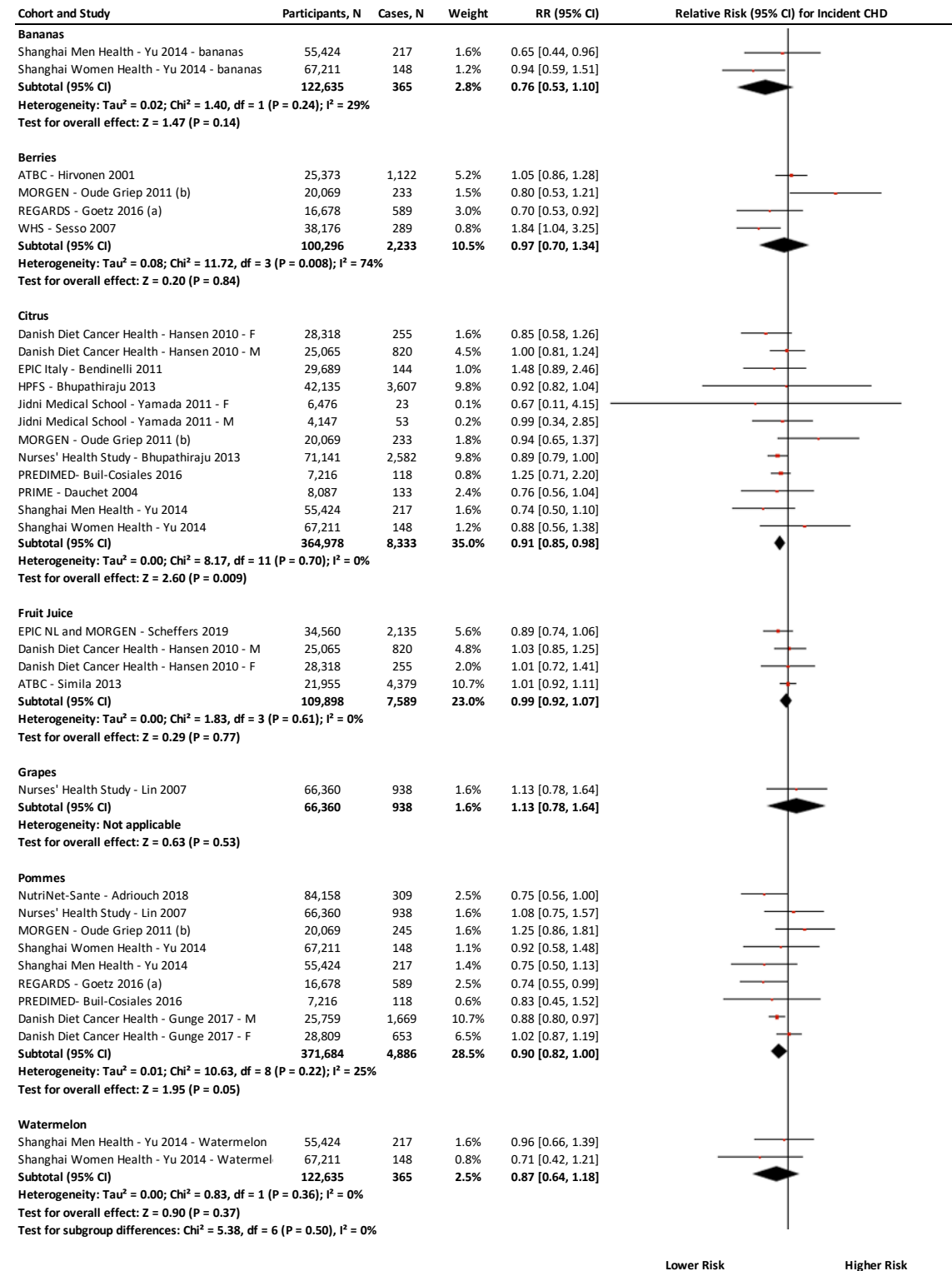
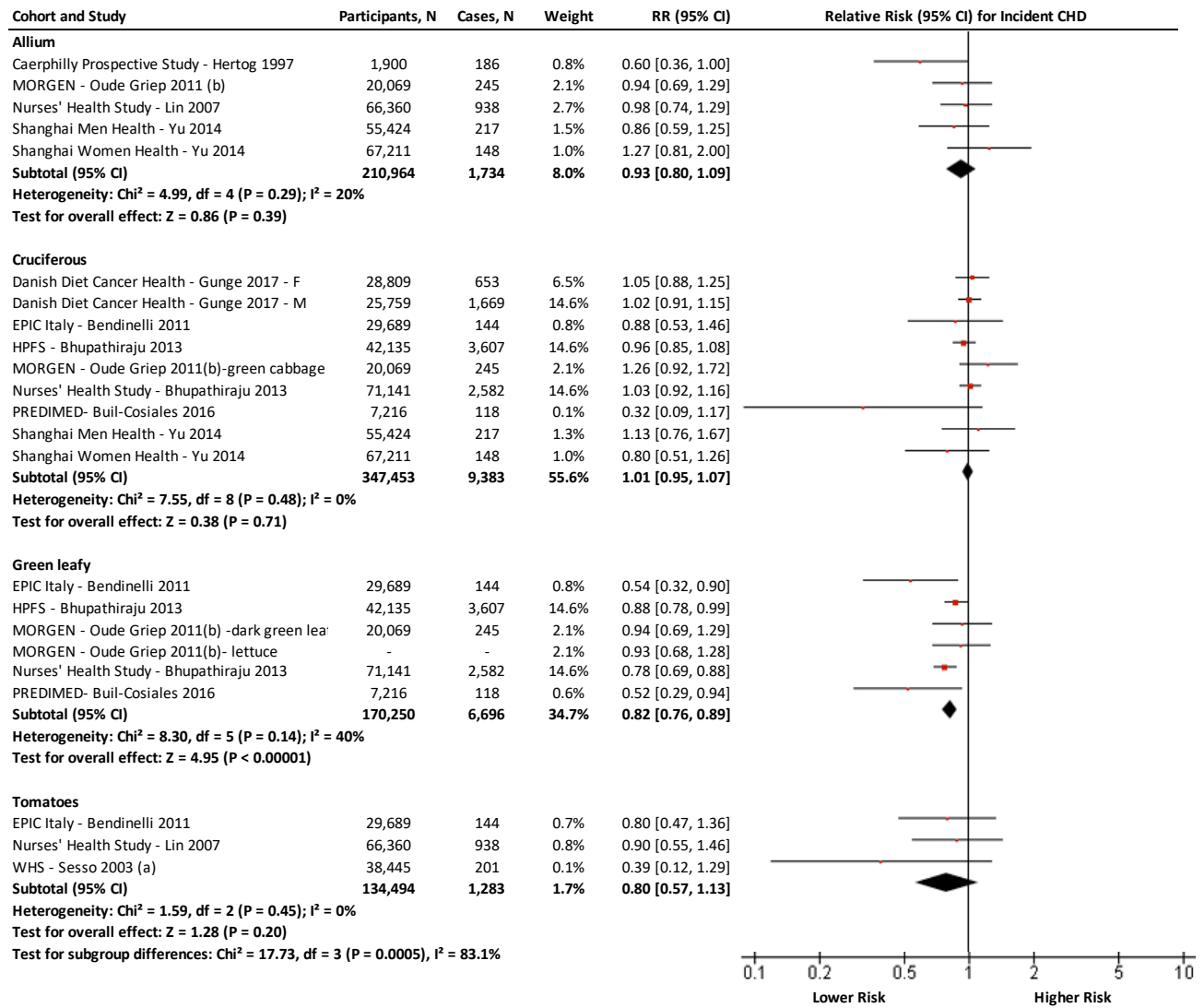


Figure S70. Relation between sources of fruit and CHD incidence (highest vs. lowest level of intake). All results are presented as relative risk (RR) with 95% confidence intervals (95% CI). Pooled risk estimate is represented by the black diamond using (A) fixed effects and (B) random effects models. Inter-study heterogeneity was assessed using the Cochran Q statistic (χ^2) at a significance level of $p < 0.10$, and quantified by I^2 , with values $\geq 50\%$ indicating substantial heterogeneity

A. Fixed Effects



B. Random Effects

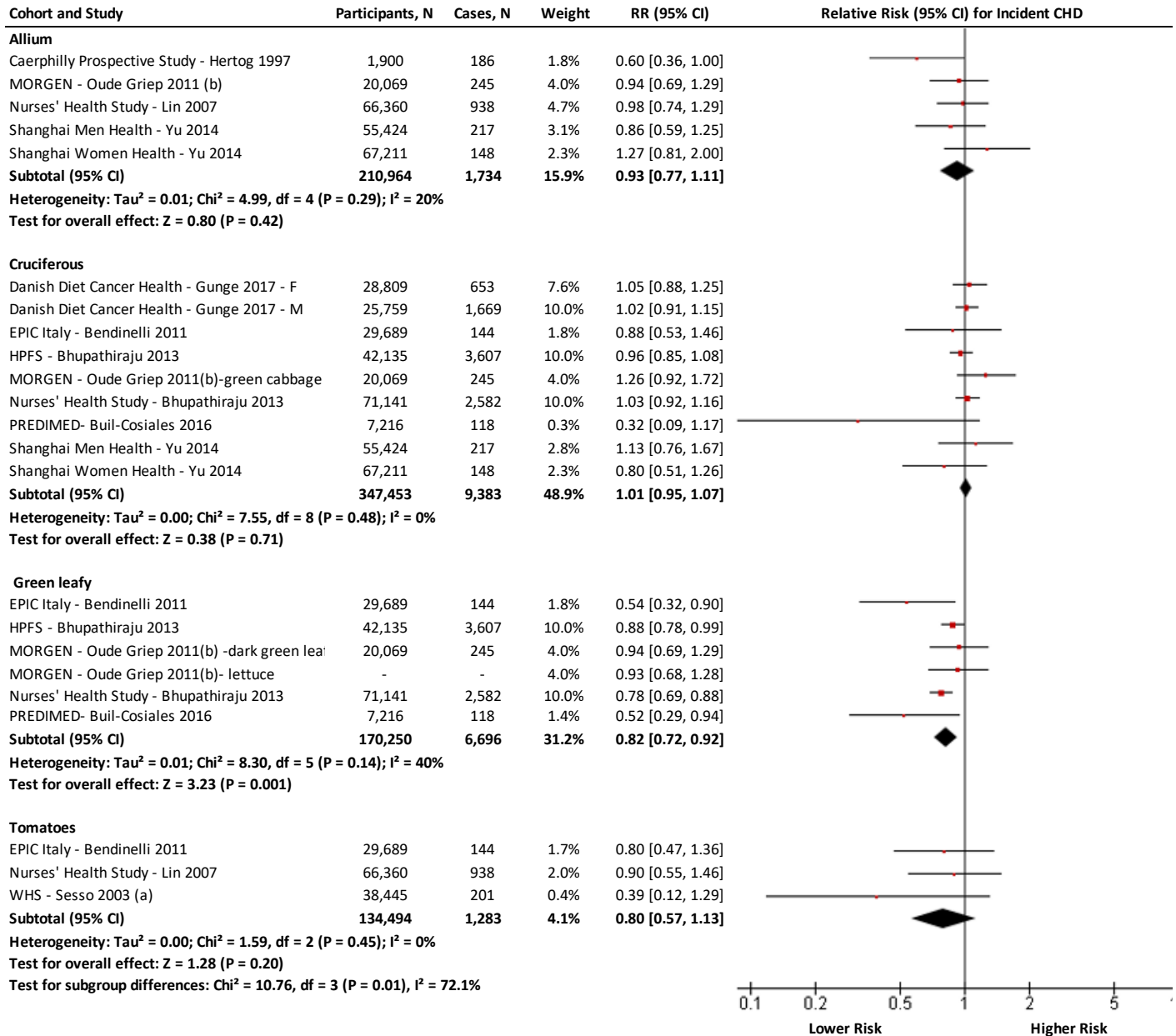
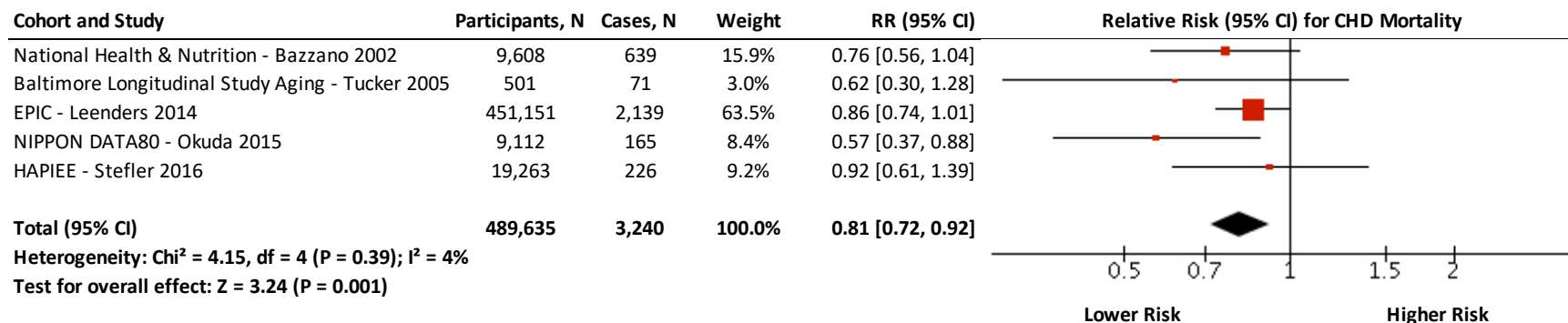


Figure S71. Relation between sources of vegetables and CHD incidence (highest vs. lowest level of intake). All results are presented as relative risk (RR) with 95% confidence intervals (95% CI). Pooled risk estimate is represented by the black diamond using (A) fixed effects and (B) random effects models. Inter-study heterogeneity was assessed using the Cochran Q statistic (Chi²) at a significance level of p<0.10, and quantified by I², with values ≥ 50% indicating substantial heterogeneity.

TOTAL FRUIT AND VEGETABLES AND CORONARY HEART DISEASE MORTALITY

A. Fixed Effects



B. Random Effects

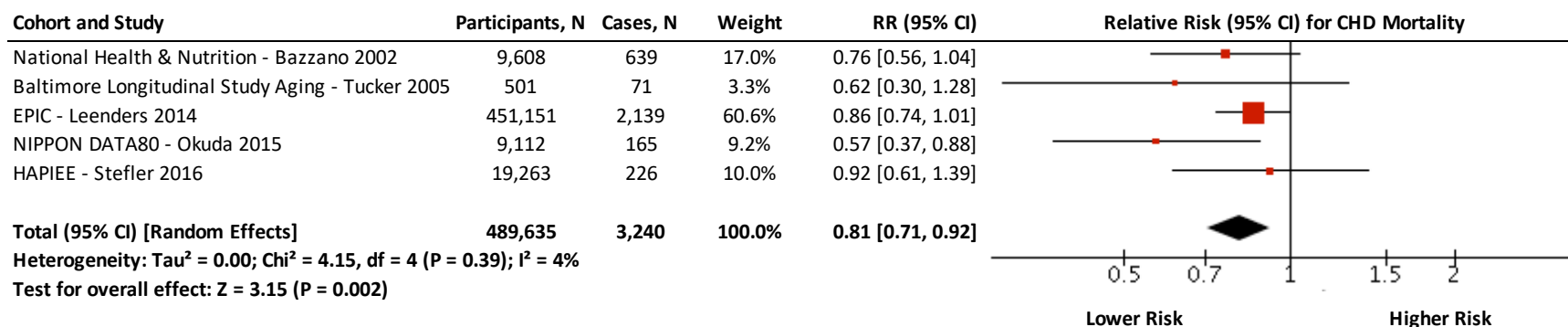
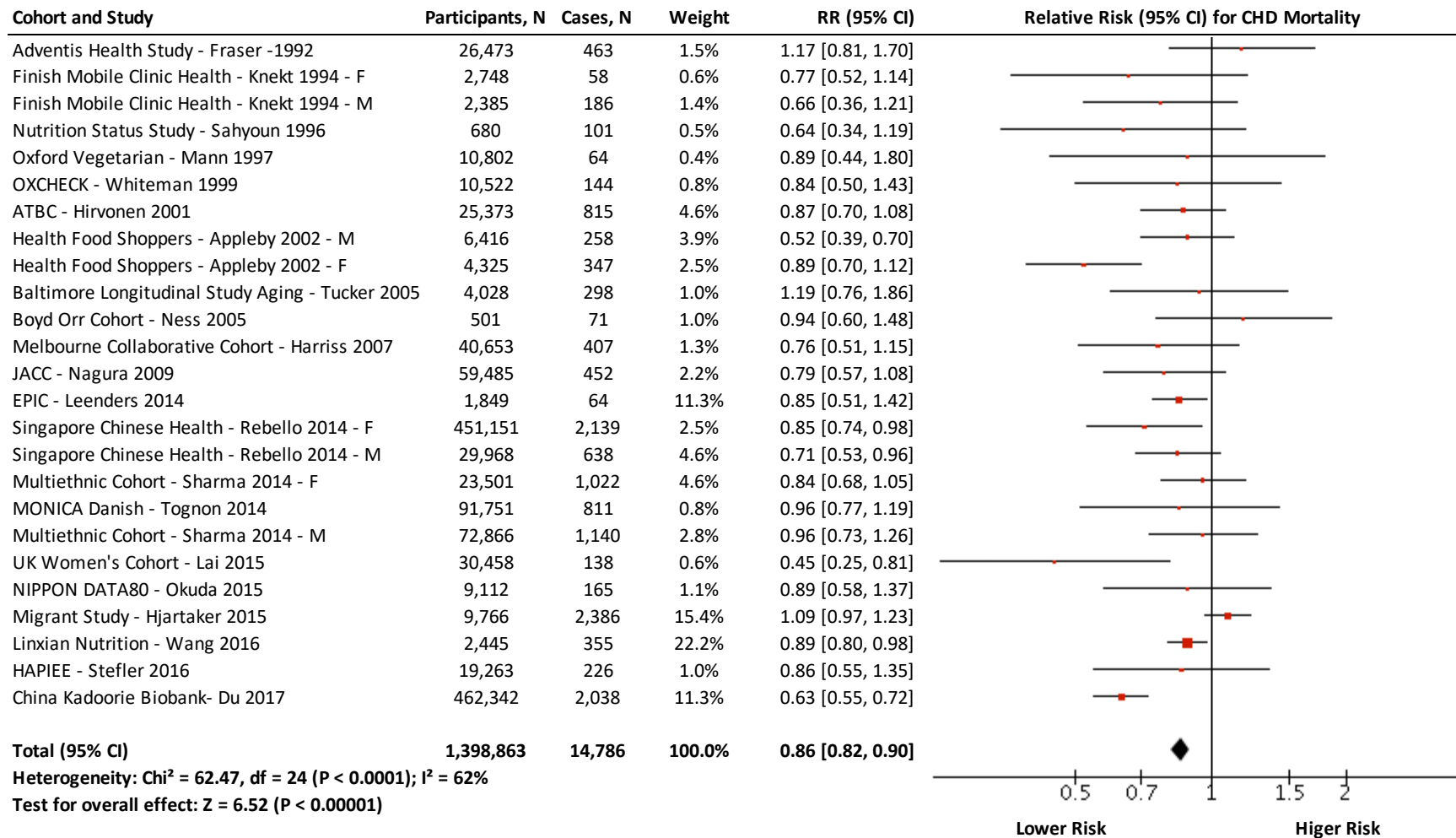


Figure S72. Relation between total fruit and vegetable intake and coronary heart disease mortality (highest vs. lowest level of intake). All results are presented as relative risk (RR) with 95% confidence intervals (95% CI). Pooled risk estimate is represented by the black diamond using (A) fixed effects and (B) random effects models. Inter-study heterogeneity was assessed using the Cochran Q statistic (χ^2) at a significance level of $p < 0.10$, and quantified by I^2 , with values $\geq 50\%$ indicating substantial heterogeneity.

FRUIT AND CORONARY HEART DISEASE MORTALITY

A. Fixed Effects



B. Random Effects

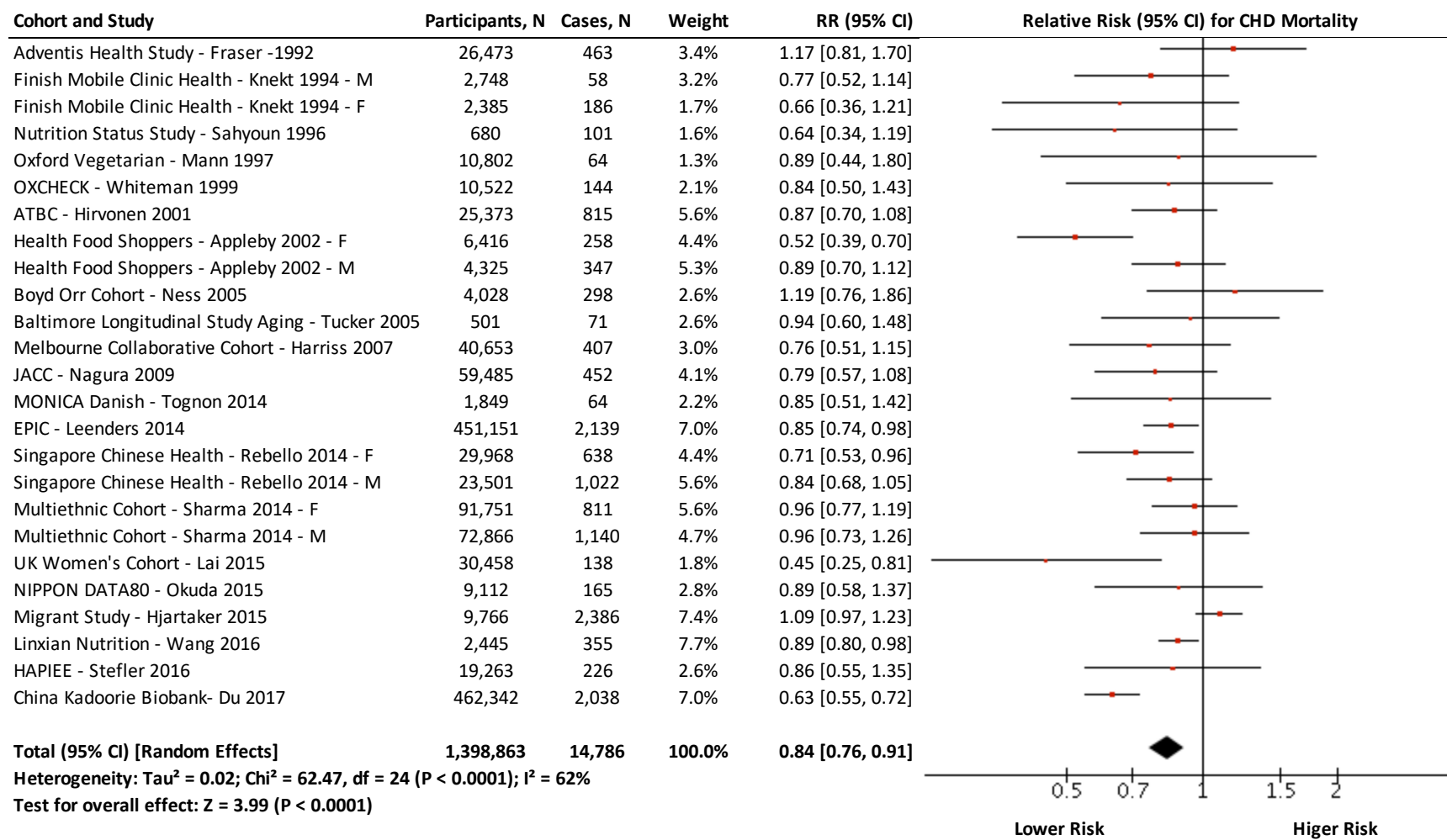
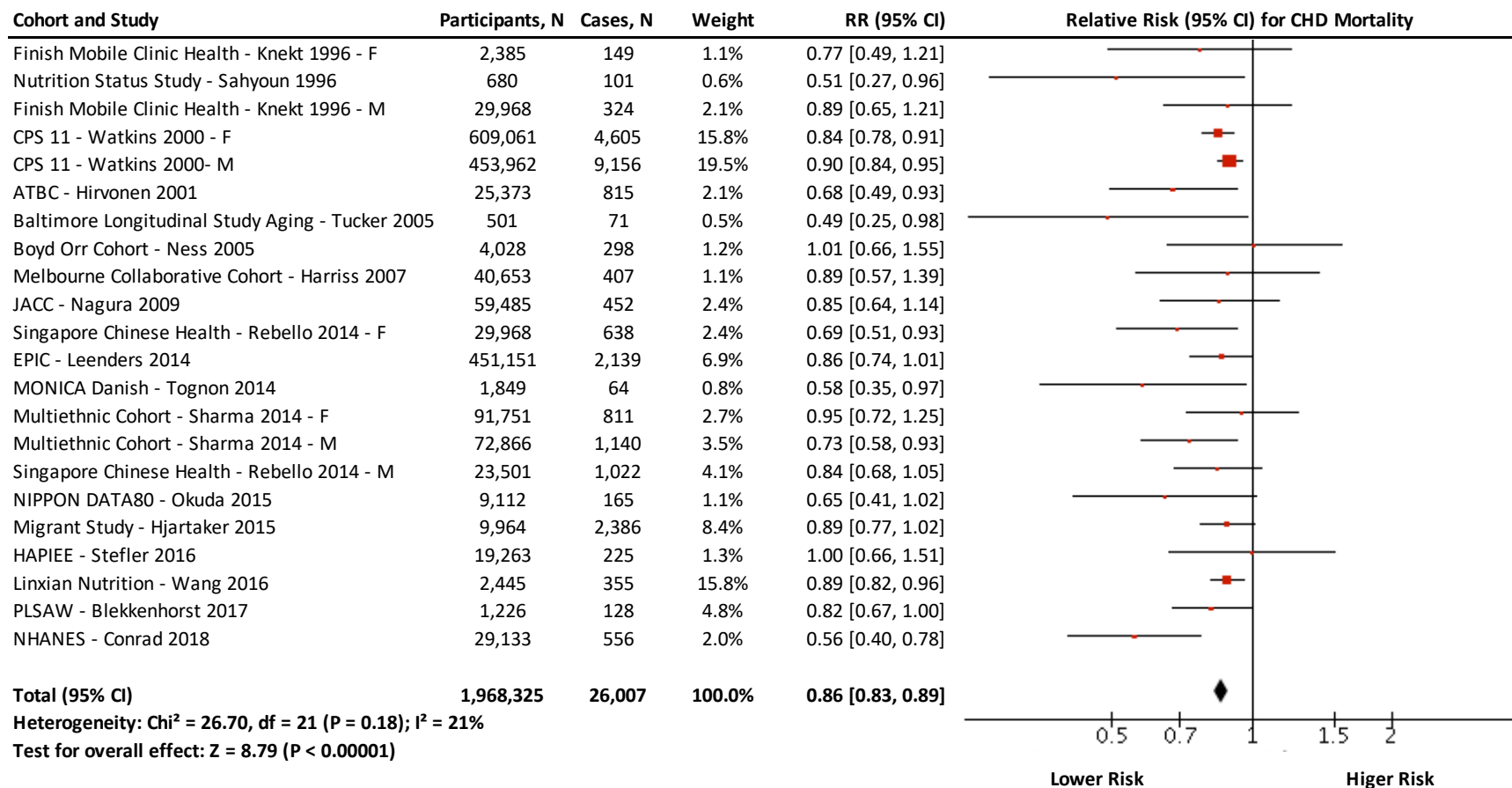


Figure S73. Relation between fruit intake and coronary heart disease mortality (highest vs. lowest level of intake). All results are presented as relative risk (RR) with 95% confidence intervals (95% CI). Pooled risk estimate is represented by the black diamond using (A) fixed effects and (B) random effects models. Inter-study heterogeneity was assessed using the Cochran Q statistic (Chi²) at a significance level of p<0.10, and quantified by I², with values ≥ 50% indicating substantial heterogeneity.

VEGETABLES AND CORONARY HEART DISEASE MORTALITY

A. Fixed Effects



B. Random Effects

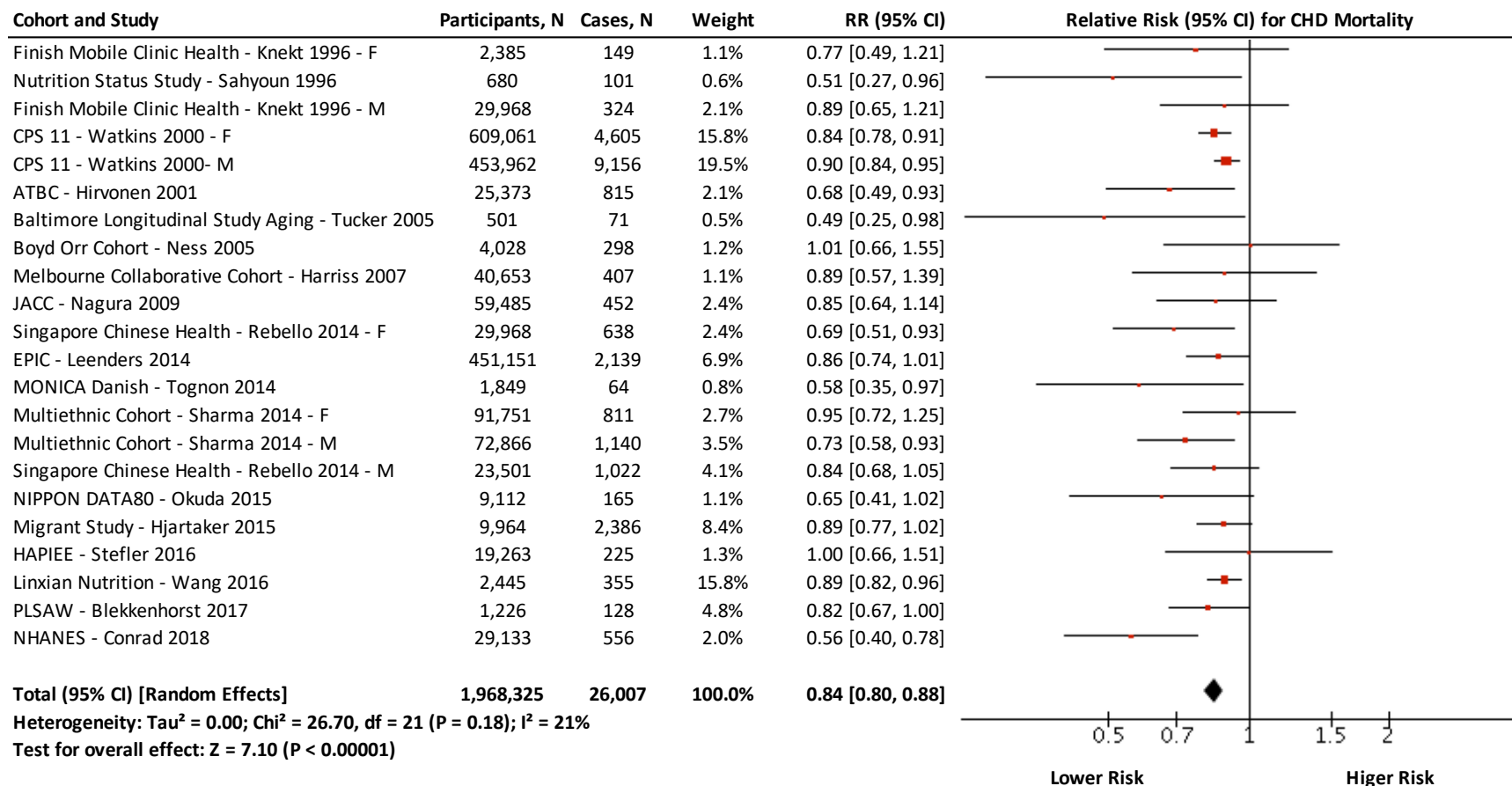


Figure S74. Relation between intake of vegetables and coronary heart disease mortality (highest vs. lowest level of intake). All results are presented as relative risk (RR) with 95% confidence intervals (95% CI). Pooled risk estimate is represented by the black diamond using (A) fixed effects and (B) random effects models. Inter-study heterogeneity was assessed using the Cochran Q statistic (χ^2) at a significance level of $p < 0.10$, and quantified by I^2 , with values $\geq 50\%$ indicating substantial heterogeneity.

BANANAS AND CORONARY HEART DISEASE MORTALITY

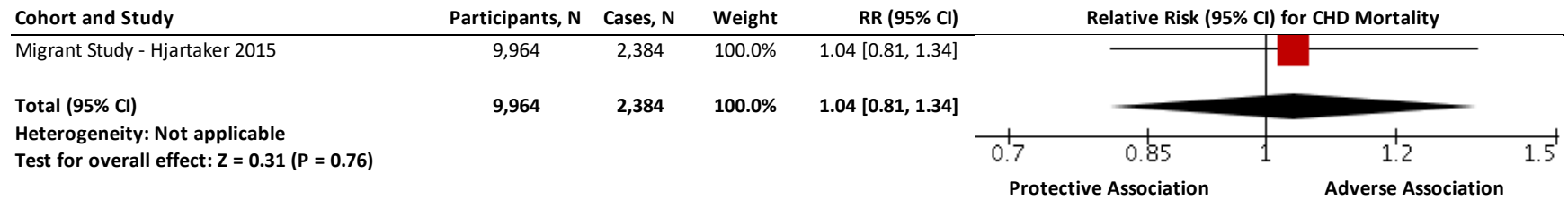
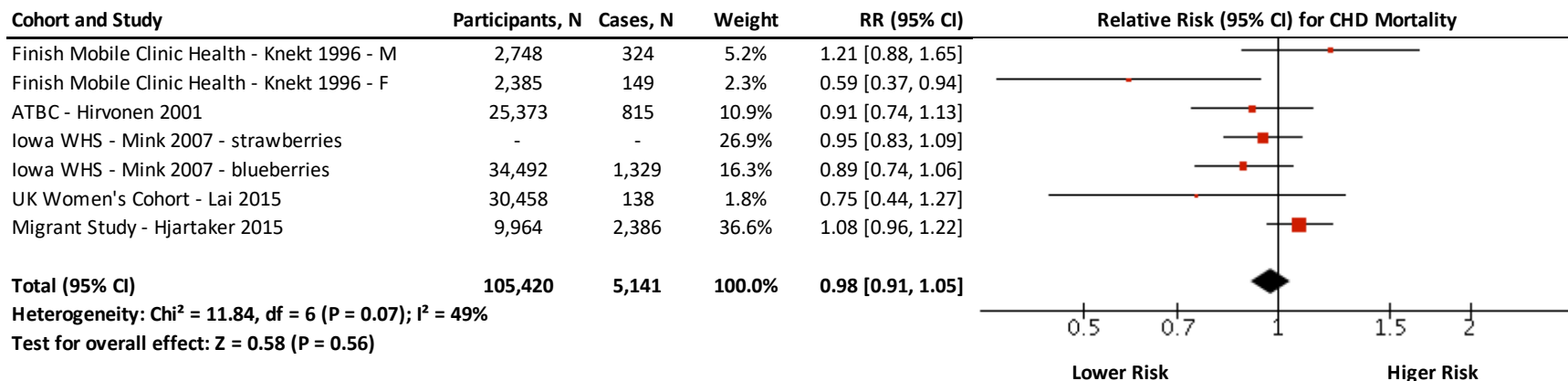


Figure S75. Relation between intake of bananas and coronary heart disease mortality (highest vs. lowest level of intake). All results are presented as relative risk (RR) with 95% confidence intervals (95% CI). Pooled risk estimate is represented by the black diamond. Inter-study heterogeneity was assessed using the Cochran Q statistic (χ^2) at a significance level of $p < 0.10$, and quantified by I^2 , with values $\geq 50\%$ indicating substantial heterogeneity.

BERRIES AND CORONARY HEART DISEASE MORTALITY

A. Fixed Effects



B. Random Effects

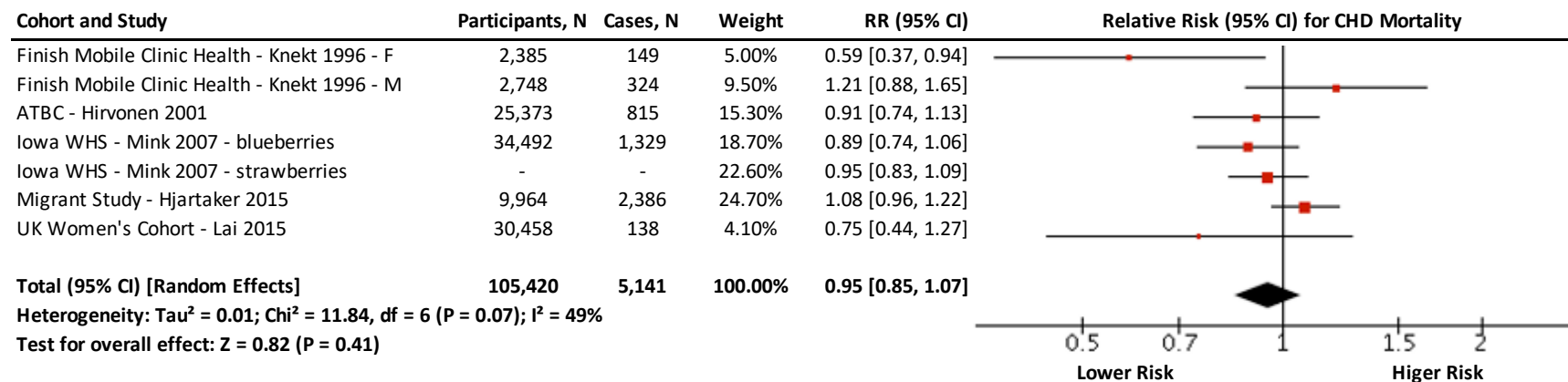
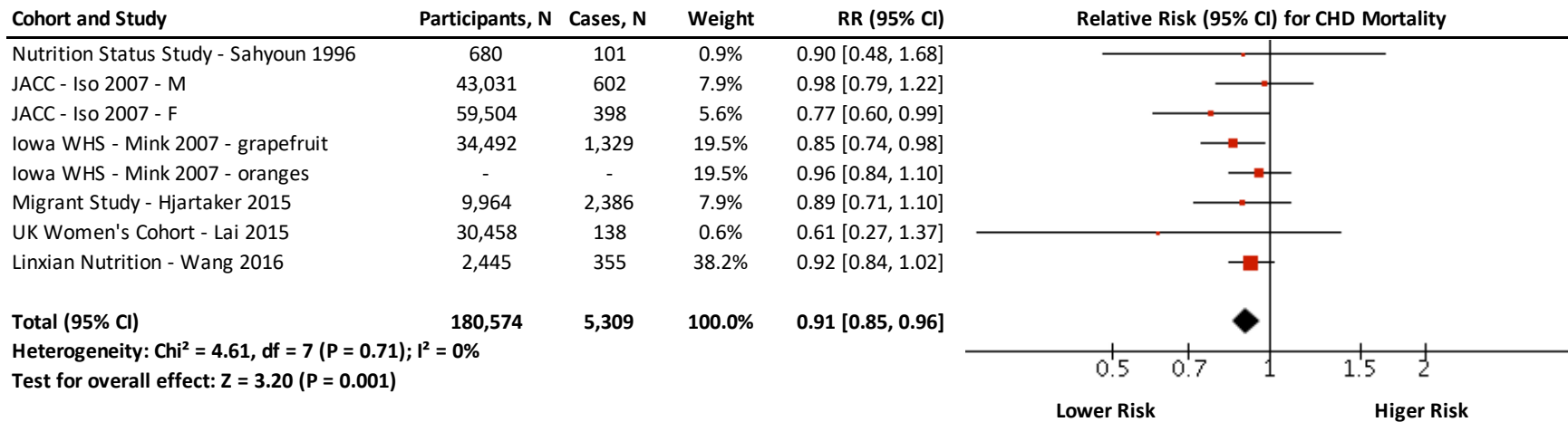


Figure S76. Relation between intake of berries and coronary heart disease mortality (highest vs. lowest level of intake). All results are presented as relative risk (RR) with 95% confidence intervals (95% CI). Pooled risk estimate is represented by the black diamond using (A) fixed effects and (B) random effects models. Inter-study heterogeneity was assessed using the Cochran Q statistic (χ^2) at a significance level of $p < 0.10$, and quantified by I^2 , with values $\geq 50\%$ indicating substantial heterogeneity.

CITRUS FRUIT AND CORONARY HEART DISEASE MORTALITY

A. Fixed Effects



B. Random Effects

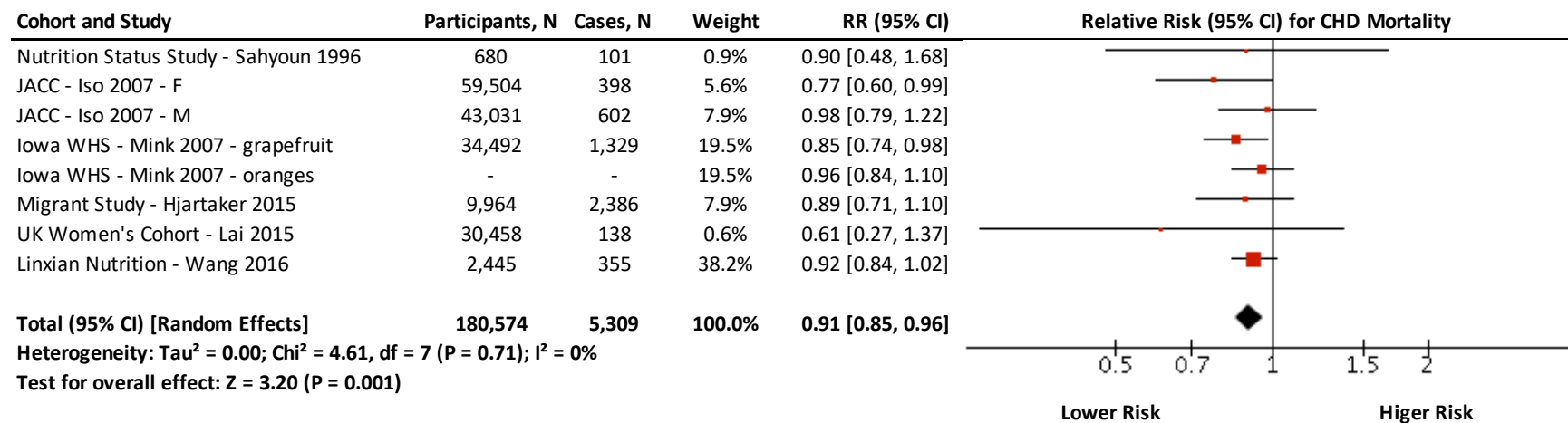


Figure S77. Relation between citrus fruit intake and coronary heart disease mortality (highest vs. lowest level of intake). All results are presented as relative risk (RR) with 95% confidence intervals (95% CI). Pooled risk estimate is represented by the black diamond using (A) fixed effects and (B) random effects models. Inter-study heterogeneity was assessed using the Cochran Q statistic (χ^2) at a significance level of $p < 0.10$, and quantified by I^2 , with values $\geq 50\%$ indicating substantial heterogeneity.

DRIED FRUIT AND CORONARY HEART DISEASE MORTALITY

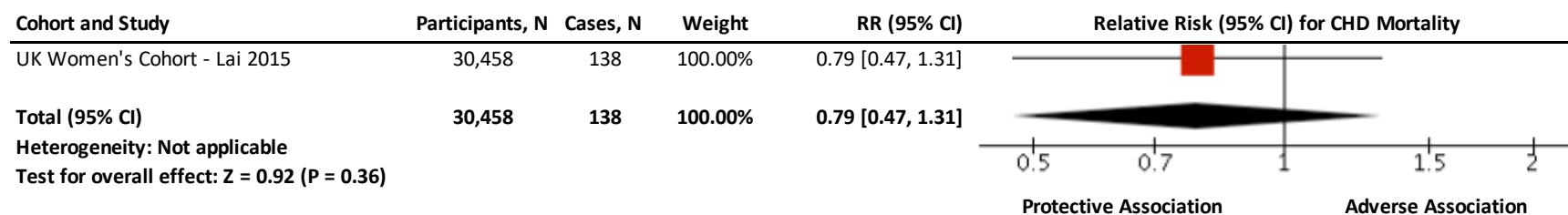
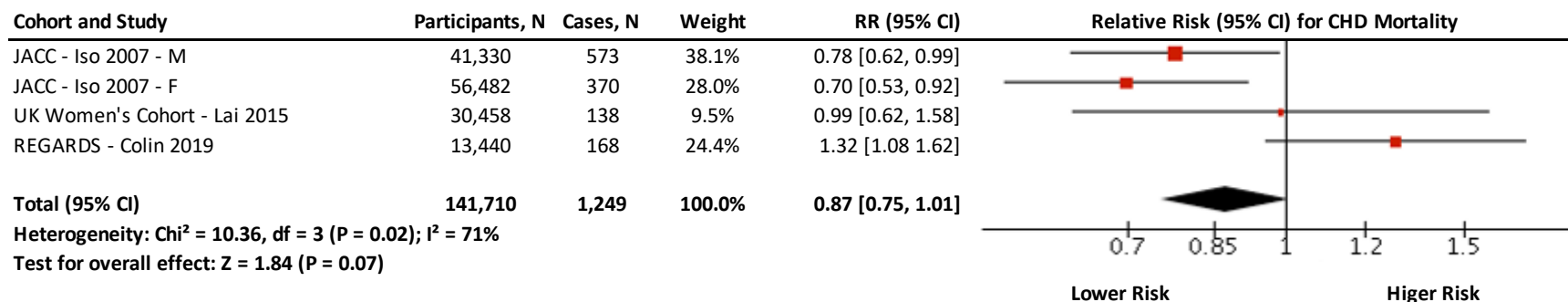


Figure S78. Relation between dried fruit intake and coronary heart disease mortality (highest vs. lowest level of intake). All results are presented as relative risk (RR) with 95% confidence intervals (95% CI). Pooled risk estimate is represented by the black diamond. Inter-study heterogeneity was assessed using the Cochran Q statistic (χ^2) at a significance level of $p < 0.10$, and quantified by I^2 , with values $\geq 50\%$ indicating substantial heterogeneity.

FRUIT JUICE AND CORONARY HEART DISEASE MORTALITY

A. Fixed Effects



B. Random Effects

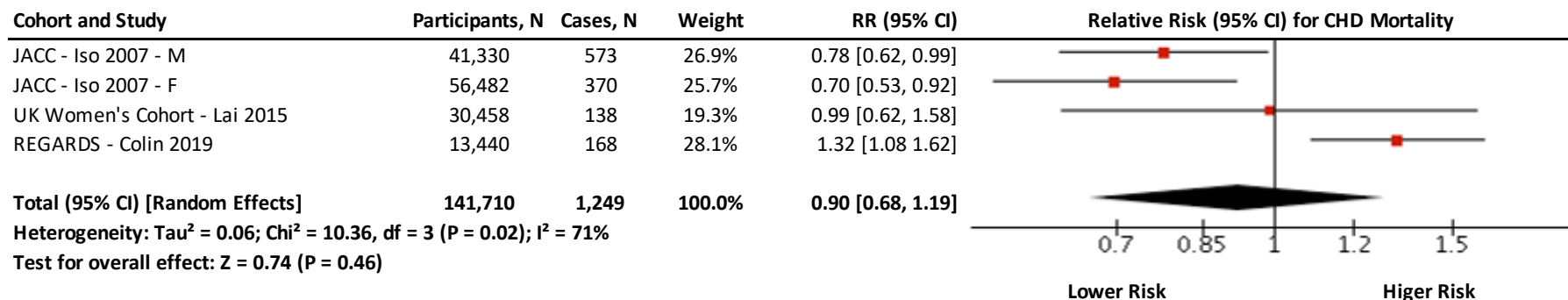
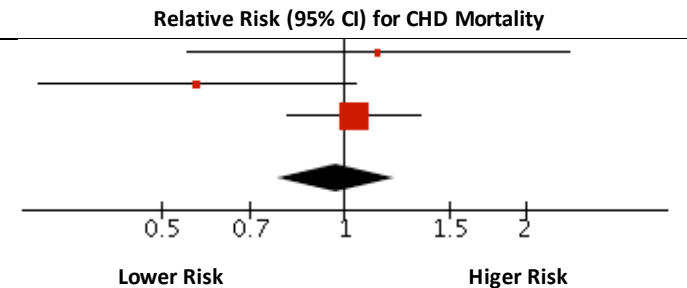


Figure S79. Relation between intake of fruit juice and coronary heart disease mortality (highest vs. lowest level of intake). All results are presented as relative risk (RR) with 95% confidence intervals (95% CI). Pooled risk estimate is represented by the black diamond using (A) fixed effects and (B) random effects models. Inter-study heterogeneity was assessed using the Cochran Q statistic (χ^2) at a significance level of $p < 0.10$, and quantified by I^2 , with values $\geq 50\%$ indicating substantial heterogeneity.

GRAPES AND CORONARY HEART DISEASE MORTALITY

A. Fixed Effects

Cohort and Study	Participants, N	Cases, N	Weight	RR (95% CI)
Nurses' Health Study - Lin 2007	66,360	324	9.5%	1.14 [0.55, 2.35]
UK Women's Cohort - Lai 2015 - grapes	30,458	138	13.5%	0.57 [0.31, 1.05]
Migrant Study - Hjartaker 2015	9,964	2,384	77.0%	1.04 [0.81, 1.34]
Total (95% CI)	106,782	2,846	100.0%	0.97 [0.77, 1.21]
Heterogeneity: $\chi^2 = 3.40$, $df = 2$ ($P = 0.18$); $I^2 = 41\%$				
Test for overall effect: $Z = 0.29$ ($P = 0.77$)				



B. Random Effects

Cohort and Study	Participants, N	Cases, N	Weight	RR (95% CI)
Nurses' Health Study - Lin 2007	66,360	324	19.5%	1.14 [0.55, 2.35]
UK Women's Cohort - Lai 2015 - grapes	30,458	138	25.0%	0.57 [0.31, 1.05]
Migrant Study - Hjartaker 2015	9,964	2,384	55.5%	1.04 [0.81, 1.34]
Total (95% CI) [Random Effects]	106,782	2,846	100.0%	0.91 [0.63, 1.32]
Heterogeneity: $\tau^2 = 0.05$; $\chi^2 = 3.40$, $df = 2$ ($P = 0.18$); $I^2 = 41\%$				
Test for overall effect: $Z = 0.49$ ($P = 0.63$)				

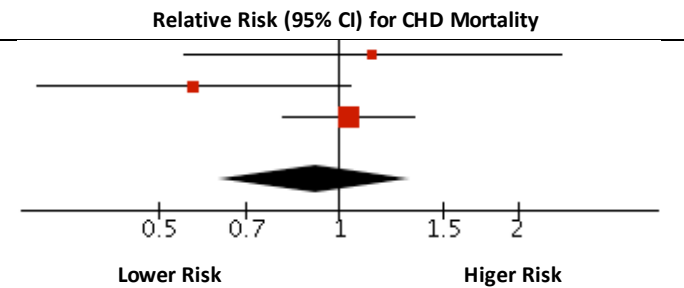
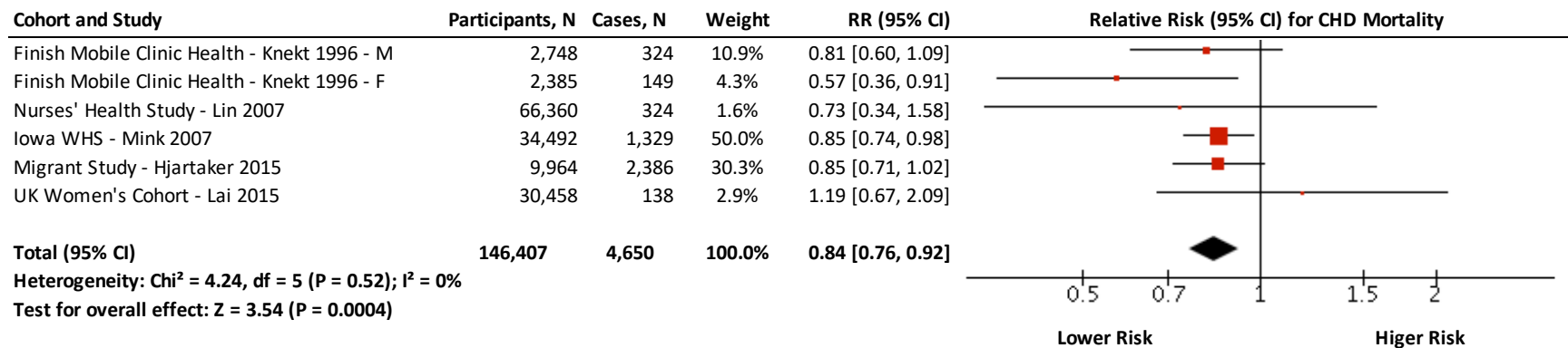


Figure S80. Relation between intake of grapes and coronary heart disease mortality (highest vs. lowest level of intake). All results are presented as relative risk (RR) with 95% confidence intervals (95% CI). Pooled risk estimate is represented by the black diamond using (A) fixed effects and (B) random effects models. Inter-study heterogeneity was assessed using the Cochran Q statistic (χ^2) at a significance level of $p < 0.10$, and quantified by I^2 , with values $\geq 50\%$ indicating substantial heterogeneity.

POMMES AND CORONARY HEART DISEASE MORTALITY

A. Fixed Effects



B. Random Effects

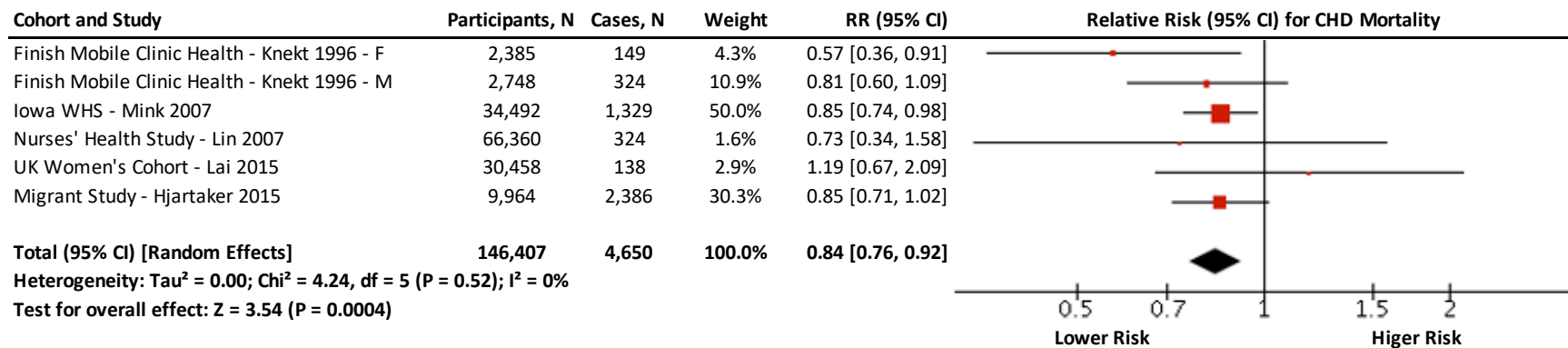
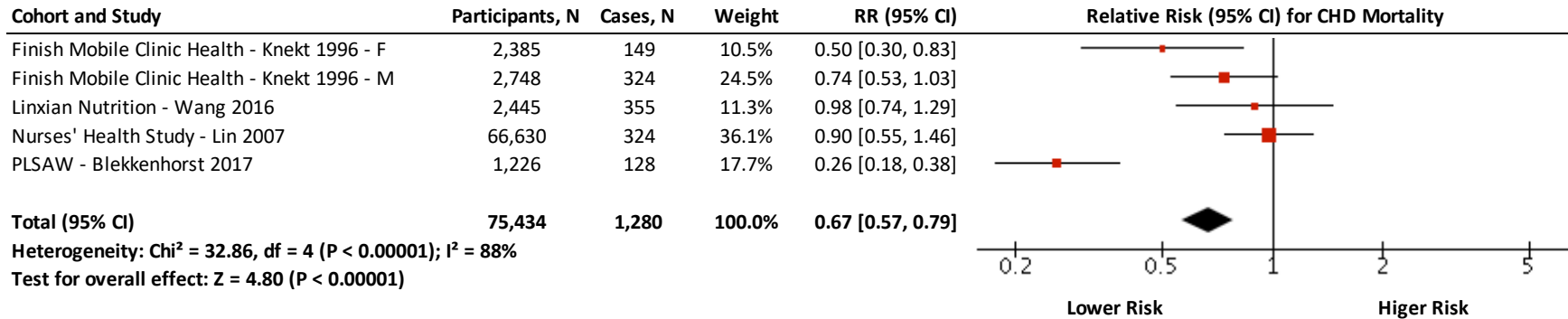


Figure S81. Relation between pomes fruit intake and coronary heart disease mortality (highest vs. lowest level of intake). All results are presented as relative risk (RR) with 95% confidence intervals (95% CI). Pooled risk estimate is represented by the black diamond using (A) fixed effects and (B) random effects models. Inter-study heterogeneity was assessed using the Cochran Q statistic (Chi^2) at a significance level of $p < 0.10$, and quantified by I^2 , with values $\geq 50\%$ indicating substantial heterogeneity.

ALLIUM VEGETABLES AND CORONARY HEART DISEASE MORTALITY

A. Fixed Effects



B. Random Effects

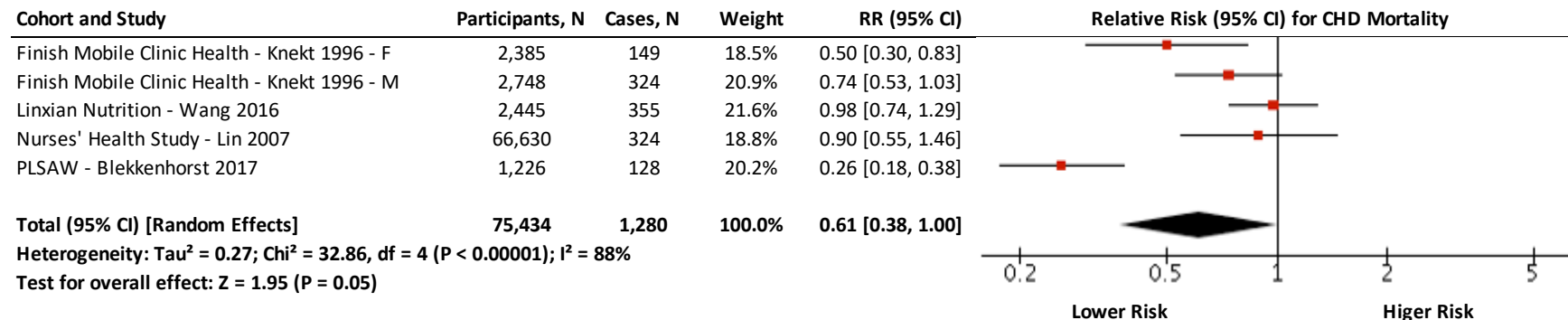
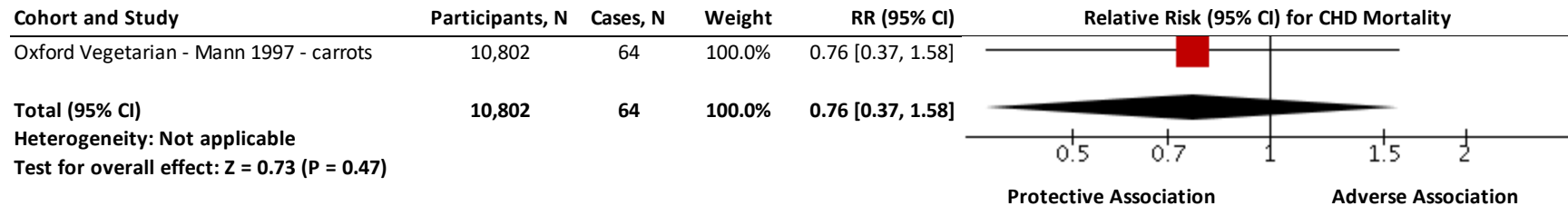


Figure S82. Relation between intake of allium vegetables and coronary heart disease mortality (highest vs. lowest level of intake). All results are presented as relative risk (RR) with 95% confidence intervals (95% CI). Pooled risk estimate is represented by the black diamond using (A) fixed effects and (B) random effects models. Inter-study heterogeneity was assessed using the Cochran Q statistic (χ^2) at a significance level of $p < 0.10$, and quantified by I^2 , with values $\geq 50\%$ indicating substantial heterogeneity.

CARROTS AND CORONARY HEART DISEASE MORTALITY



Supplementary Figure 83. Relation between intake of carrots and coronary heart disease mortality (highest vs. lowest level of intake). All results are presented as relative risk (RR) with 95% confidence intervals (95% CI). Pooled risk estimate is represented by the black diamond. Inter-study heterogeneity was assessed using the Cochran Q statistic (χ^2) at a significance level of $p < 0.10$, and quantified by I^2 , with values $\geq 50\%$ indicating substantial heterogeneity.

CELERY AND CORONARY HEART DISEASE MORTALITY

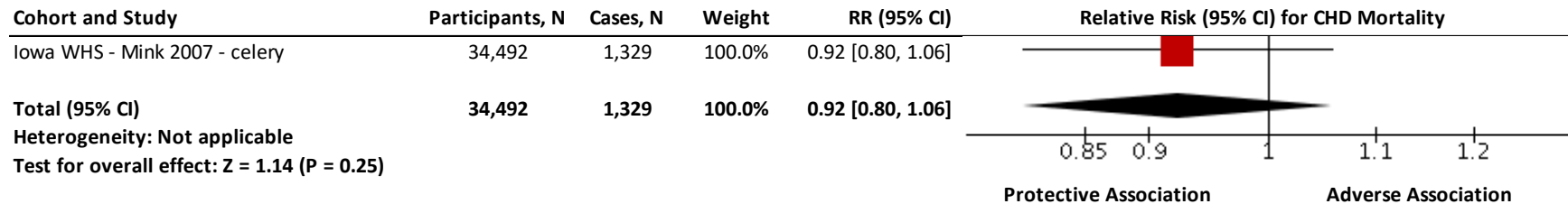
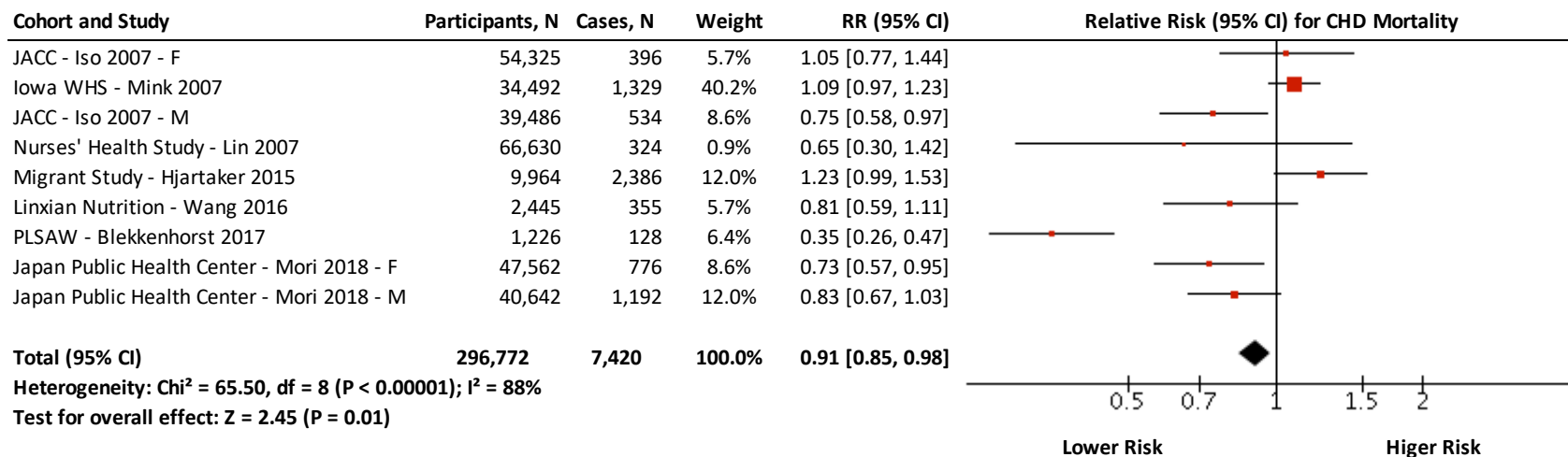


Figure S84. Relation between intake of celery and coronary heart disease mortality (highest vs. lowest level of intake). All results are presented as relative risk (RR) with 95% confidence intervals (95% CI). Pooled risk estimate is represented by the black diamond. Inter-study heterogeneity was assessed using the Cochran Q statistic (χ^2) at a significance level of $p < 0.10$, and quantified by I^2 , with values $\geq 50\%$ indicating substantial heterogeneity.

CRUCIFEROUS VEGETABLES AND CORONARY HEART DISEASE MORTALITY

A. Fixed Effects



B. Random Effects

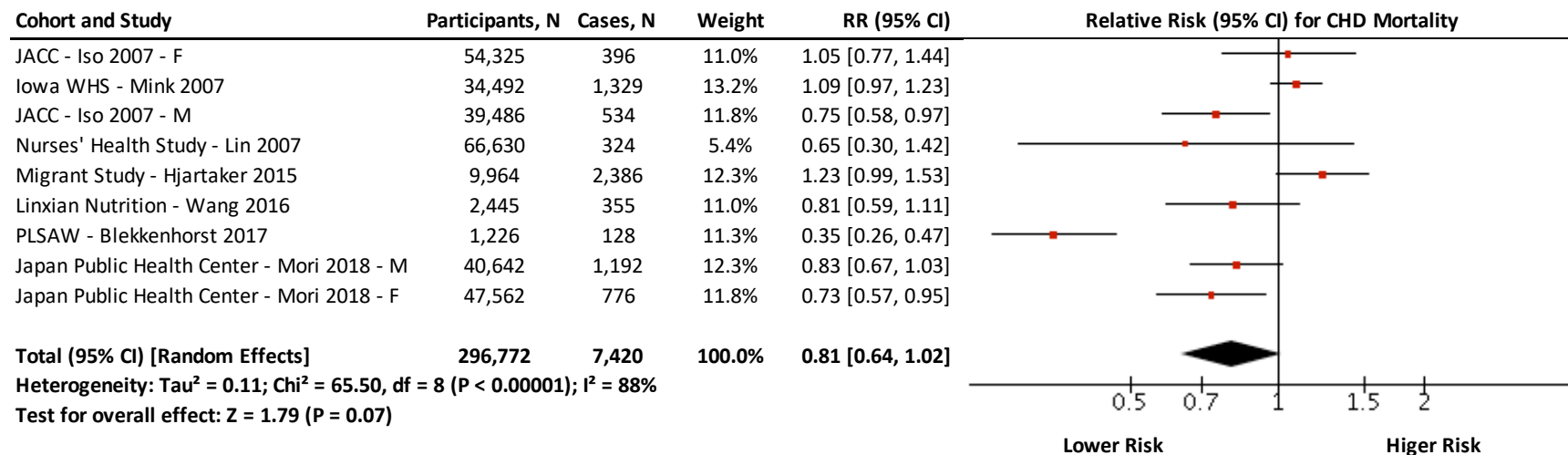
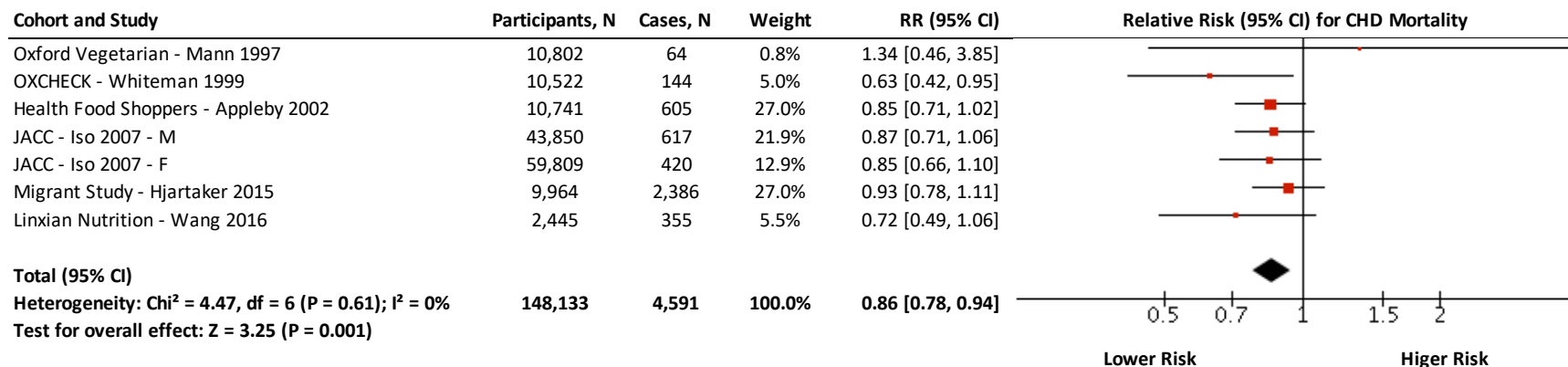


Figure S85. Relation between intake of cruciferous vegetables and coronary heart disease mortality (highest vs. lowest level of intake). All results are presented as relative risk (RR) with 95% confidence intervals (95% CI). Pooled risk estimate is represented by the black diamond using (A) fixed effects and (B) random effects models. Inter-study heterogeneity was assessed using the Cochran Q statistic (χ^2) at a significance level of $p < 0.10$, and quantified by I^2 , with values $\geq 50\%$ indicating substantial heterogeneity.

GREEN LEAFY VEGETABLES AND CORONARY HEART DISEASE MORTALITY

A. Fixed Effects



B. Random Effects

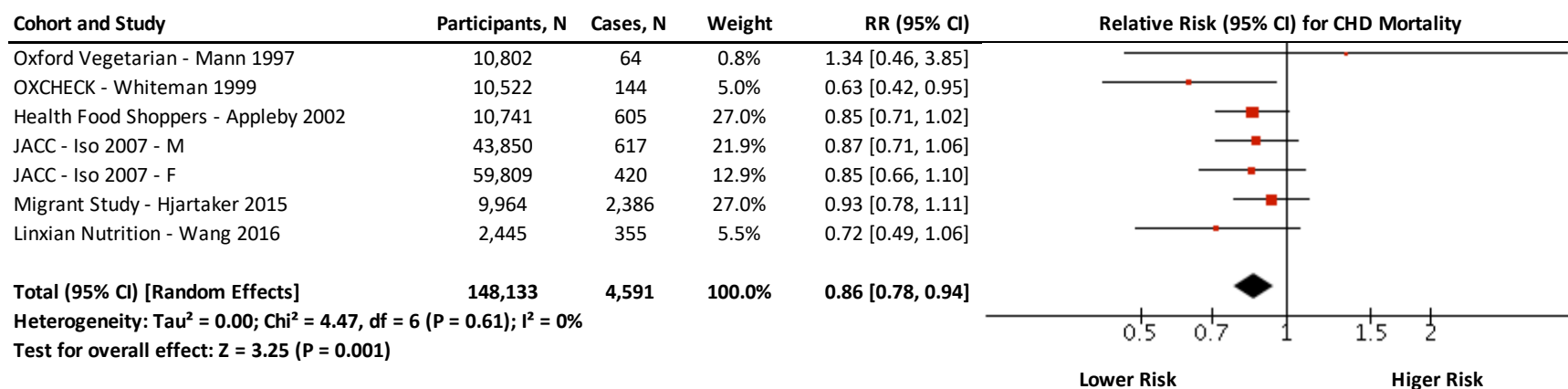
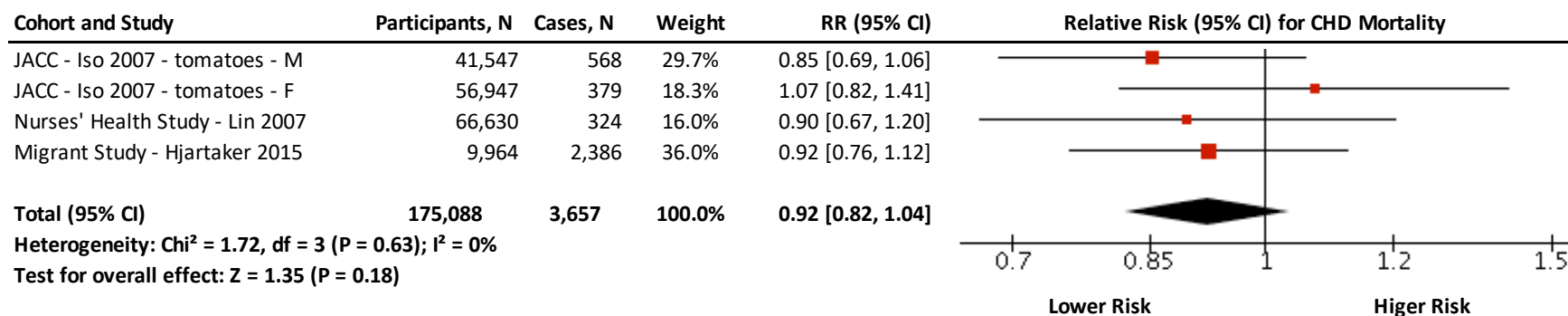


Figure S86. Relation between intake of green leafy vegetables and coronary heart disease mortality (highest vs. lowest level of intake). All results are presented as relative risk (RR) with 95% confidence intervals (95% CI). Pooled risk estimate is represented by the black diamond using (A) fixed effects and (B) random effects models. Inter-study heterogeneity was assessed using the Cochran Q statistic (χ^2) at a significance level of $p < 0.10$, and quantified by I^2 , with values $\geq 50\%$ indicating substantial heterogeneity.

TOMATOES AND CORONARY HEART DISEASE MORTALITY

A. Fixed Effects



B. Random Effects

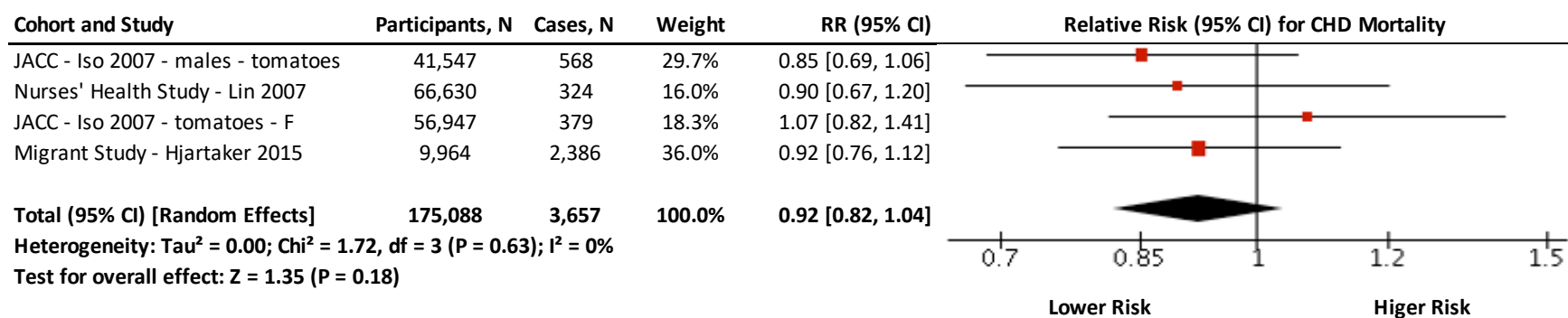
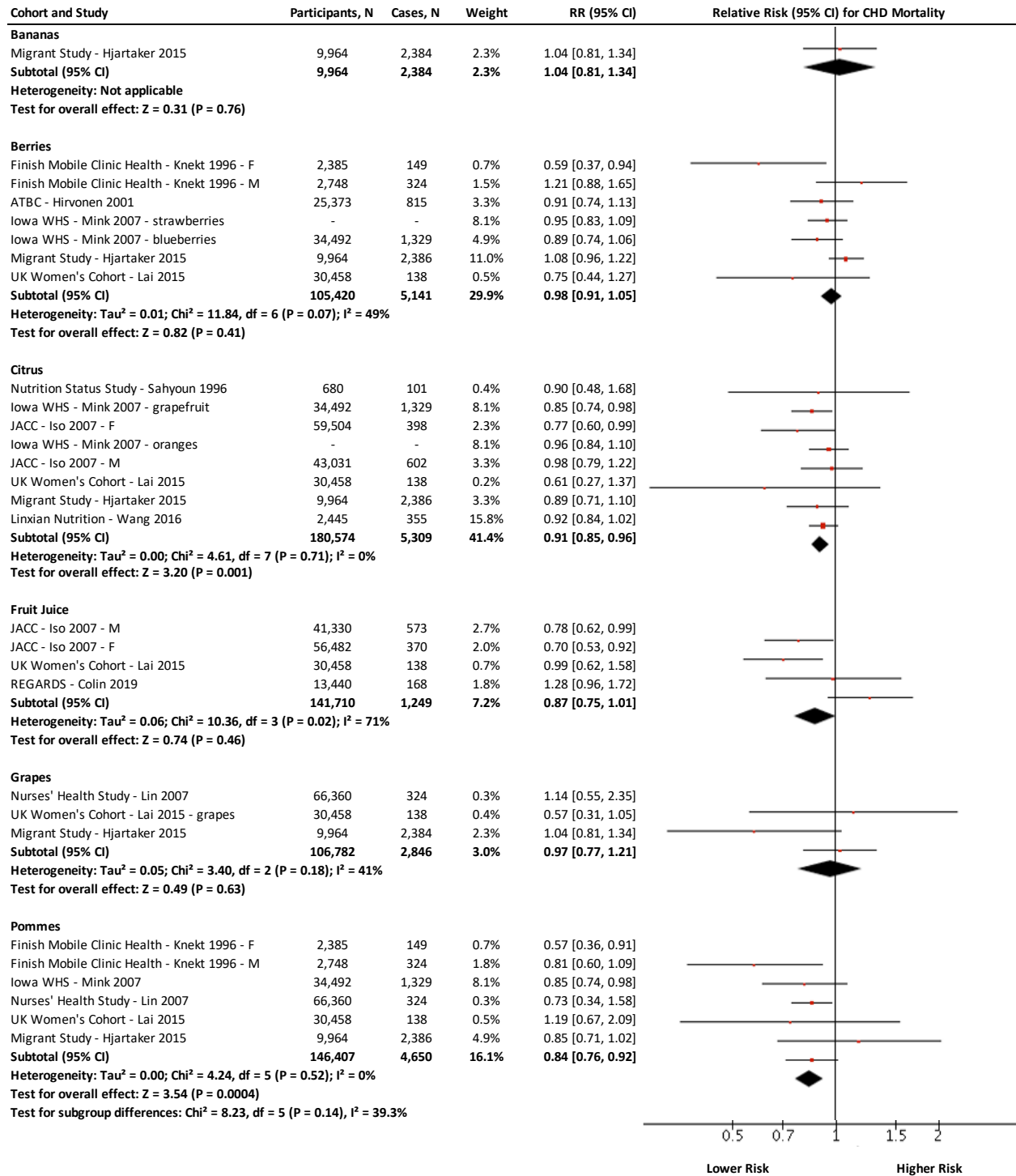


Figure S87. Relation between intake of tomatoes and coronary heart disease mortality (highest vs. lowest level of intake). All results are presented as relative risk (RR) with 95% confidence intervals (95% CI). Pooled risk estimate is represented by the black diamond using (A) fixed effects and (B) random effects models. Inter-study heterogeneity was assessed using the Cochran Q statistic (χ^2) at a significance level of $p < 0.10$, and quantified by I^2 , with values $\geq 50\%$ indicating substantial heterogeneity.

A. Fixed Effects



B. Random Effects

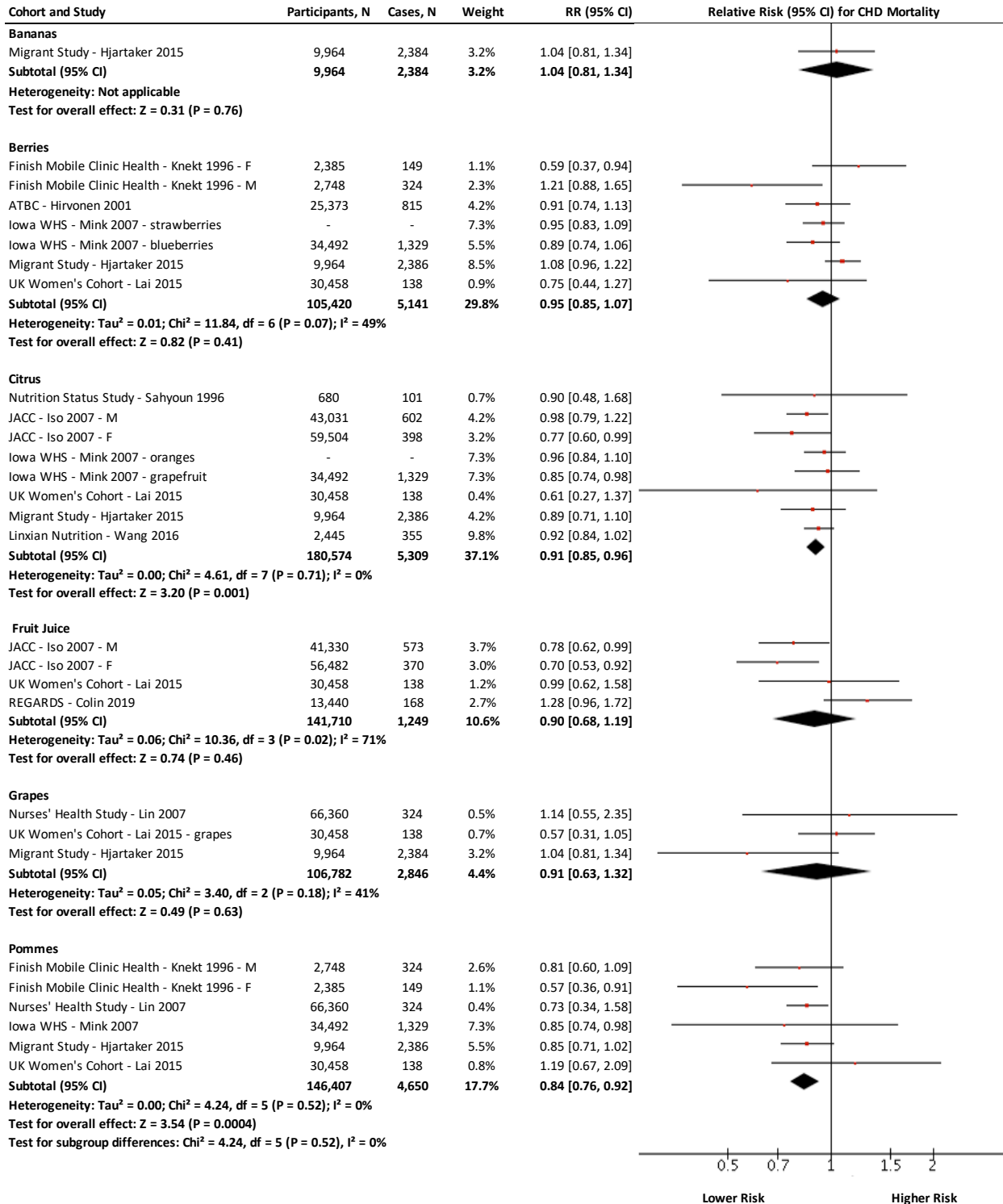
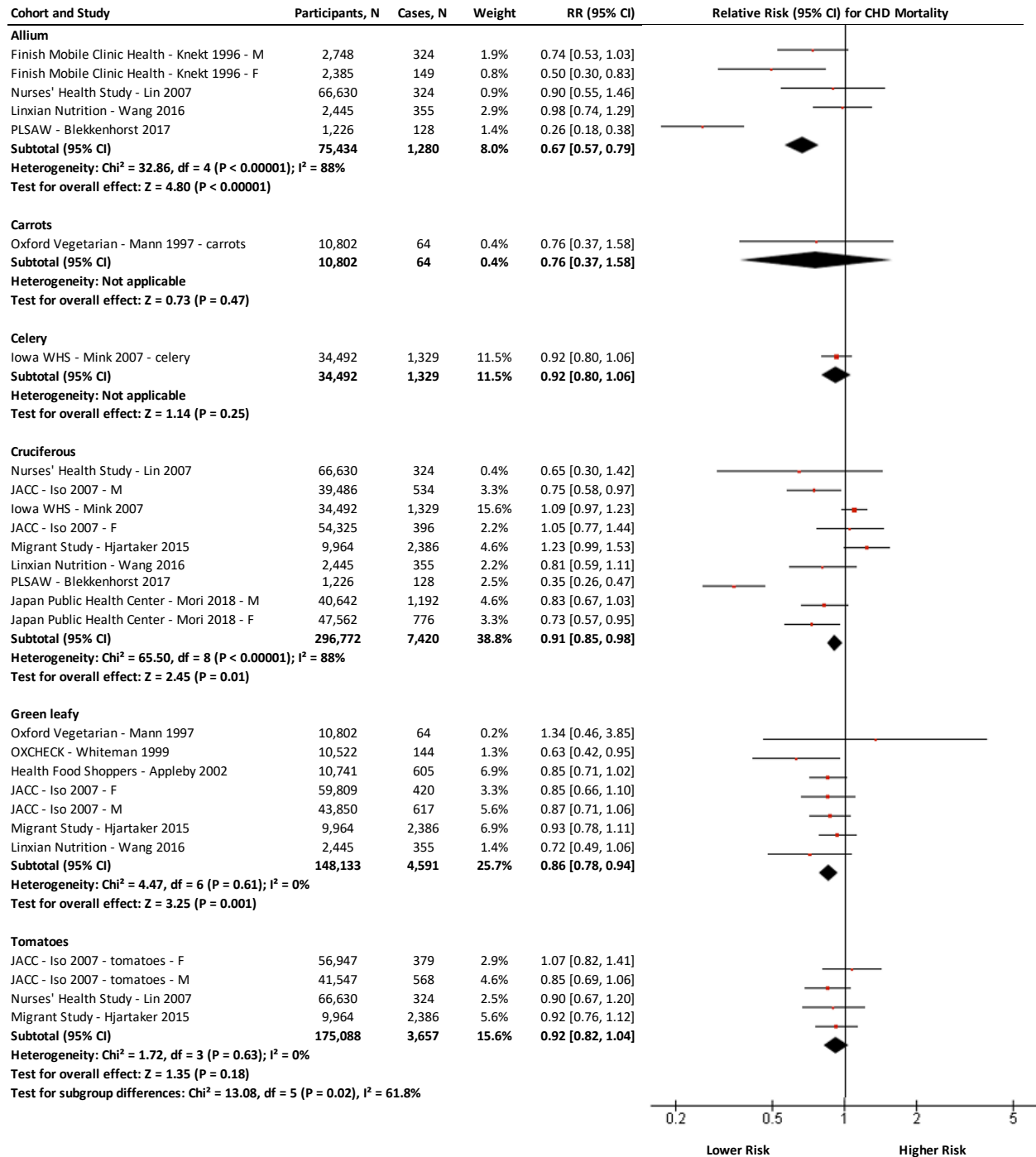


Figure S88. Relation between sources of fruit and CHD mortality (highest vs. lowest level of intake). All results are presented as relative risk (RR) with 95% confidence intervals (95% CI). Pooled risk estimate is represented by the black diamond using (A) fixed effects and (B) random effects models. Inter-study heterogeneity was assessed using the Cochran Q statistic (Chi²) at a significance level of p<0.10, and quantified by I², with values ≥ 50% indicating substantial heterogeneity.

A. Fixed Effects



B. Random Effects

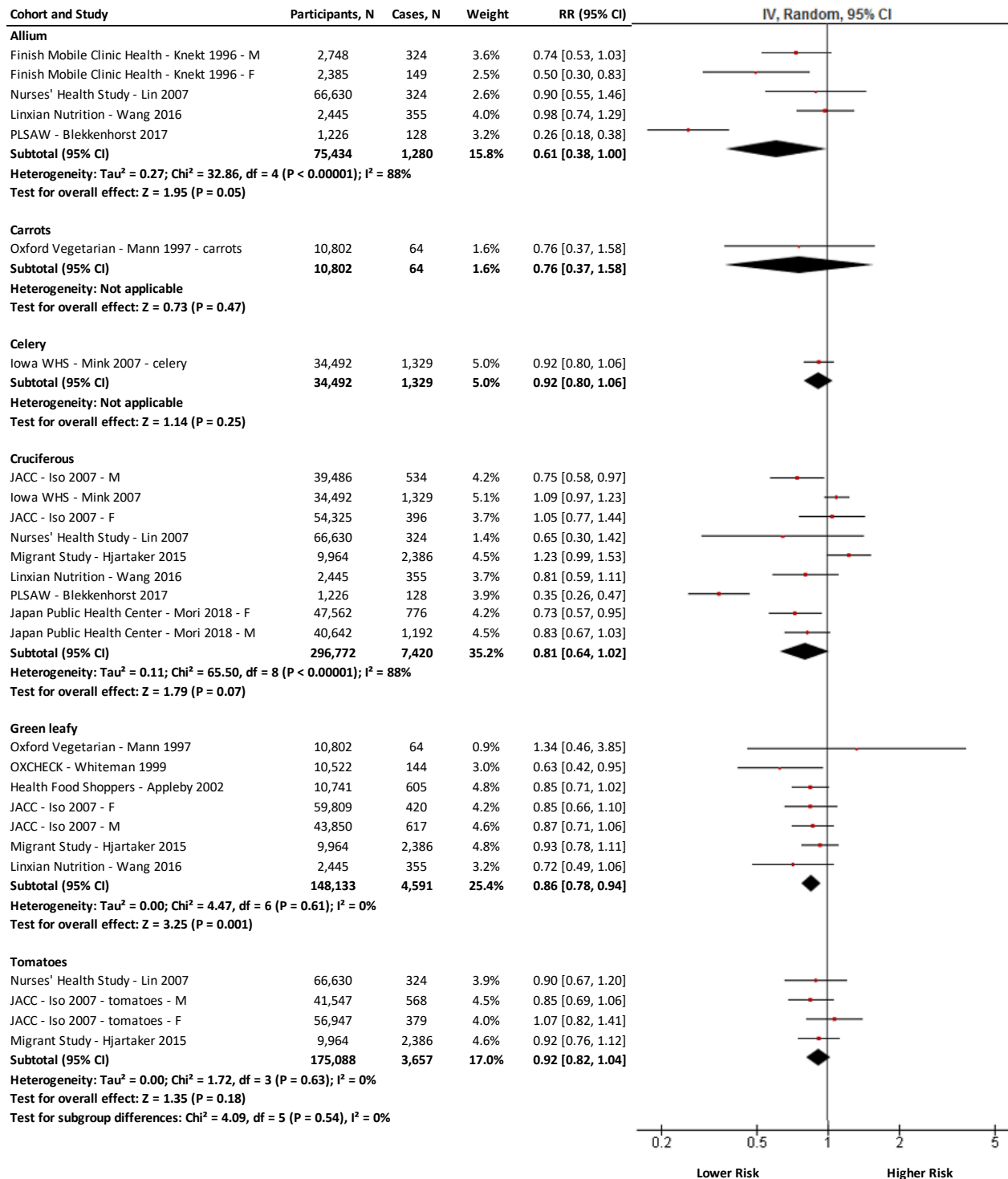


Figure S89. Relation between sources of vegetables and CHD mortality (highest vs. lowest level of intake). All results are presented as relative risk (RR) with 95% confidence intervals (95% CI). Pooled risk estimate is represented by the black diamond using (A) fixed effects and (B) random effects models. Inter-study heterogeneity was assessed using the Cochran Q statistic (χ^2) at a significance level of $p < 0.10$, and quantified by I^2 , with values $\geq 50\%$ indicating substantial heterogeneity.

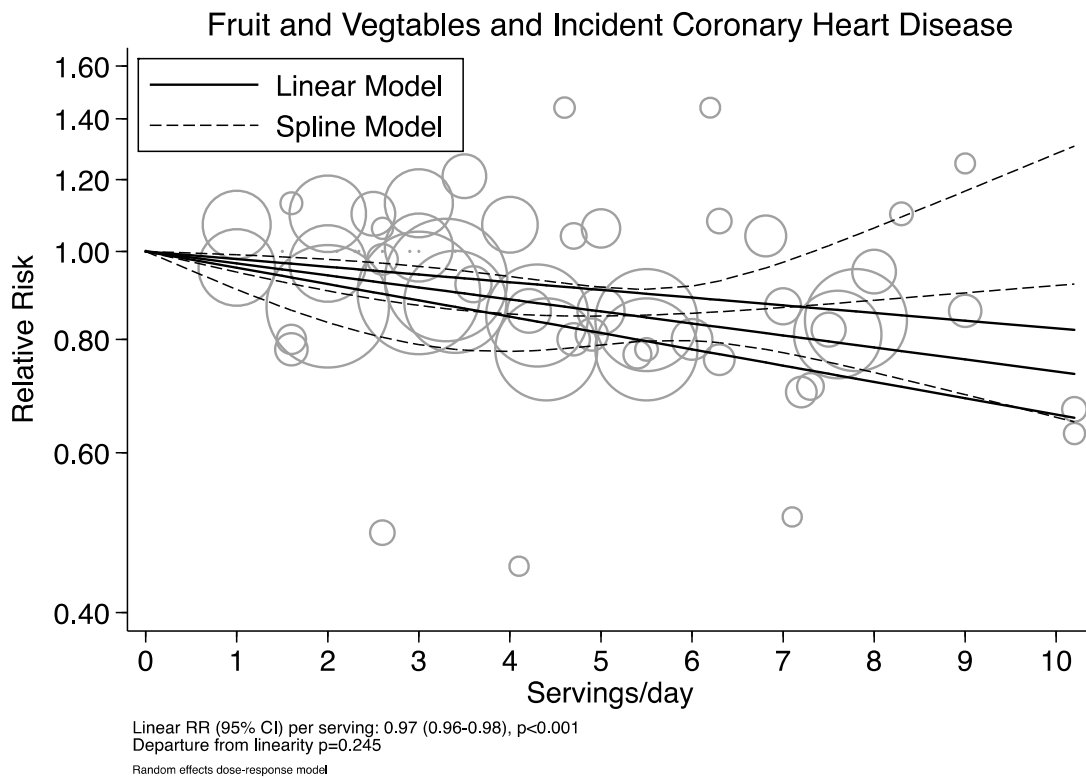


Figure S90. Linear and cubic-spline dose-response relation between increasing fruit and vegetable intake and incidence of coronary heart disease. Linear dose-response data was modeled using the Greenland and Longnecker²³ method to estimate the covariances of multivariable-adjusted relative risk. Cubic spline data were modeled with fixed-effects restricted cubic spline with 3 knots and using the Greenland and Longnecker²³ method to estimate the covariances of multivariable-adjusted relative risk. All data was kept on the original dose scale. The fitted trend for each model is represented by a central line (solid lines for linear model; dashed lines for cubic spline model) with 95% confidence intervals represented by the outer lines. Individual observations are represented by the circles, with the weight of the study in the overall analysis represented by the size of the circles.

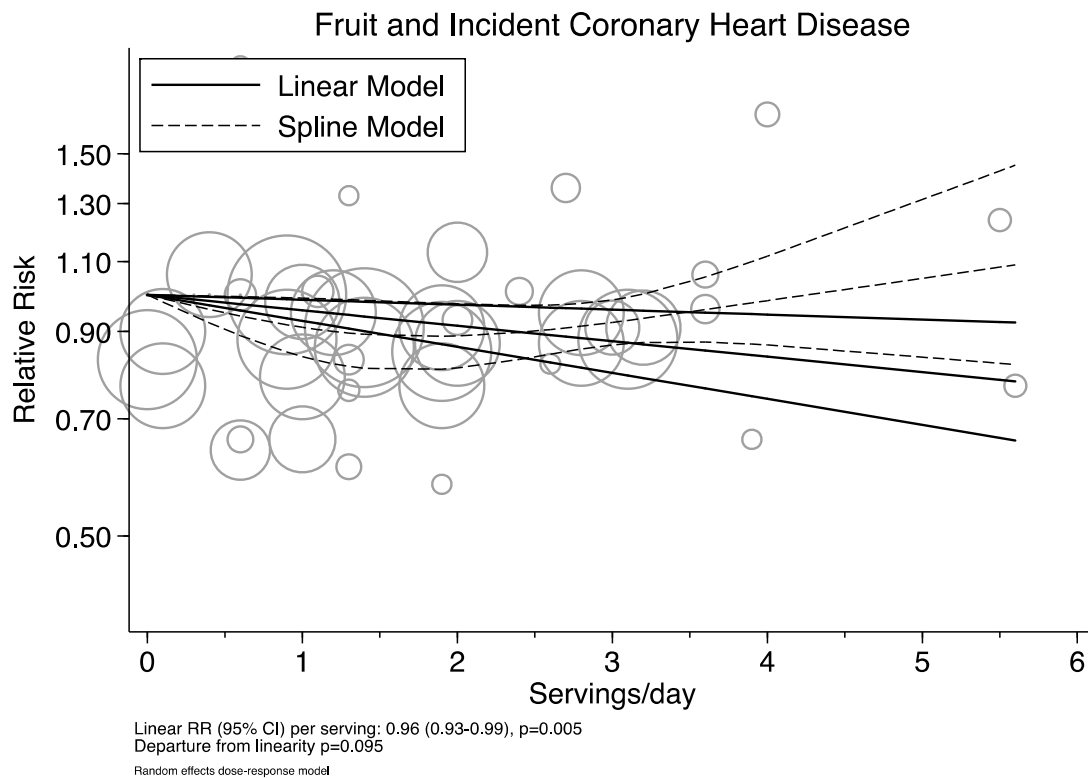


Figure S91. Linear and cubic-spline dose-response relation between increasing fruit intake and incidence of coronary heart disease. Linear dose-response data was modeled using the Greenland and Longnecker²³ method to estimate the covariances of multivariable-adjusted relative risk. Cubic spline data were modeled with fixed-effects restricted cubic spline with 3 knots and using the Greenland and Longnecker²³ method to estimate the covariances of multivariable-adjusted relative risk. All data was kept on the original dose scale. The fitted trend for each model is represented by a central line (solid lines for linear model; dashed lines for cubic spline model) with 95% confidence intervals represented by the outer lines. Individual observations are represented by the circles, with the weight of the study in the overall analysis represented by the size of the circles.

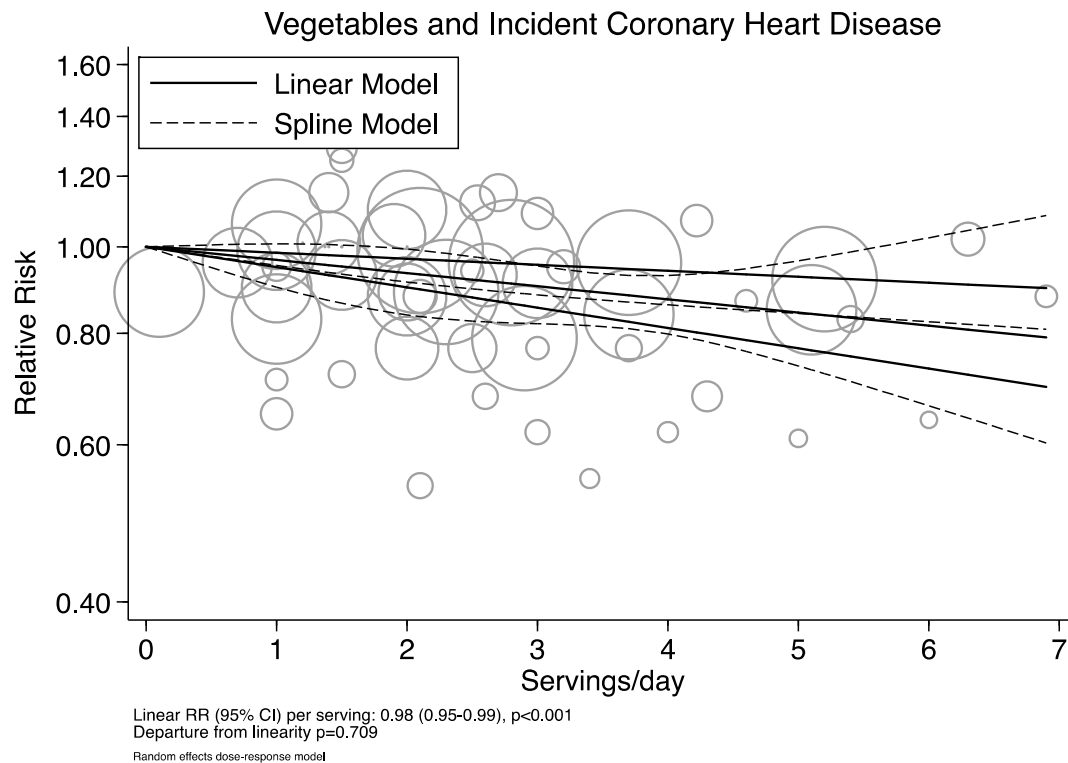


Figure S92. Linear and cubic-spline dose-response relation between increasing intake of vegetables and incidence of coronary heart disease. Linear dose-response data was modeled using the Greenland and Longnecker²³ method to estimate the covariances of multivariable-adjusted relative risk. Cubic spline data were modeled with fixed-effects restricted cubic spline with 3 knots and using the Greenland and Longnecker²³ method to estimate the covariances of multivariable-adjusted relative risk. All data was kept on the original dose scale. The fitted trend for each model is represented by a central line (solid lines for linear model; dashed lines for cubic spline model) with 95% confidence intervals represented by the outer lines. Individual observations are represented by the circles, with the weight of the study in the overall analysis represented by the size of the circles.

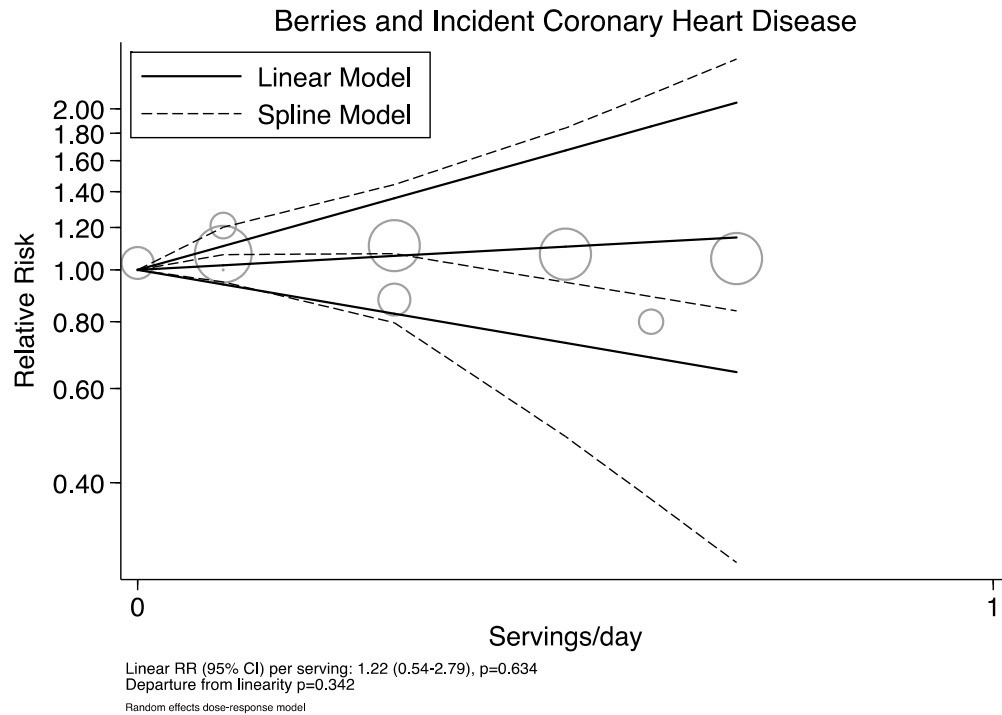


Figure S93. Linear and cubic-spline dose-response relation between increasing berries intake and incidence of coronary heart disease. Linear dose-response data was modeled using the Greenland and Longnecker²³ method to estimate the covariances of multivariable-adjusted relative risk. Cubic spline data were modeled with fixed-effects restricted cubic spline with 3 knots and using the Greenland and Longnecker²³ method to estimate the covariances of multivariable-adjusted relative risk. All data was kept on the original dose scale. The fitted trend for each model is represented by a central line (solid lines for linear model; dashed lines for cubic spline model) with 95% confidence intervals represented by the outer lines. Individual observations are represented by the circles, with the weight of the study in the overall analysis represented by the size of the circles.

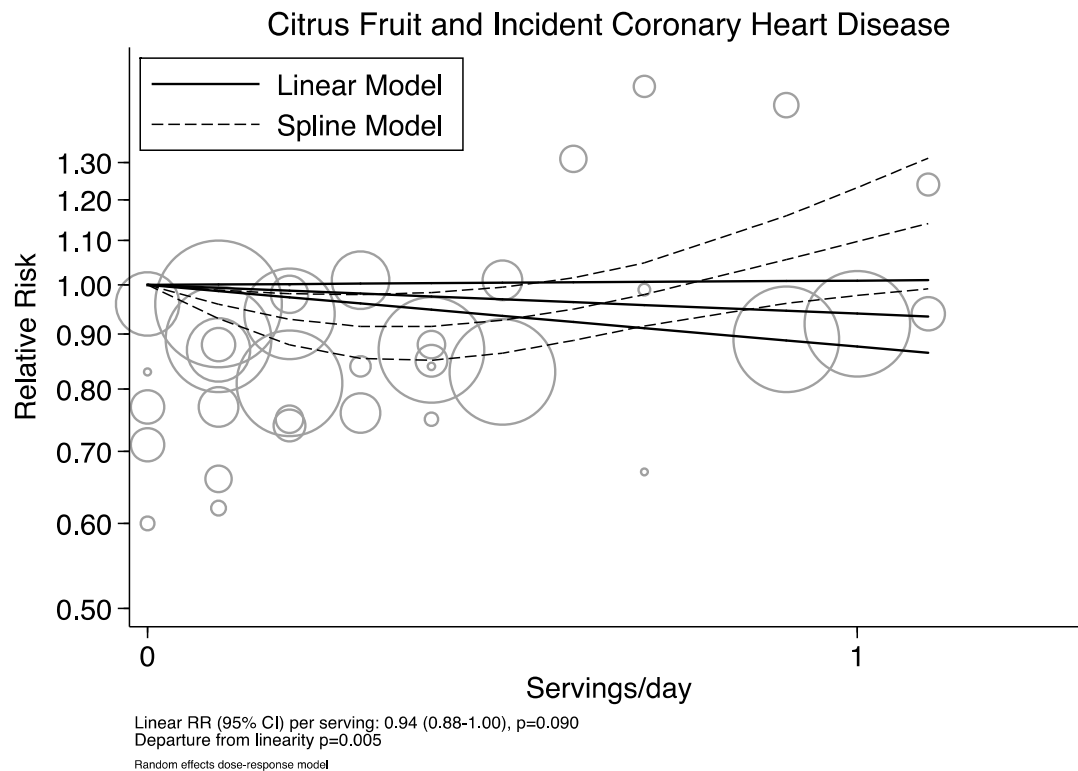


Figure S94. Linear and cubic-spline dose-response relation between increasing citrus fruit intake and incidence of coronary heart disease. Linear dose-response data was modeled using the Greenland and Longnecker²³ method to estimate the covariances of multivariable-adjusted relative risk. Cubic spline data were modeled with fixed-effects restricted cubic spline with 3 knots and using the Greenland and Longnecker²³ method to estimate the covariances of multivariable-adjusted relative risk. All data was kept on the original dose scale. The fitted trend for each model is represented by a central line (solid lines for linear model; dashed lines for cubic spline model) with 95% confidence intervals represented by the outer lines. Individual observations are represented by the circles, with the weight of the study in the overall analysis represented by the size of the circles.

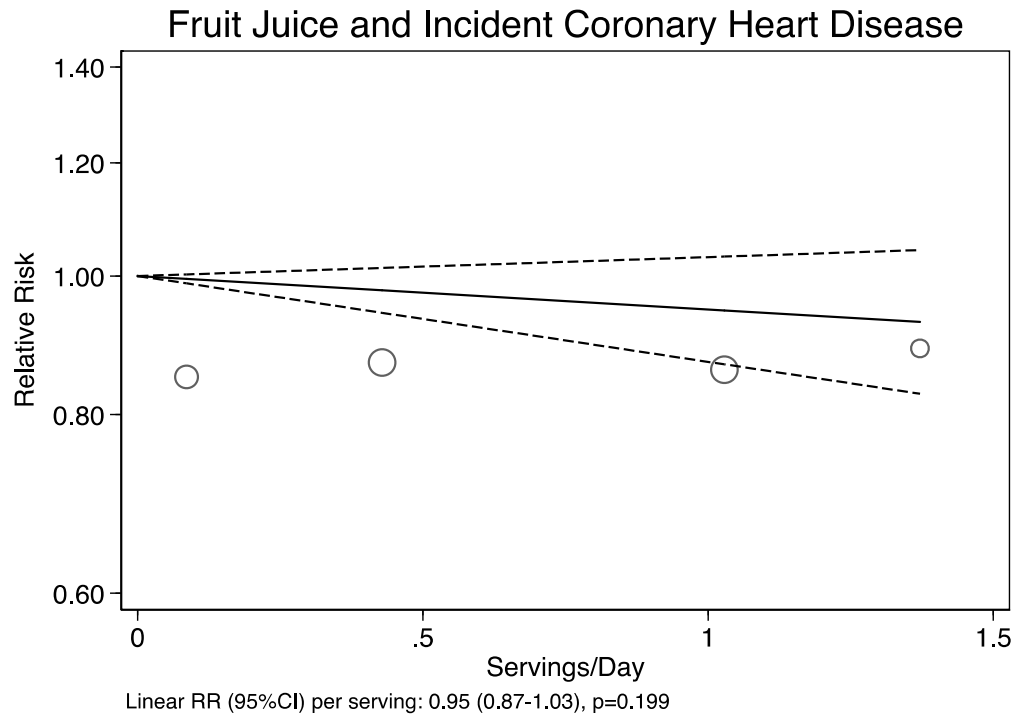


Figure S95. Linear and cubic-spline dose-response relation between increasing fruit juice intake and incidence of coronary heart disease. Linear dose-response data was modeled using the Greenland and Longnecker²³ method to estimate the covariances of multivariable-adjusted relative risk. Cubic spline data were modeled with fixed-effects restricted cubic spline with 3 knots and using the Greenland and Longnecker²³ method to estimate the covariances of multivariable-adjusted relative risk. All data was kept on the original dose scale. The fitted trend for each model is represented by a central line (solid lines for linear model; dashed lines for cubic spline model) with 95% confidence intervals represented by the outer lines. Individual observations are represented by the circles, with the weight of the study in the overall analysis represented by the size of the circles.

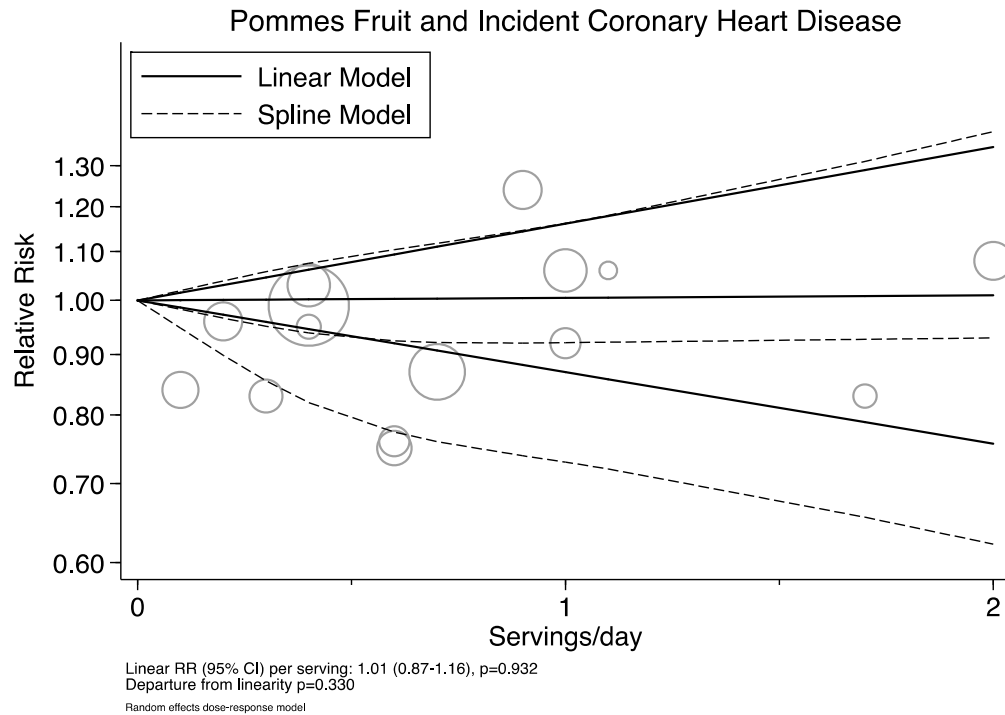


Figure S96. Linear and cubic-spline dose-response relation between increasing pommes intake and incidence of coronary heart disease. Linear dose-response data was modeled using the Greenland and Longnecker²³ method to estimate the covariances of multivariable-adjusted relative risk. Cubic spline data were modeled with fixed-effects restricted cubic spline with 3 knots and using the Greenland and Longnecker²³ method to estimate the covariances of multivariable-adjusted relative risk. All data was kept on the original dose scale. The fitted trend for each model is represented by a central line (solid lines for linear model; dashed lines for cubic spline model) with 95% confidence intervals represented by the outer lines. Individual observations are represented by the circles, with the weight of the study in the overall analysis represented by the size of the circles.

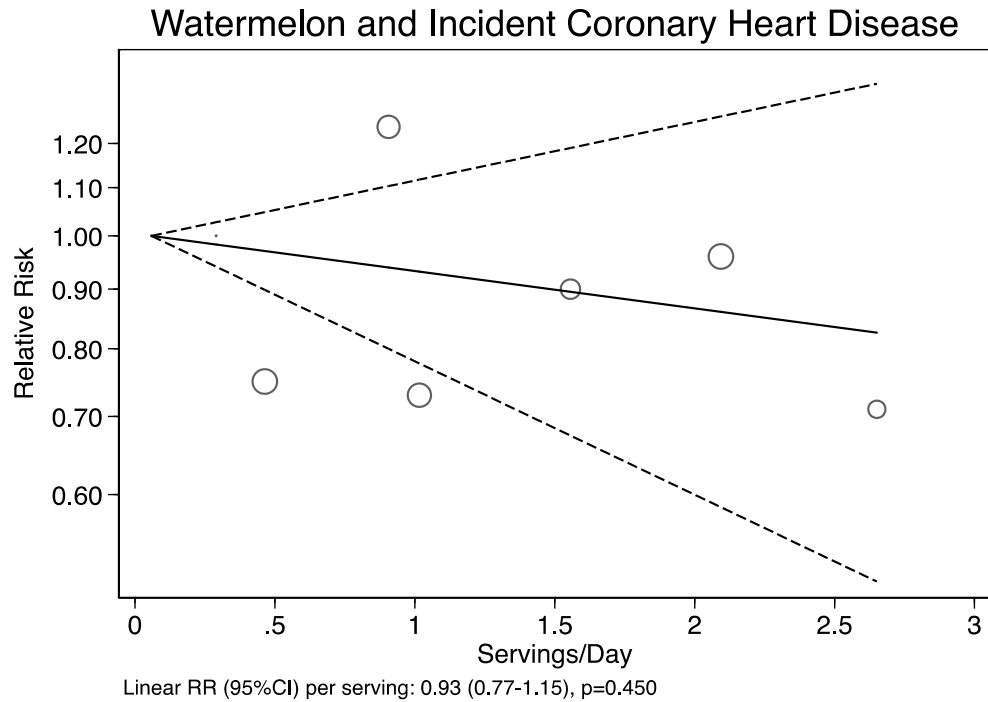


Figure S97. Linear dose-response relation between increasing watermelon intake and cardiovascular disease mortality. Linear dose-response data was modeled using the Greenland and Longnecker²³ method to estimate the covariances of multivariable-adjusted relative risk, with kept on the original dose scale. Dashed lines represent the pointwise 95% confidence intervals for the fitted linear trend represented by a solid line. Individual observations are represented by the circles, with the weight of the study in the overall analysis represented by the size of the circles.

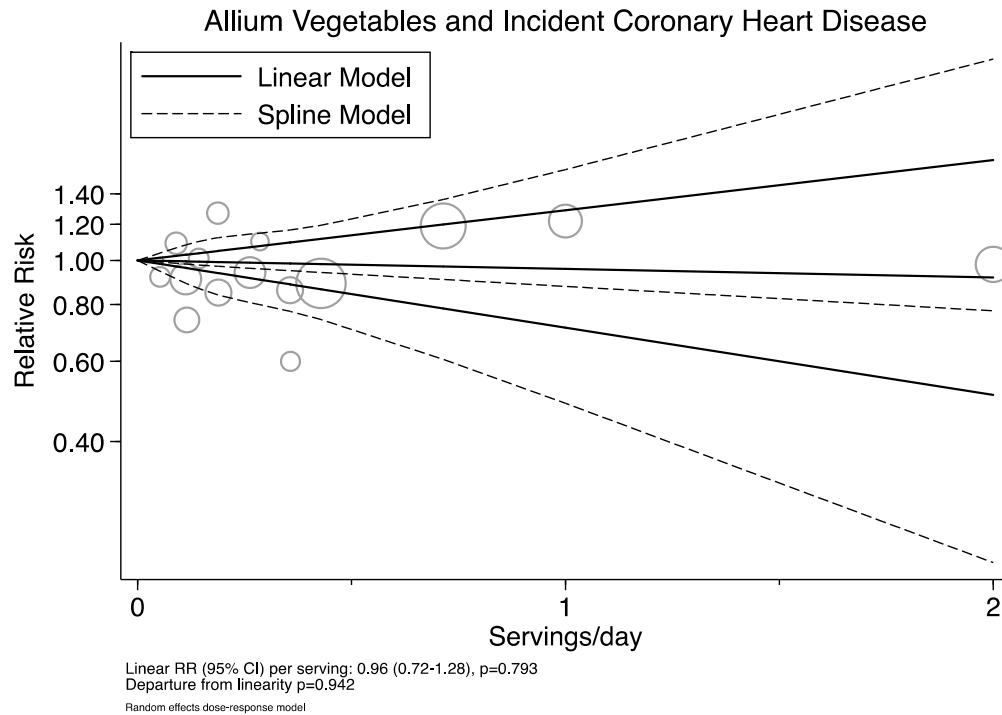


Figure S98. Linear and cubic-spline dose-response relation between increasing intake of allium vegetables and incidence of coronary heart disease. Linear dose-response data was modeled using the Greenland and Longnecker²³ method to estimate the covariances of multivariable-adjusted relative risk. Cubic spline data were modeled with fixed-effects restricted cubic spline with 3 knots and using the Greenland and Longnecker²³ method to estimate the covariances of multivariable-adjusted relative risk. All data was kept on the original dose scale. The fitted trend for each model is represented by a central line (solid lines for linear model; dashed lines for cubic spline model) with 95% confidence intervals represented by the outer lines. Individual observations are represented by the circles, with the weight of the study in the overall analysis represented by the size of the circles.

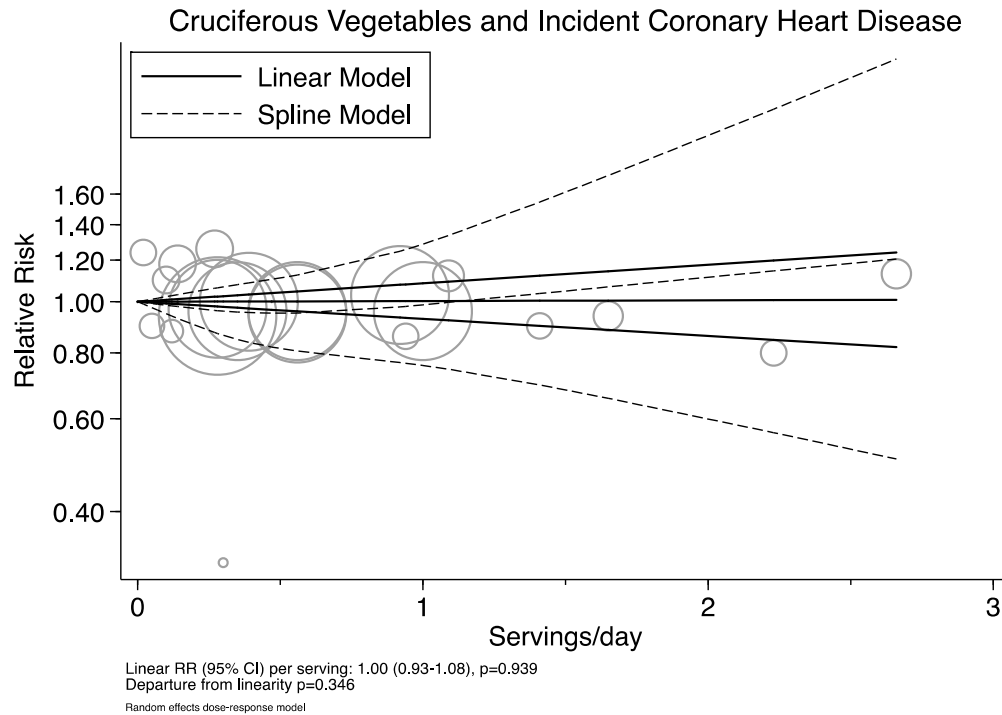


Figure S99. Linear and cubic-spline dose-response relation between increasing intake of cruciferous vegetables and coronary heart disease mortality. Linear dose-response data was modeled using the Greenland and Longnecker²³ method to estimate the covariances of multivariable-adjusted relative risk. Cubic spline data were modeled with fixed-effects restricted cubic spline with 3 knots and using the Greenland and Longnecker²³ method to estimate the covariances of multivariable-adjusted relative risk. All data was kept on the original dose scale. The fitted trend for each model is represented by a central line (solid lines for linear model; dashed lines for cubic spline model) with 95% confidence intervals represented by the outer lines. Individual observations are represented by the circles, with the weight of the study in the overall analysis represented by the size of the circles.

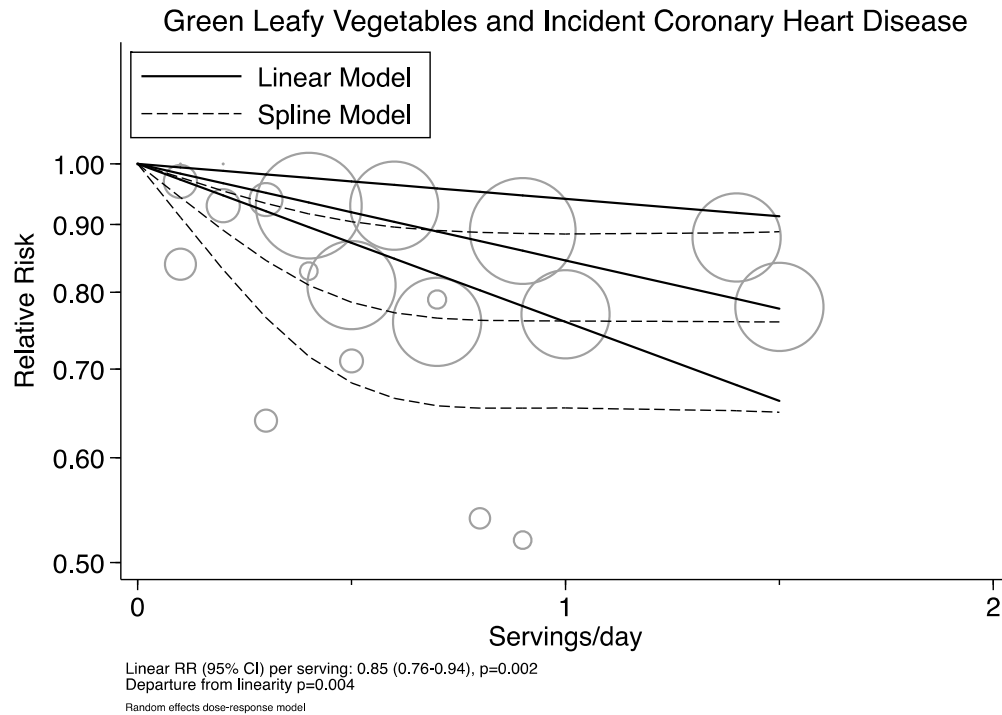


Figure S100. Linear and cubic-spline dose-response relation between increasing intake of green leafy vegetables and incidence of coronary heart disease. Linear dose-response data was modeled using the Greenland and Longnecker²³ method to estimate the covariances of multivariable-adjusted relative risk. Cubic spline data were modeled with fixed-effects restricted cubic spline with 3 knots and using the Greenland and Longnecker²³ method to estimate the covariances of multivariable-adjusted relative risk. All data was kept on the original dose scale. The fitted trend for each model is represented by a central line (solid lines for linear model; dashed lines for cubic spline model) with 95% confidence intervals represented by the outer lines. Individual observations are represented by the circles, with the weight of the study in the overall analysis represented by the size of the circles.

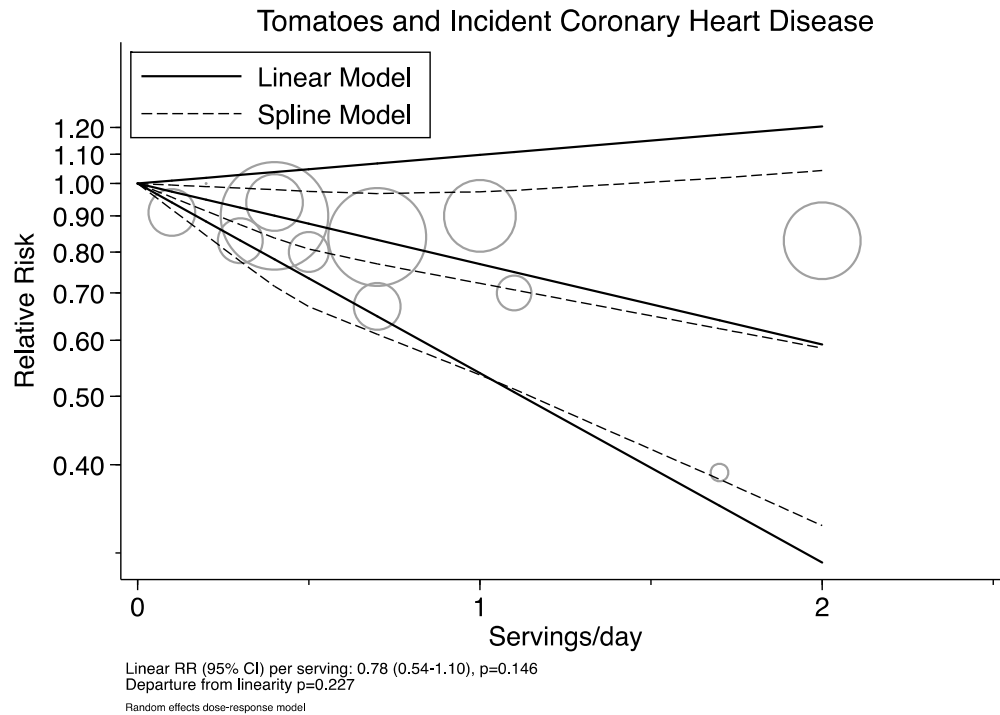


Figure S101. Linear and cubic-spline dose-response relation between increasing tomato intake and incidence of coronary heart disease. Linear dose-response data was modeled using the Greenland and Longnecker²³ method to estimate the covariances of multivariable-adjusted relative risk. Cubic spline data were modeled with fixed-effects restricted cubic spline with 3 knots and using the Greenland and Longnecker²³ method to estimate the covariances of multivariable-adjusted relative risk. All data was kept on the original dose scale. The fitted trend for each model is represented by a central line (solid lines for linear model; dashed lines for cubic spline model) with 95% confidence intervals represented by the outer lines. Individual observations are represented by the circles, with the weight of the study in the overall analysis represented by the size of the circles.

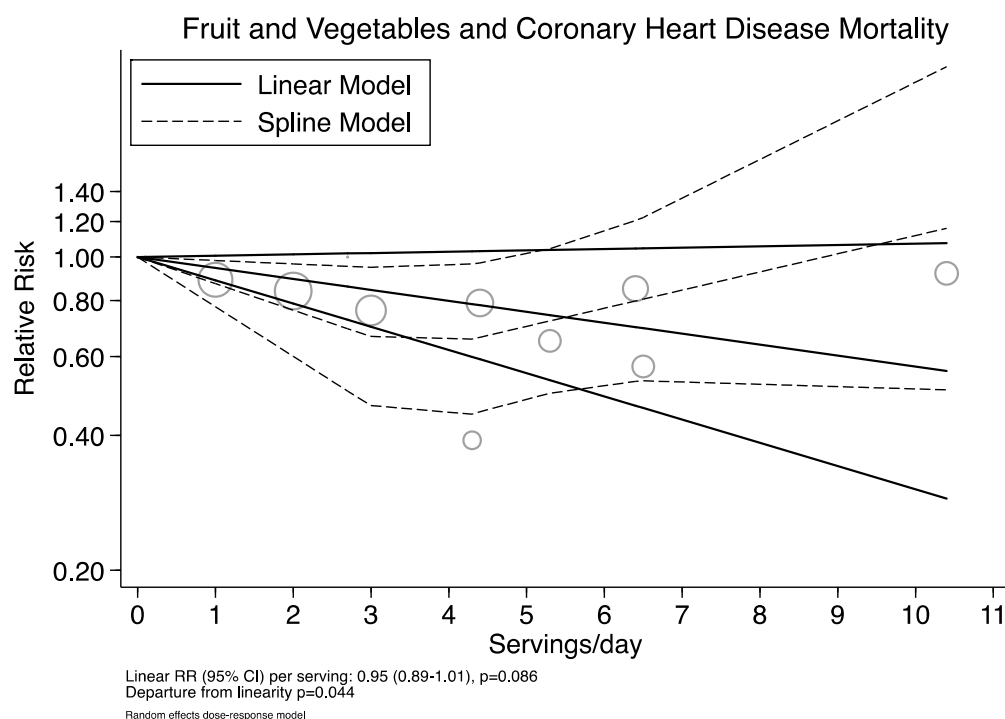


Figure S102. Linear and cubic-spline dose-response relation between increasing fruit and vegetable intake and coronary heart disease mortality. Linear dose-response data was modeled using the Greenland and Longnecker²³ method to estimate the covariances of multivariable-adjusted relative risk. Cubic spline data were modeled with fixed-effects restricted cubic spline with 3 knots and using the Greenland and Longnecker²³ method to estimate the covariances of multivariable-adjusted relative risk. All data was kept on the original dose scale. The fitted trend for each model is represented by a central line (solid lines for linear model; dashed lines for cubic spline model) with 95% confidence intervals represented by the outer lines. Individual observations are represented by the circles, with the weight of the study in the overall analysis represented by the size of the circles.

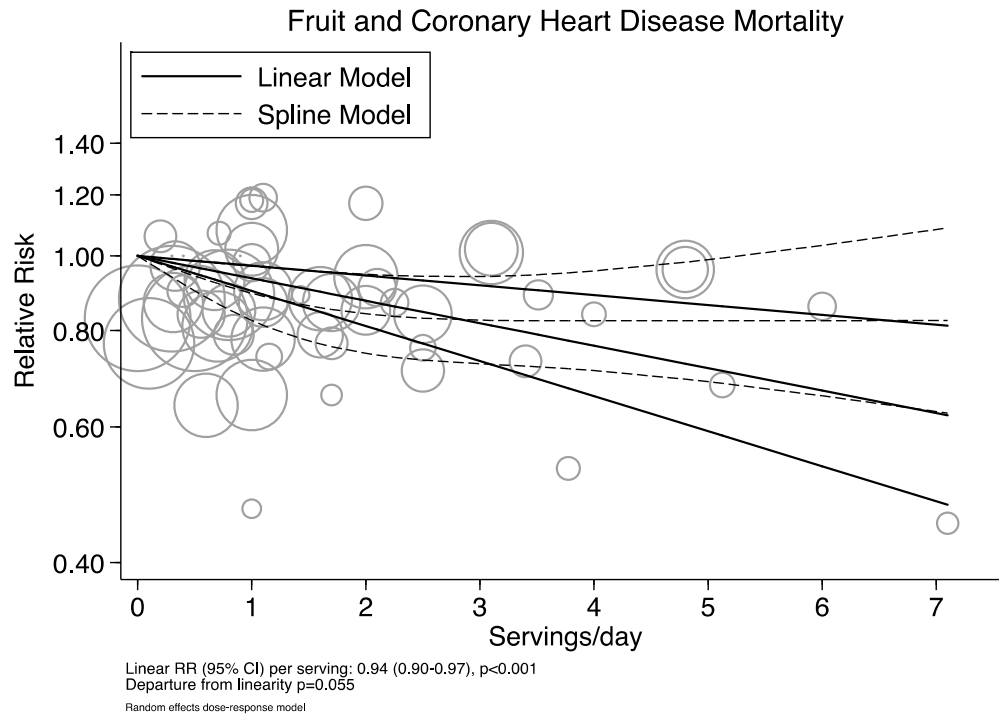


Figure S103. Linear and cubic-spline dose-response relation between increasing fruit intake and coronary heart disease mortality. Linear dose-response data was modeled using the Greenland and Longnecker²³ method to estimate the covariances of multivariable-adjusted relative risk. Cubic spline data were modeled with fixed-effects restricted cubic spline with 3 knots and using the Greenland and Longnecker²³ method to estimate the covariances of multivariable-adjusted relative risk. All data was kept on the original dose scale. The fitted trend for each model is represented by a central line (solid lines for linear model; dashed lines for cubic spline model) with 95% confidence intervals represented by the outer lines. Individual observations are represented by the circles, with the weight of the study in the overall analysis represented by the size of the circles.

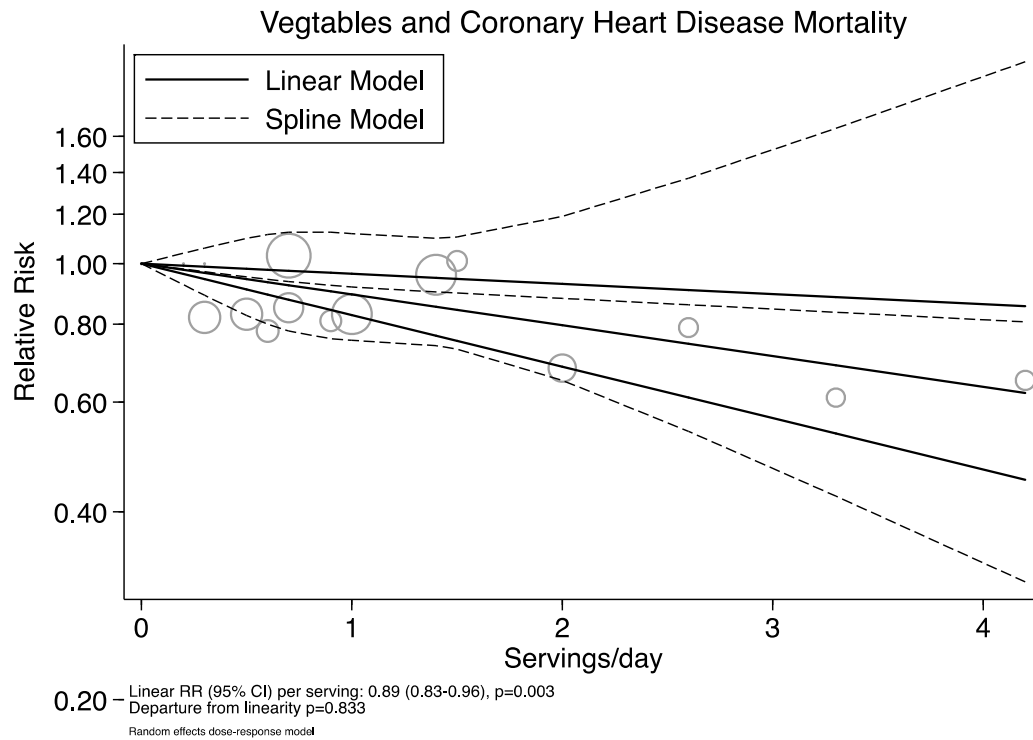


Figure S104. Linear and cubic-spline dose-response relation between increasing intake of vegetables and coronary heart disease mortality. Linear dose-response data was modeled using the Greenland and Longnecker²³ method to estimate the covariances of multivariable-adjusted relative risk. Cubic spline data were modeled with fixed-effects restricted cubic spline with 3 knots and using the Greenland and Longnecker²³ method to estimate the covariances of multivariable-adjusted relative risk. All data was kept on the original dose scale. The fitted trend for each model is represented by a central line (solid lines for linear model; dashed lines for cubic spline model) with 95% confidence intervals represented by the outer lines. Individual observations are represented by the circles, with the weight of the study in the overall analysis represented by the size of the circles.

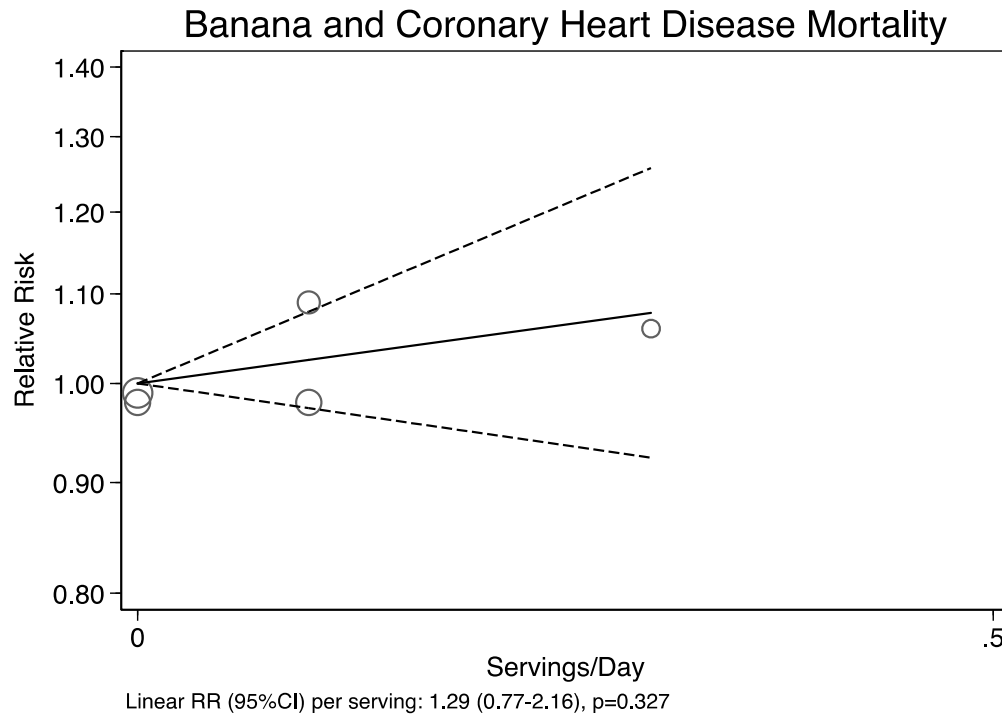


Figure S105. Linear dose-response relation between increasing banana intake and cardiovascular disease mortality. Linear dose-response data was modeled using the Greenland and Longnecker²³ method to estimate the covariances of multivariable-adjusted relative risk, with kept on the original dose scale. Dashed lines represent the pointwise 95% confidence intervals for the fitted linear trend represented by a solid line. Individual observations are represented by the circles, with the weight of the study in the overall analysis represented by the size of the circles.

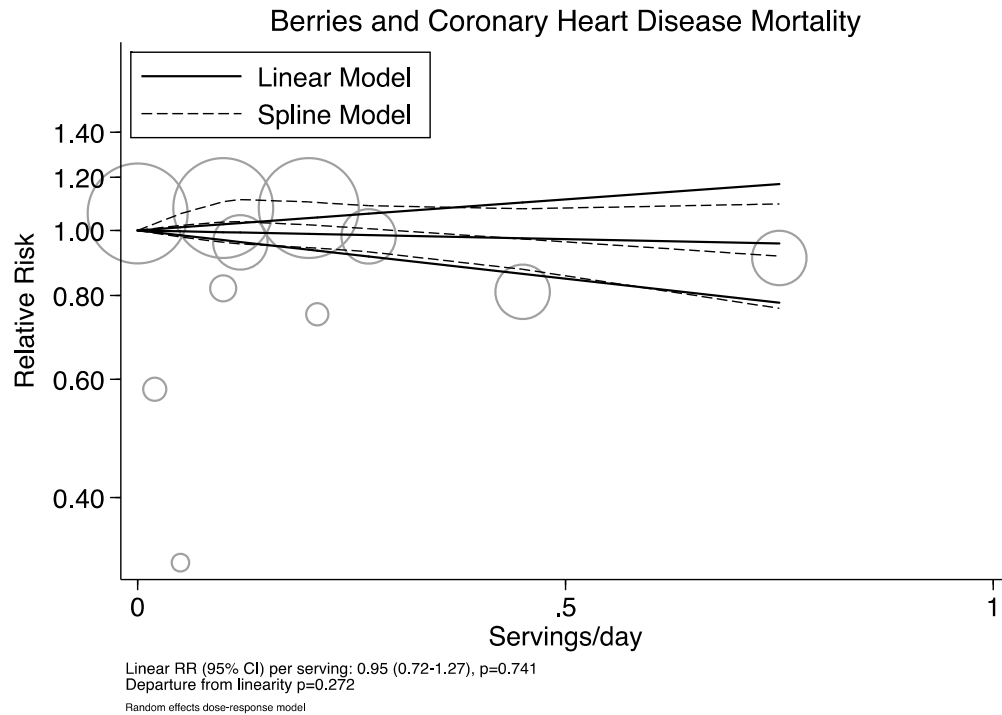


Figure S106. Linear dose-response relation between increasing berries intake and coronary heart disease mortality. Linear dose-response data was modeled using the Greenland and Longnecker²³ method to estimate the covariances of multivariable-adjusted relative risk, with kept on the original dose scale. Dashed lines represent the pointwise 95% confidence intervals for the fitted linear trend represented by a solid line. Individual observations are represented by the circles, with the weight of the study in the overall analysis represented by the size of the circles.

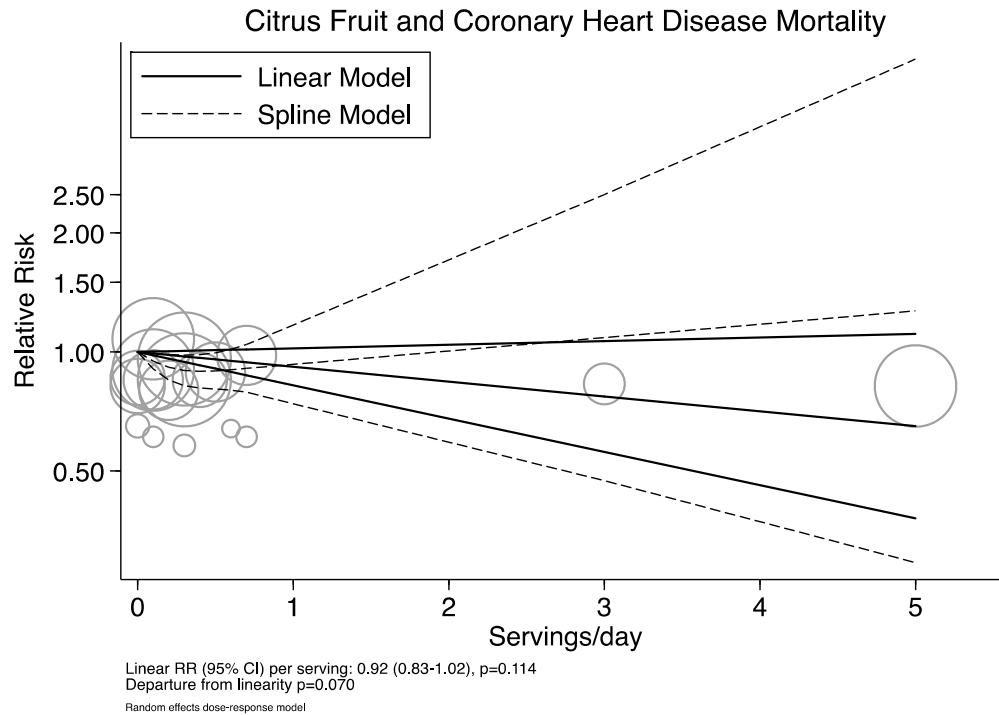


Figure S107. Linear and cubic-spline dose-response relation between increasing citrus fruit intake and coronary heart disease mortality. Linear dose-response data was modeled using the Greenland and Longnecker²³ method to estimate the covariances of multivariable-adjusted relative risk. Cubic spline data were modeled with fixed-effects restricted cubic spline with 3 knots and using the Greenland and Longnecker²³ method to estimate the covariances of multivariable-adjusted relative risk. All data was kept on the original dose scale. The fitted trend for each model is represented by a central line (solid lines for linear model; dashed lines for cubic spline model) with 95% confidence intervals represented by the outer lines. Individual observations are represented by the circles, with the weight of the study in the overall analysis represented by the size of the circles.

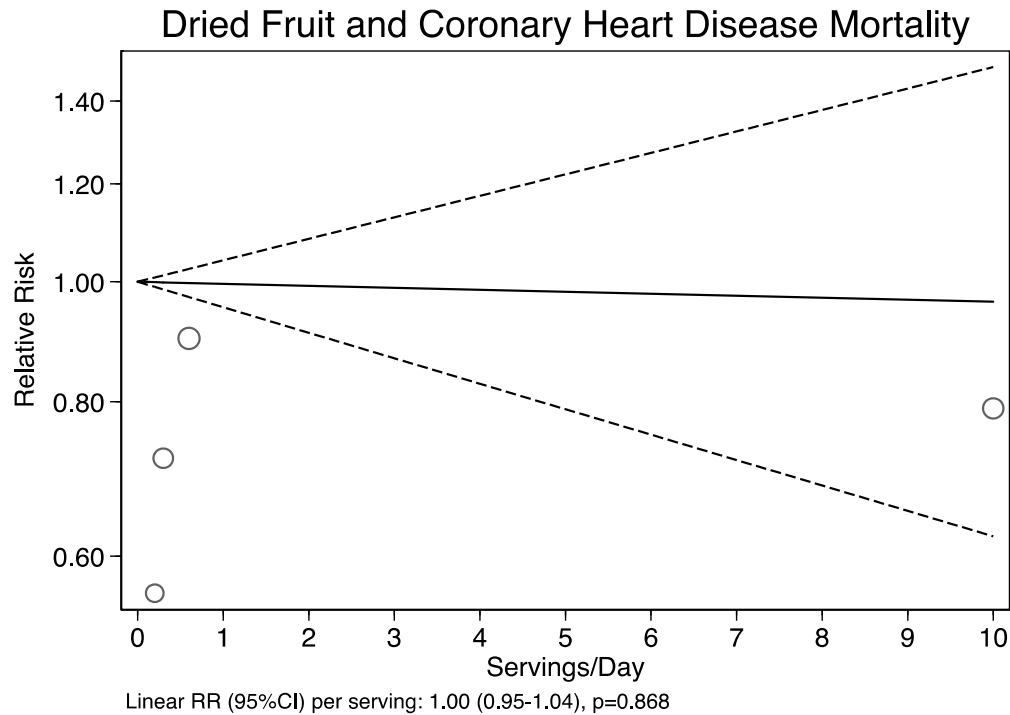


Figure S108. Linear and cubic-spline dose-response relation between increasing dried fruit intake and coronary heart disease mortality. Linear dose-response data was modeled using the Greenland and Longnecker²³ method to estimate the covariances of multivariable-adjusted relative risk. Cubic spline data were modeled with fixed-effects restricted cubic spline with 3 knots and using the Greenland and Longnecker²³ method to estimate the covariances of multivariable-adjusted relative risk. All data was kept on the original dose scale. The fitted trend for each model is represented by a central line (solid lines for linear model; dashed lines for cubic spline model) with 95% confidence intervals represented by the outer lines. Individual observations are represented by the circles, with the weight of the study in the overall analysis represented by the size of the circles.

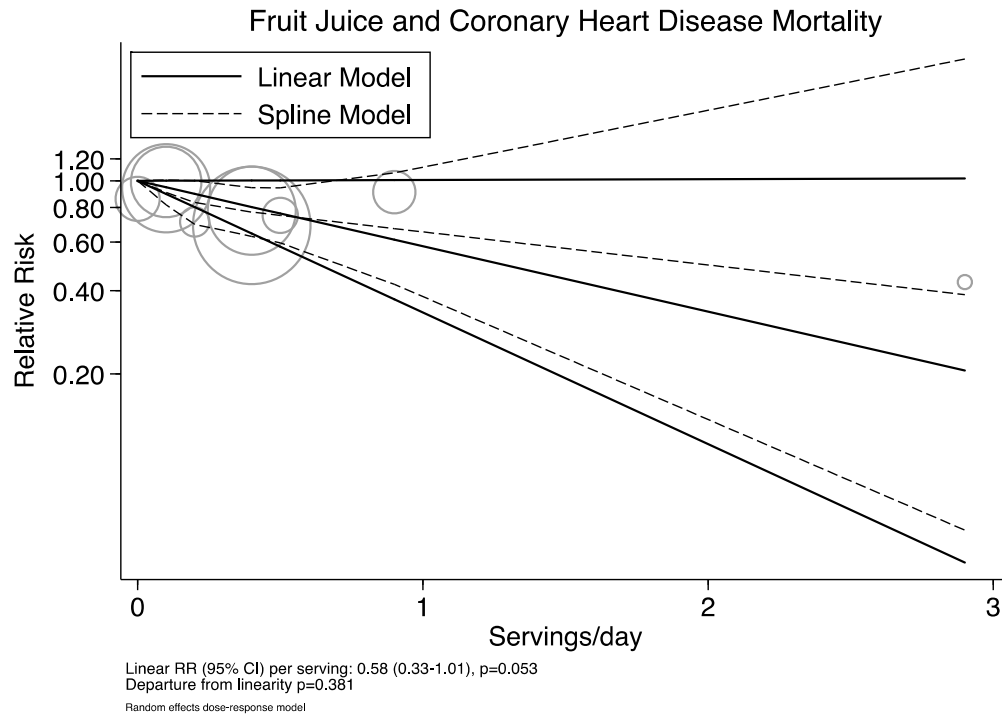


Figure S109. Linear and cubic-spline dose-response relation between increasing fruit juice intake and coronary heart disease mortality. Linear dose-response data was modeled using the Greenland and Longnecker²³ method to estimate the covariances of multivariable-adjusted relative risk. Cubic spline data were modeled with fixed-effects restricted cubic spline with 3 knots and using the Greenland and Longnecker²³ method to estimate the covariances of multivariable-adjusted relative risk. All data was kept on the original dose scale. The fitted trend for each model is represented by a central line (solid lines for linear model; dashed lines for cubic spline model) with 95% confidence intervals represented by the outer lines. Individual observations are represented by the circles, with the weight of the study in the overall analysis represented by the size of the circles.

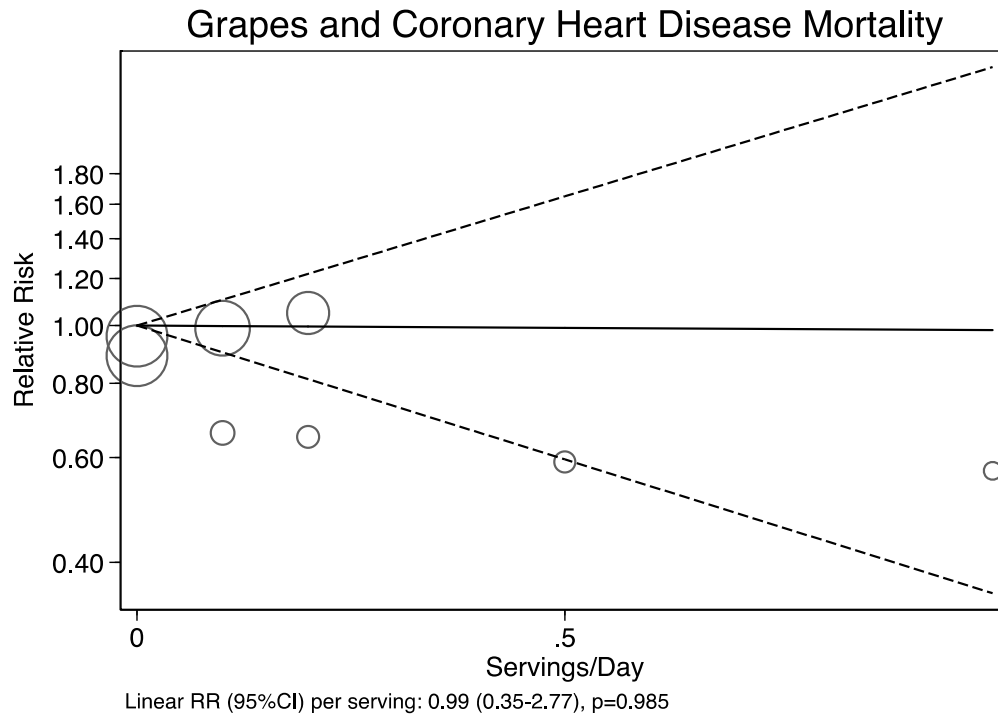


Figure S110. Linear dose-response relation between increasing grape intake and coronary heart disease mortality. Linear dose-response data was modeled using the Greenland and Longnecker²³ method to estimate the covariances of multivariable-adjusted relative risk, with kept on the original dose scale. Dashed lines represent the pointwise 95% confidence intervals for the fitted linear trend represented by a solid line. Individual observations are represented by the circles, with the weight of the study in the overall analysis represented by the size of the circles.

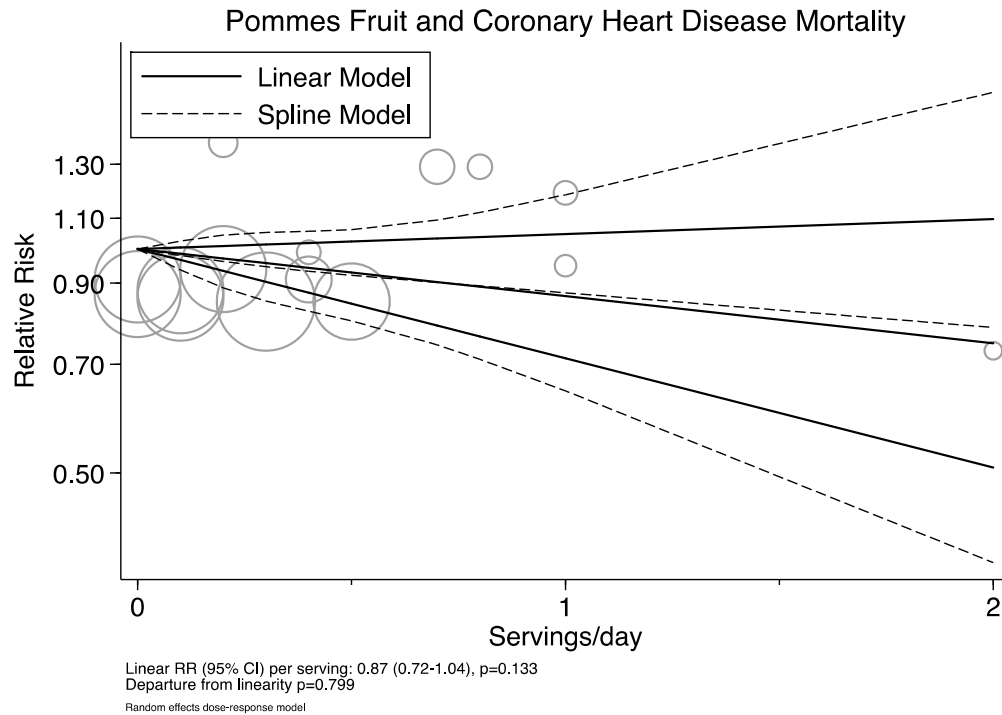


Figure S111. Linear and cubic-spline dose-response relation between increasing pommes intake and coronary heart disease mortality. Linear dose-response data was modeled using the Greenland and Longnecker²³ method to estimate the covariances of multivariable-adjusted relative risk. Cubic spline data were modeled with fixed-effects restricted cubic spline with 3 knots and using the Greenland and Longnecker²³ method to estimate the covariances of multivariable-adjusted relative risk. All data was kept on the original dose scale. The fitted trend for each model is represented by a central line (solid lines for linear model; dashed lines for cubic spline model) with 95% confidence intervals represented by the outer lines. Individual observations are represented by the circles, with the weight of the study in the overall analysis represented by the size of the circles.

Allium Vegetables and Coronary Heart Disease Mortality

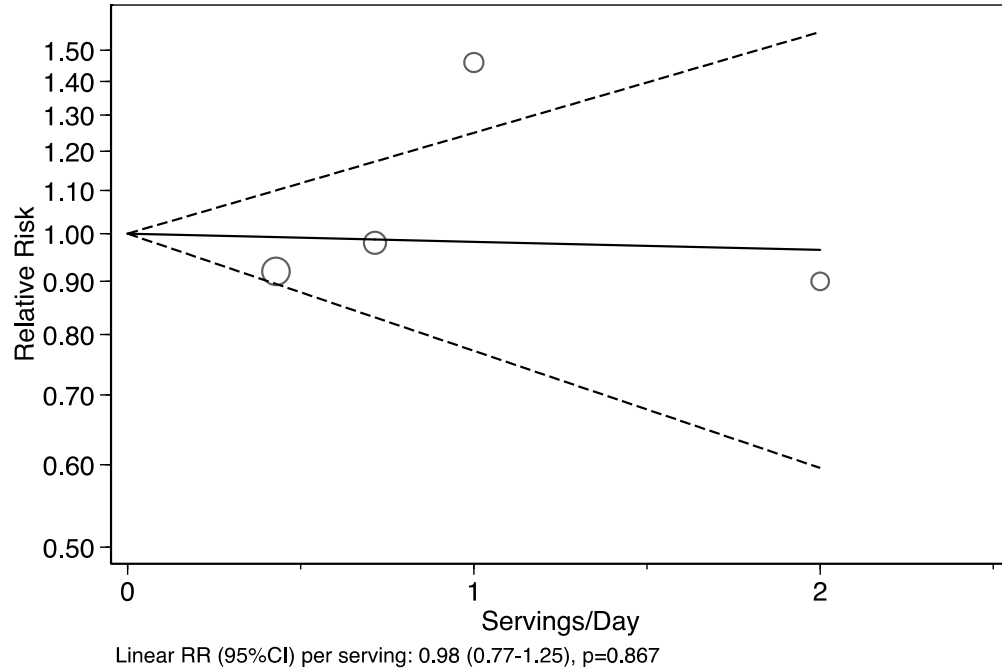


Figure S112. Linear dose-response relation between increasing intake of allium vegetables and coronary heart disease mortality. Linear dose-response data was modeled using the Greenland and Longnecker²³ method to estimate the covariances of multivariable-adjusted relative risk, with kept on the original dose scale. Dashed lines represent the pointwise 95% confidence intervals for the fitted linear trend represented by a solid line. Individual observations are represented by the circles, with the weight of the study in the overall analysis represented by the size of the circles.

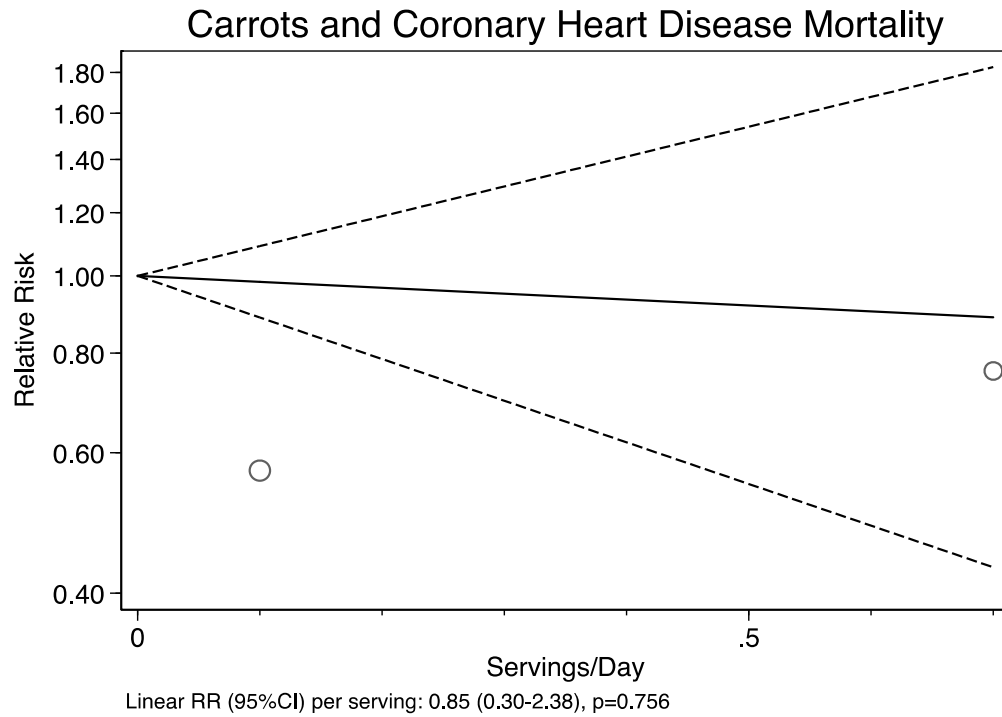


Figure S113. Linear dose-response relation between increasing intake of carrots and coronary heart disease mortality. Linear dose-response data was modeled using the Greenland and Longnecker²³ method to estimate the covariances of multivariable-adjusted relative risk, with kept on the original dose scale. Dashed lines represent the pointwise 95% confidence intervals for the fitted linear trend represented by a solid line. Individual observations are represented by the circles, with the weight of the study in the overall analysis represented by the size of the circles.

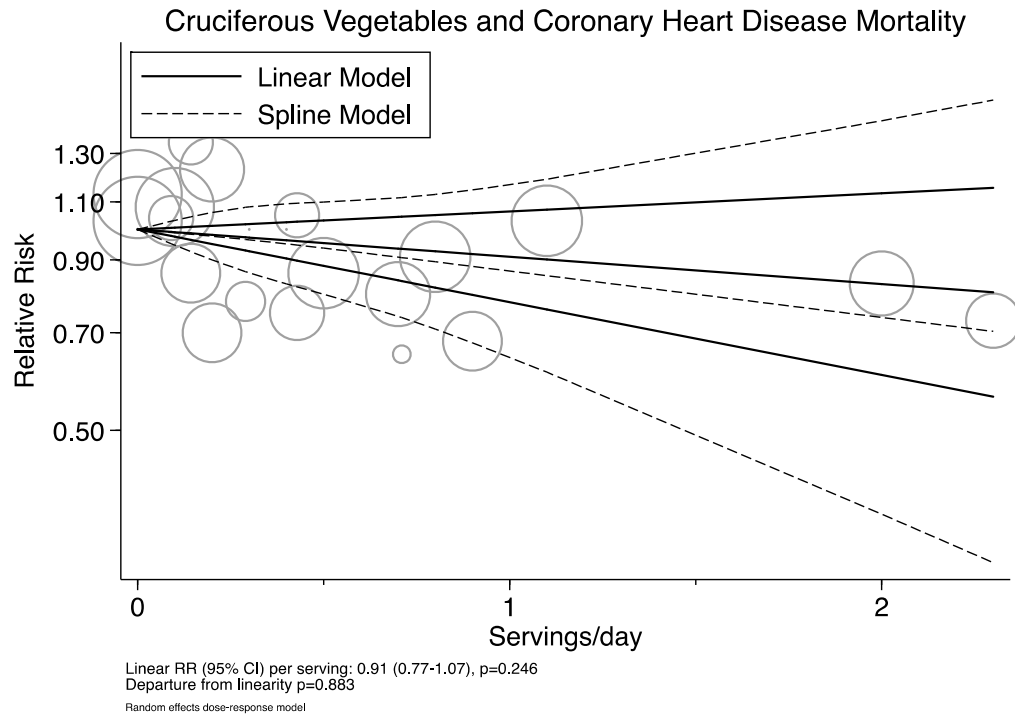


Figure S114. Linear and cubic-spline dose-response relation between increasing intake of cruciferous vegetables and coronary heart disease mortality. Linear dose-response data was modeled using the Greenland and Longnecker²³ method to estimate the covariances of multivariable-adjusted relative risk. Cubic spline data were modeled with fixed-effects restricted cubic spline with 3 knots and using the Greenland and Longnecker²³ method to estimate the covariances of multivariable-adjusted relative risk. All data was kept on the original dose scale. The fitted trend for each model is represented by a central line (solid lines for linear model; dashed lines for cubic spline model) with 95% confidence intervals represented by the outer lines. Individual observations are represented by the circles, with the weight of the study in the overall analysis represented by the size of the circles.

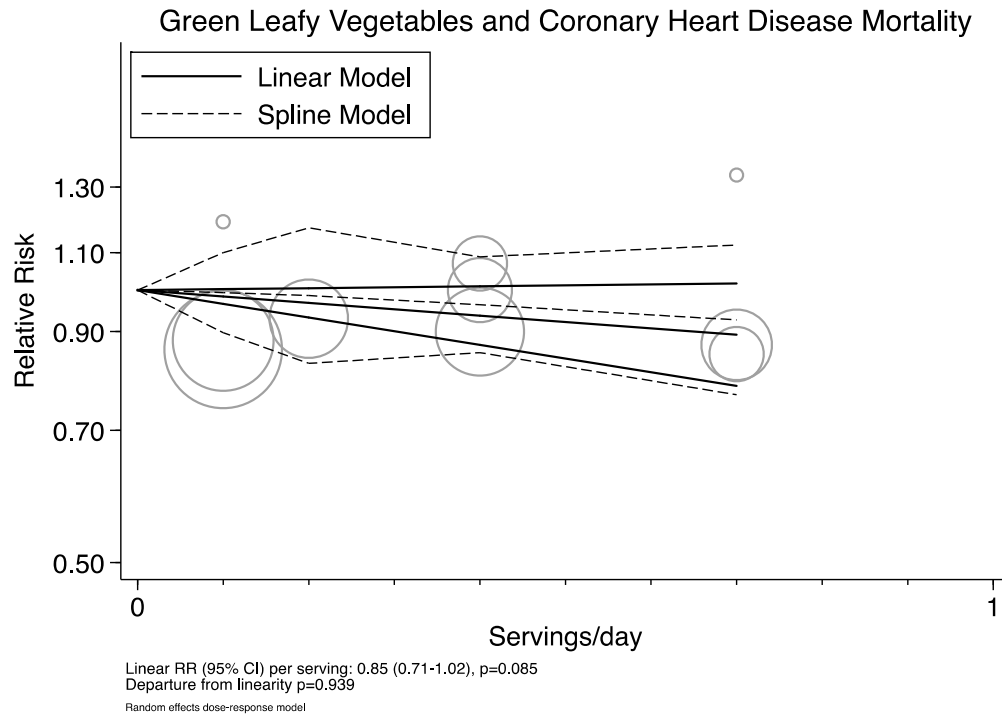


Figure S115. Linear dose-response relation between increasing intake of green leafy vegetables and coronary heart disease mortality. Linear dose-response data was modeled using the Greenland and Longnecker²³ method to estimate the covariances of multivariable-adjusted relative risk, with kept on the original dose scale. Dashed lines represent the pointwise 95% confidence intervals for the fitted linear trend represented by a solid line. Individual observations are represented by the circles, with the weight of the study in the overall analysis represented by the size of the circles.

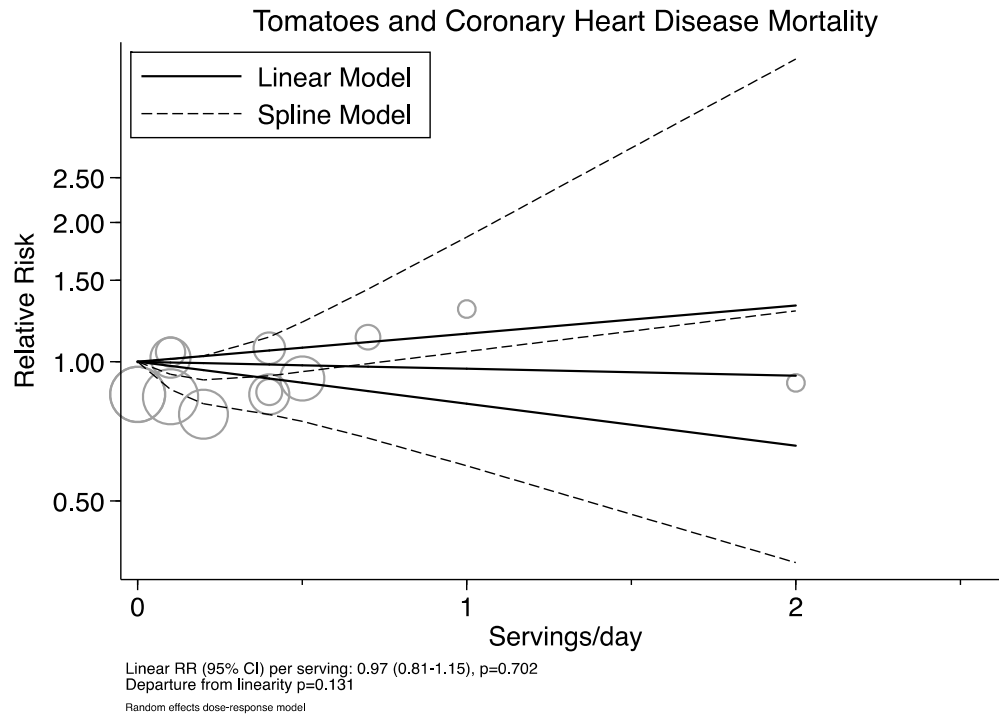
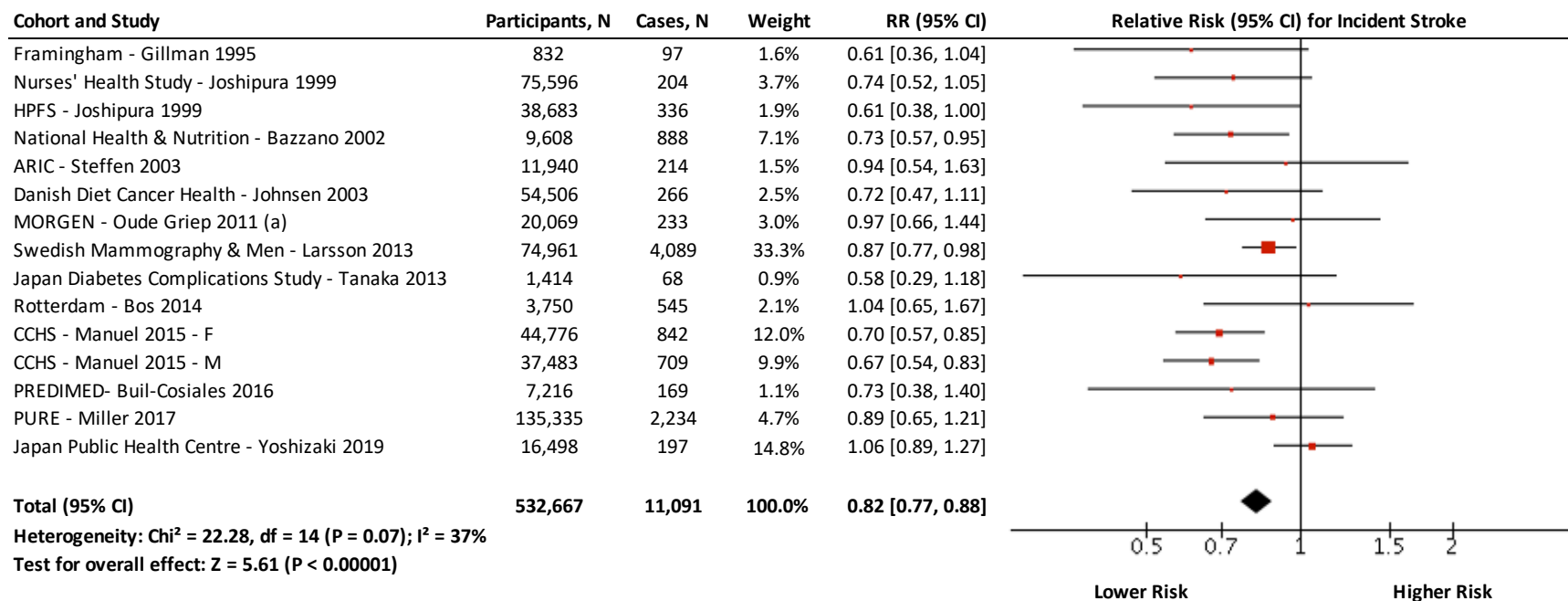


Figure S116. Linear dose-response relation between increasing tomato intake and coronary heart disease mortality. Linear dose-response data was modeled using the Greenland and Longnecker²³ method to estimate the covariances of multivariable-adjusted relative risk, with kept on the original dose scale. Dashed lines represent the pointwise 95% confidence intervals for the fitted linear trend represented by a solid line. Individual observations are represented by the circles, with the weight of the study in the overall analysis represented by the size of the circles.

TOTAL FRUIT AND VEGETABLES AND STROKE INCIDENCE

A. Fixed Effects



B. Random Effects

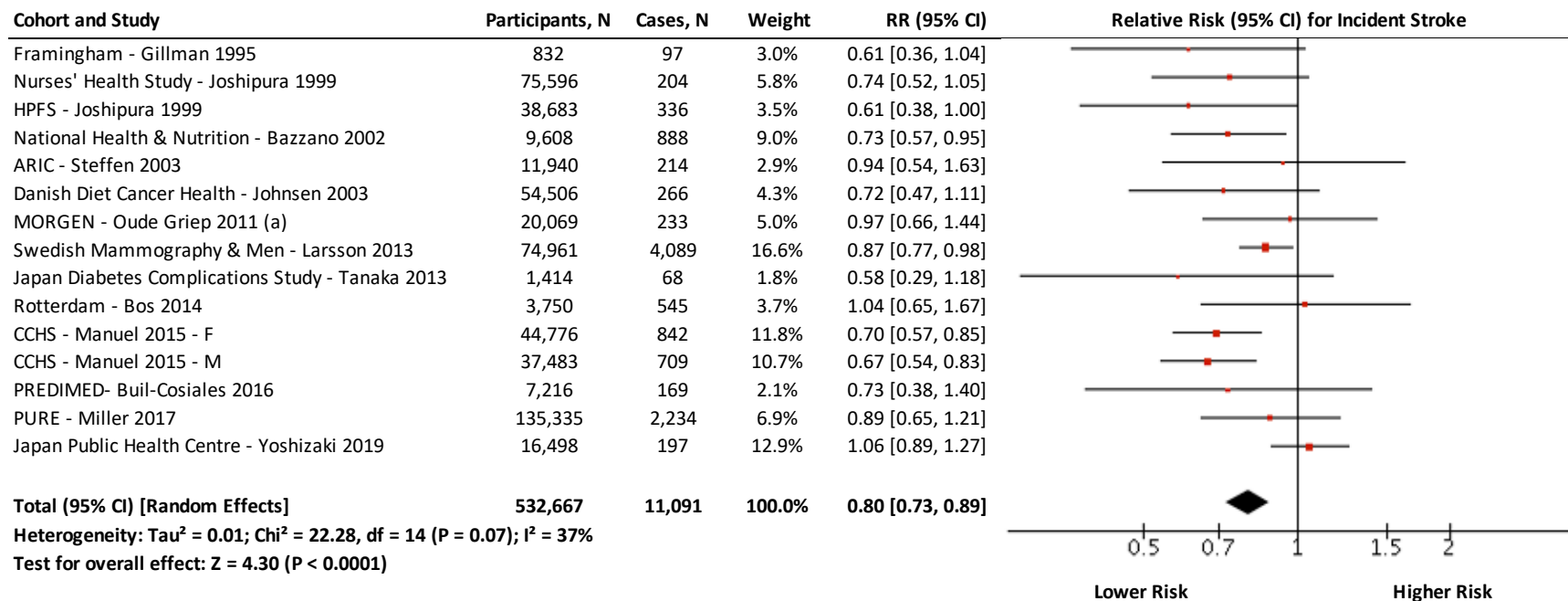
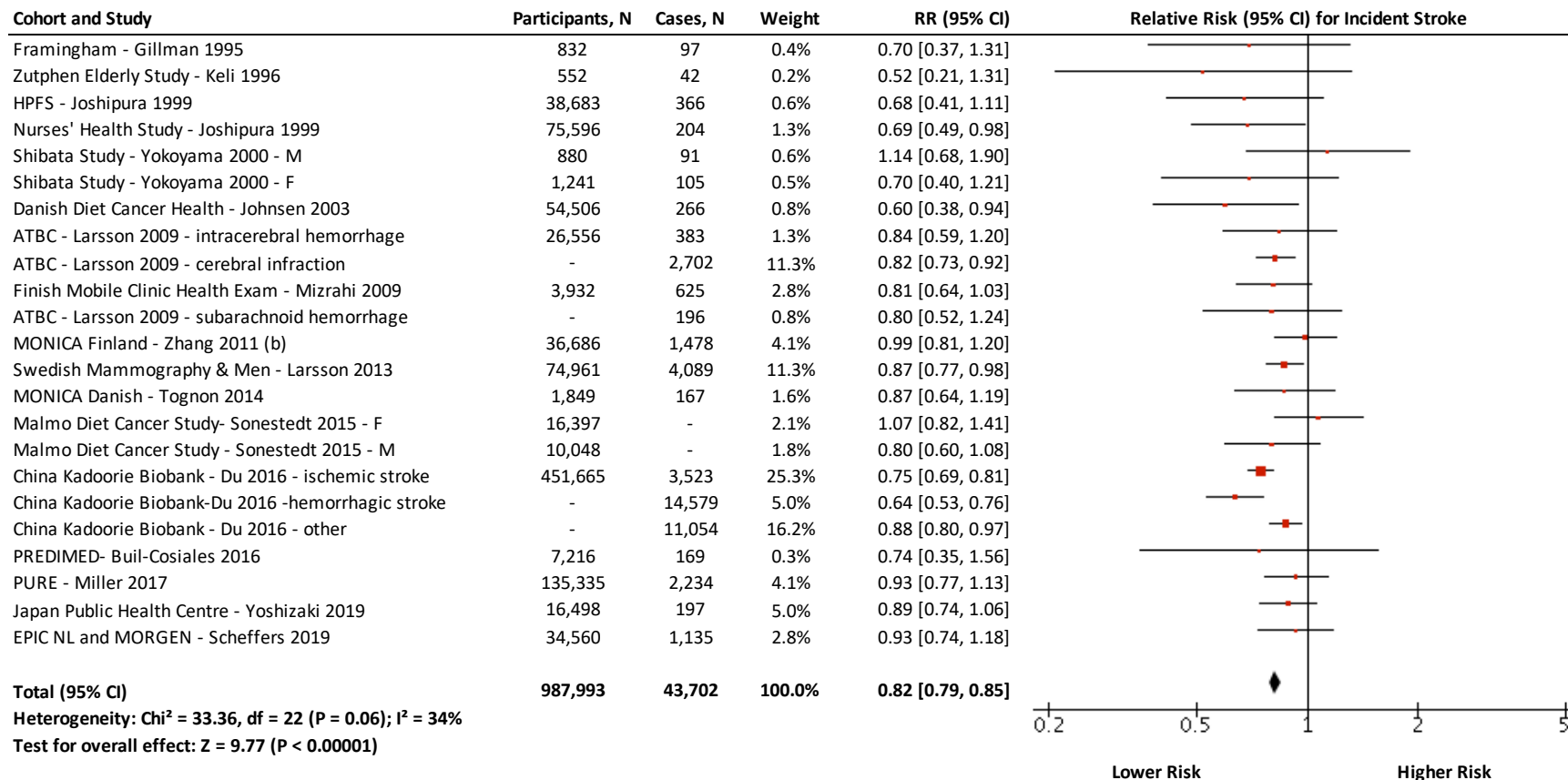


Figure S117. Relation between total fruit and vegetables intake and stroke incidence (highest vs. lowest level of intake). All results are presented as relative risk (RR) with 95% confidence intervals (95% CI). Pooled risk estimate is represented by the black diamond using (A) fixed effects and (B) random effects models. Inter-study heterogeneity was assessed using the Cochran Q statistic (χ^2) at a significance level of $p < 0.10$, and quantified by I^2 , with values $\geq 50\%$ indicating substantial heterogeneity.

FRUIT AND STROKE INCIDENCE

A. Fixed Effects



B. Random Effects

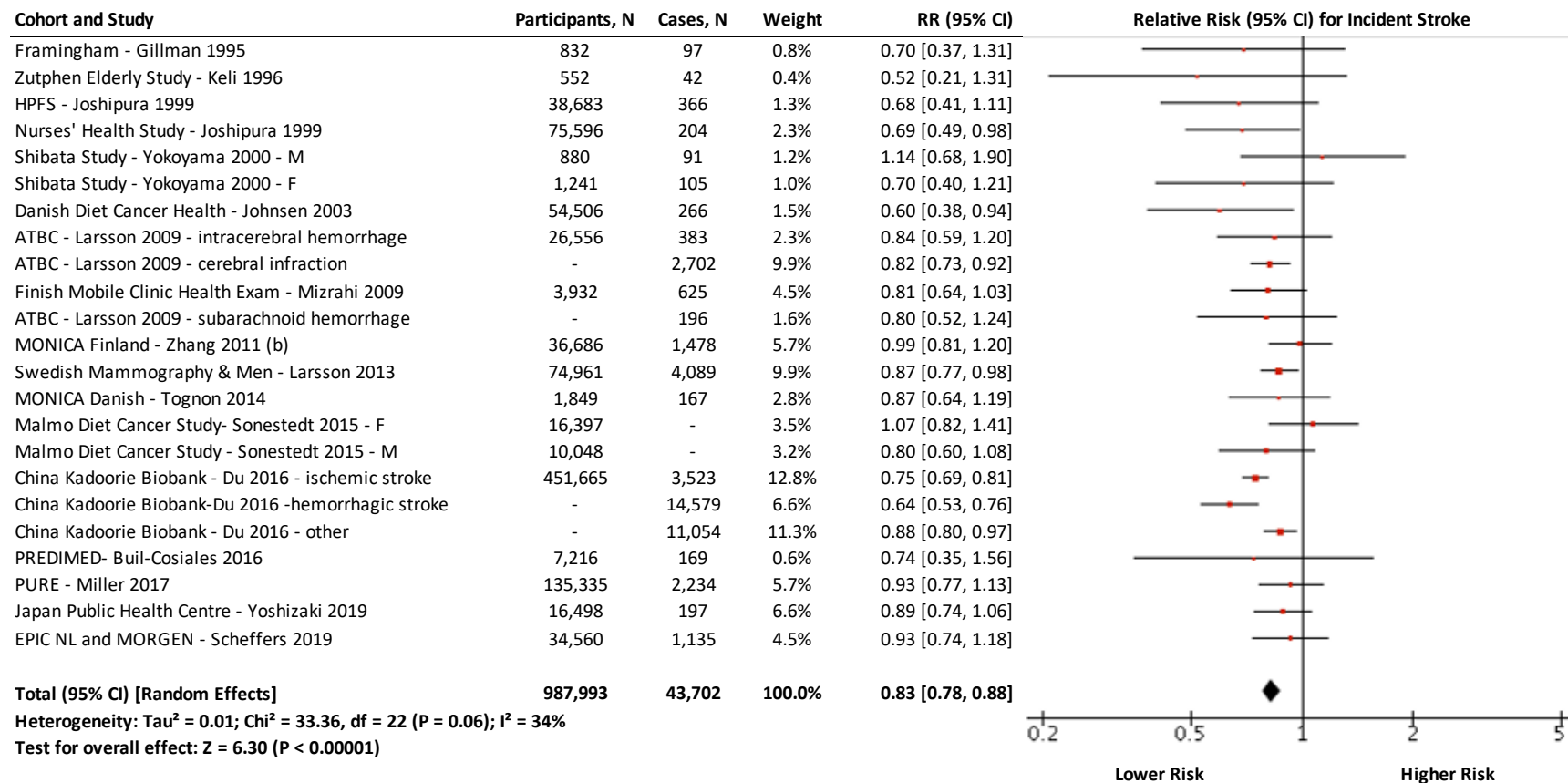
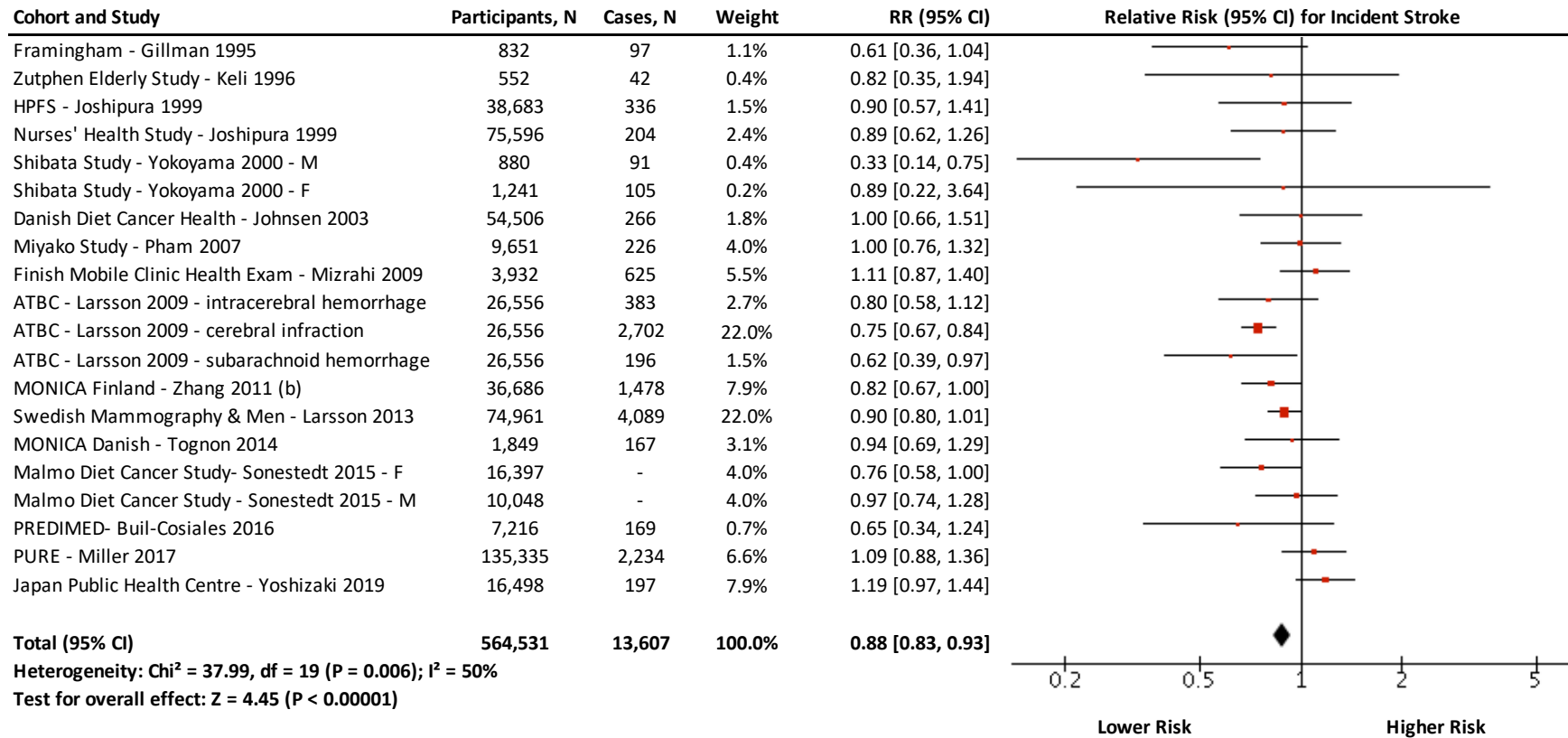


Figure S118. Relation between fruit intake and stroke incidence (highest vs. lowest level of intake). All results are presented as relative risk (RR) with 95% confidence intervals (95% CI). Pooled risk estimate is represented by the black diamond using (A) fixed effects and (B) random effects models. Inter-study heterogeneity was assessed using the Cochran Q statistic (χ^2) at a significance level of $p < 0.10$, and quantified by I^2 , with values $\geq 50\%$ indicating substantial heterogeneity.

VEGETABLES AND STROKE INCIDENCE

A. Fixed Effects



B. Random Effects

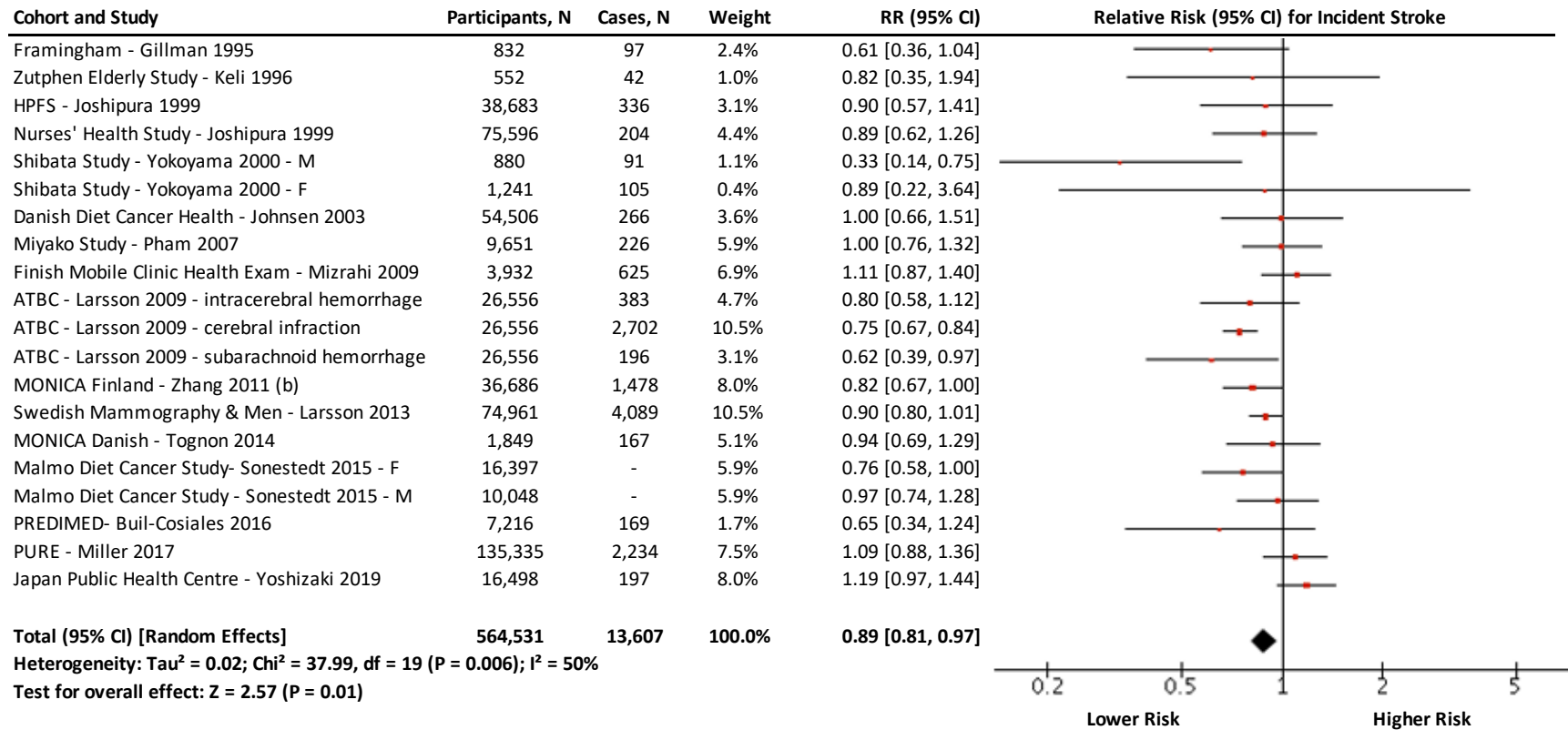
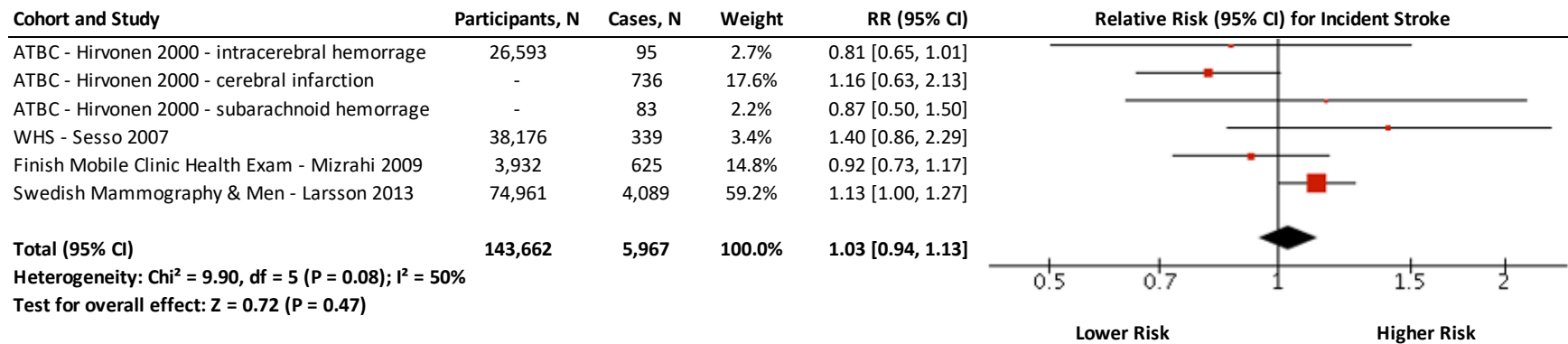


Figure S119. Relation between intake of vegetables and stroke incidence (highest vs. lowest level of intake). All results are presented as relative risk (RR) with 95% confidence intervals (95% CI). Pooled risk estimate is represented by the black diamond using (A) fixed effects and (B) random effects models. Inter-study heterogeneity was assessed using the Cochran Q statistic (χ^2) at a significance level of $p < 0.10$, and quantified by I^2 , with values $\geq 50\%$ indicating substantial heterogeneity.

BERRIES AND STROKE INCIDENCE

A. Fixed Effects



B. Random Effects

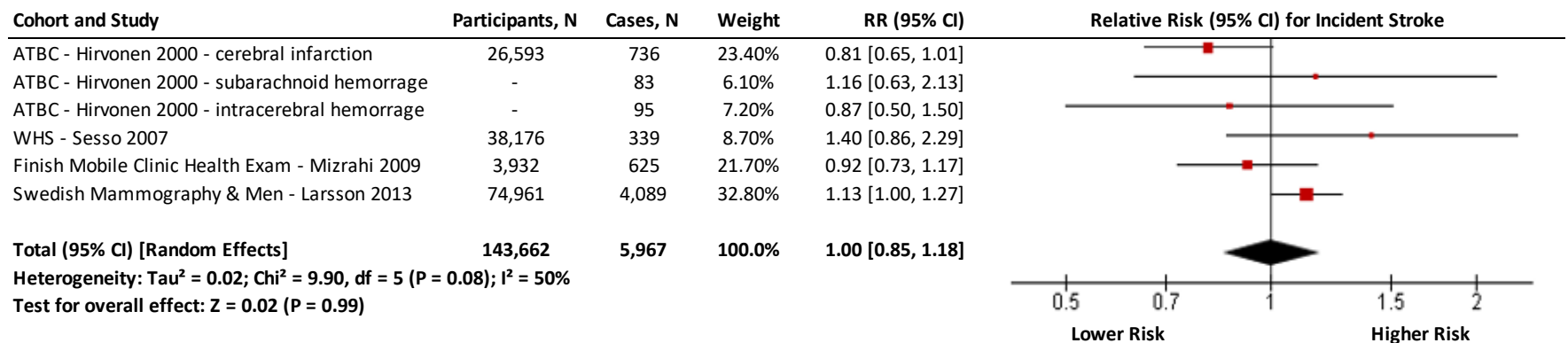
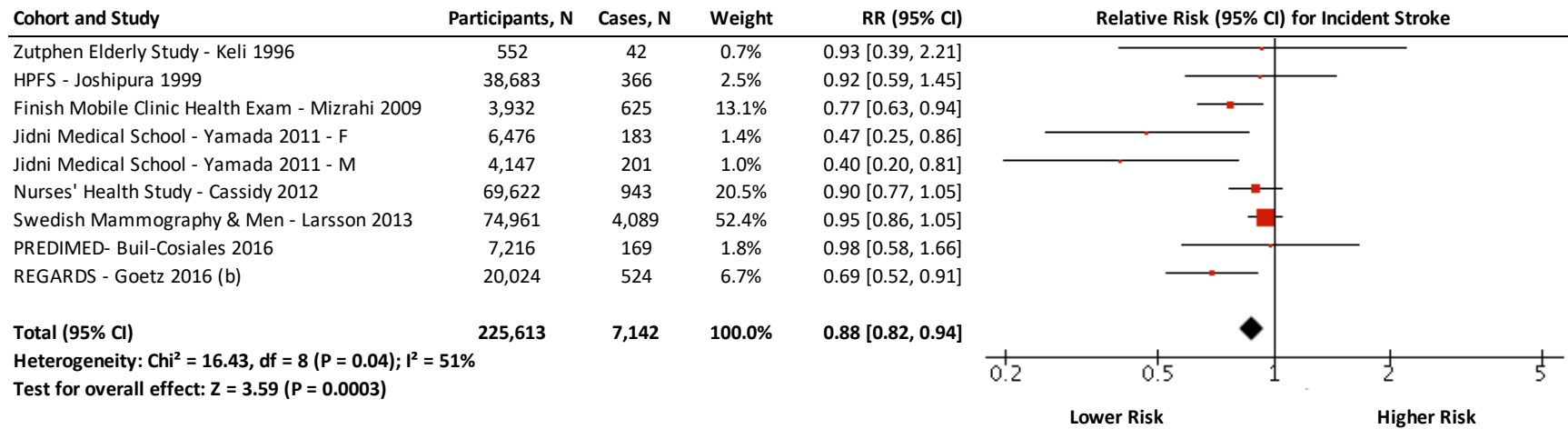


Figure S120. Relation between intake of berries and stroke incidence (highest vs. lowest level of intake). All results are presented as relative risk (RR) with 95% confidence intervals (95% CI). Pooled risk estimate is represented by the black diamond using (A) fixed effects and (B) random effects models. Inter-study heterogeneity was assessed using the Cochran Q statistic (χ^2) at a significance level of $p < 0.10$, and quantified by I^2 , with values $\geq 50\%$ indicating substantial heterogeneity.

CITRUS FRUIT AND STROKE INCIDENCE

A. Fixed Effects



B. Random Effects

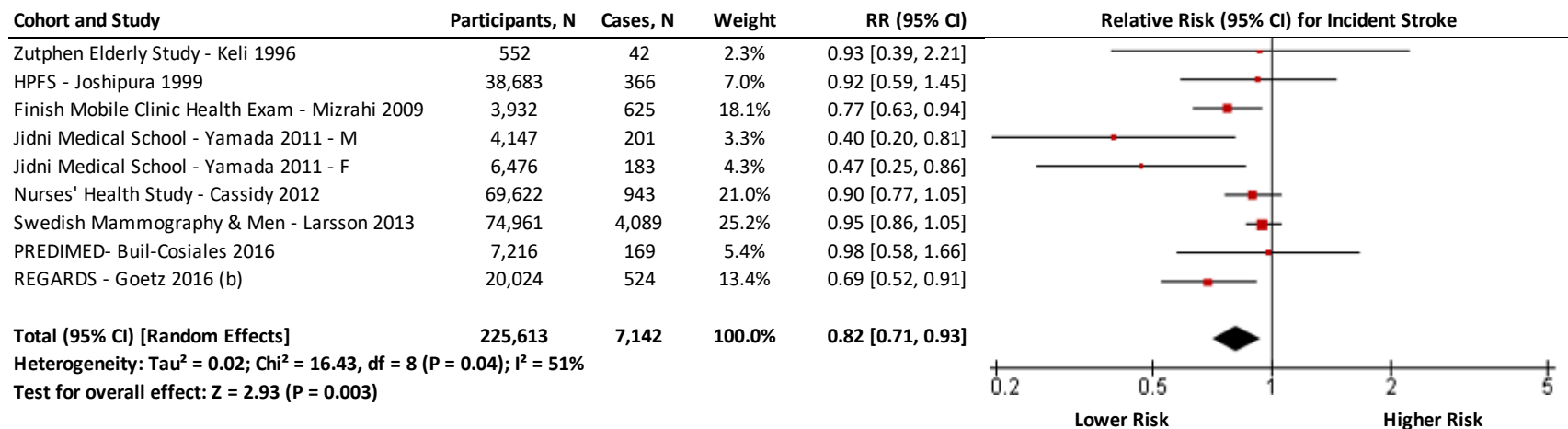
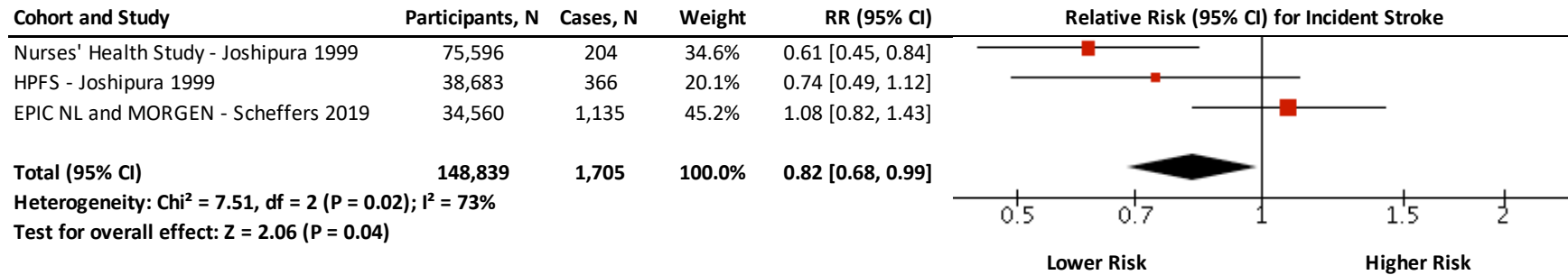


Figure S121. Relation between citrus fruit intake and stroke incidence (highest vs. lowest level of intake). All results are presented as relative risk (RR) with 95% confidence intervals (95% CI). Pooled risk estimate is represented by the black diamond using (A) fixed effects and (B) random effects models. Inter-study heterogeneity was assessed using the Cochran Q statistic (χ^2) at a significance level of $p < 0.10$, and quantified by I^2 , with values $\geq 50\%$ indicating substantial heterogeneity.

FRUIT JUICE AND STROKE INCIDENCE

A. Fixed Effects



B. Random Effects

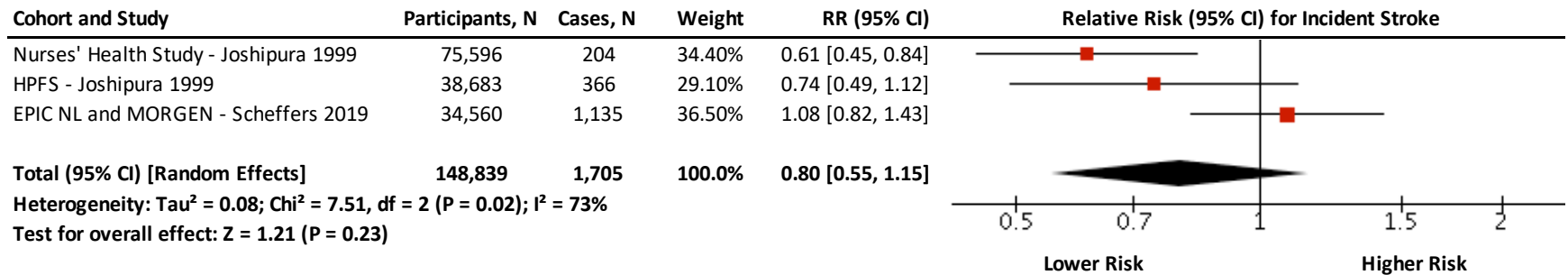
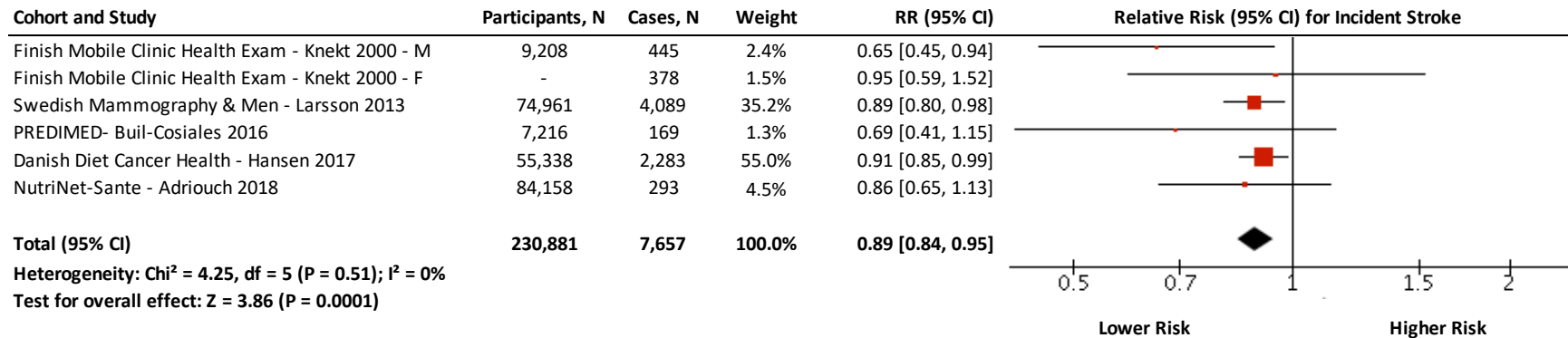


Figure S122. Relation between intake of fruit juice and stroke incidence (highest vs. lowest level of intake). All results are presented as relative risk (RR) with 95% confidence intervals (95% CI). Pooled risk estimate is represented by the black diamond using (A) fixed effects and (B) random effects models. Inter-study heterogeneity was assessed using the Cochran Q statistic (χ^2) at a significance level of $p < 0.10$, and quantified by I^2 , with values $\geq 50\%$ indicating substantial heterogeneity.

POMMES AND STROKE INCIDENCE

A. Fixed Effects



B. Random Effects

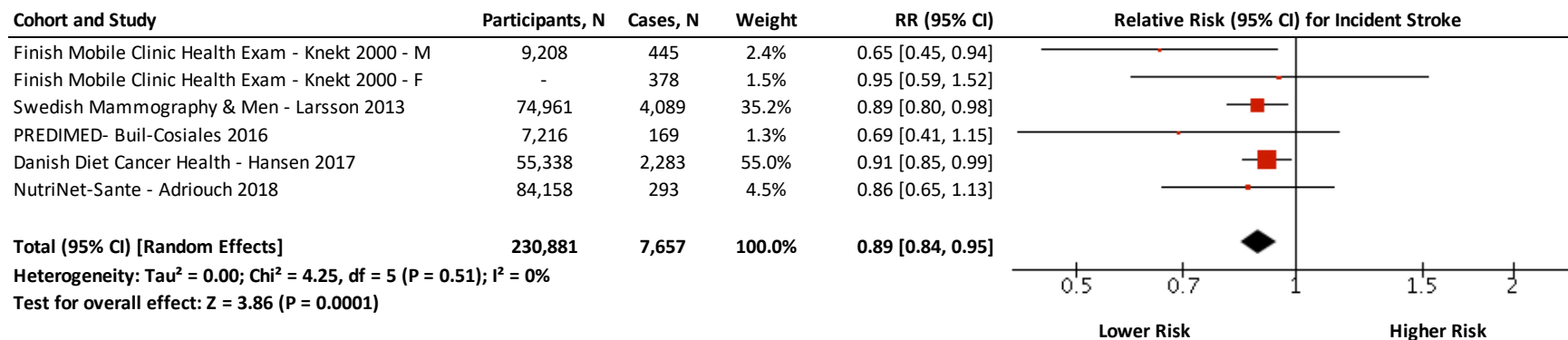
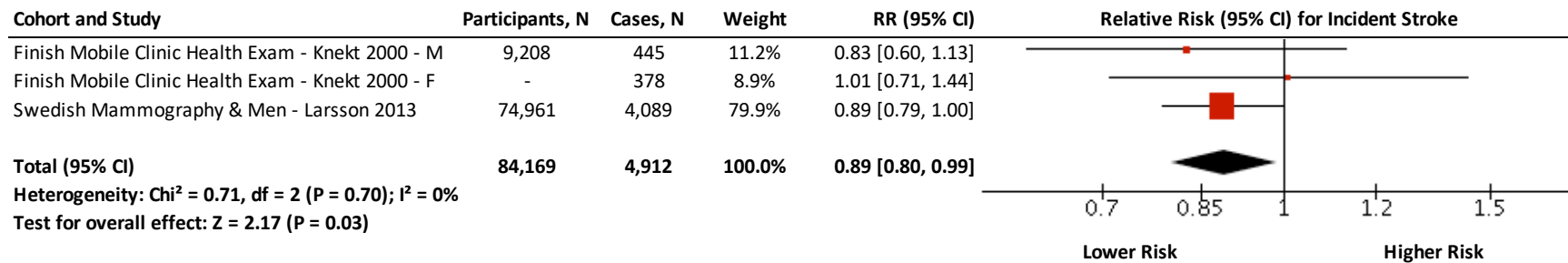


Figure S123. Relation between intake of pomes fruit and stroke incidence (highest vs. lowest level of intake). All results are presented as relative risk (RR) with 95% confidence intervals (95% CI). Pooled risk estimate is represented by the black diamond using (A) fixed effects and (B) random effects models. Inter-study heterogeneity was assessed using the Cochran Q statistic (χ^2) at a significance level of $p < 0.10$, and quantified by I^2 , with values $\geq 50\%$ indicating substantial heterogeneity.

ALLIUM VEGETABLES AND STROKE INCIDENCE

A. Fixed Effects



B. Random Effects

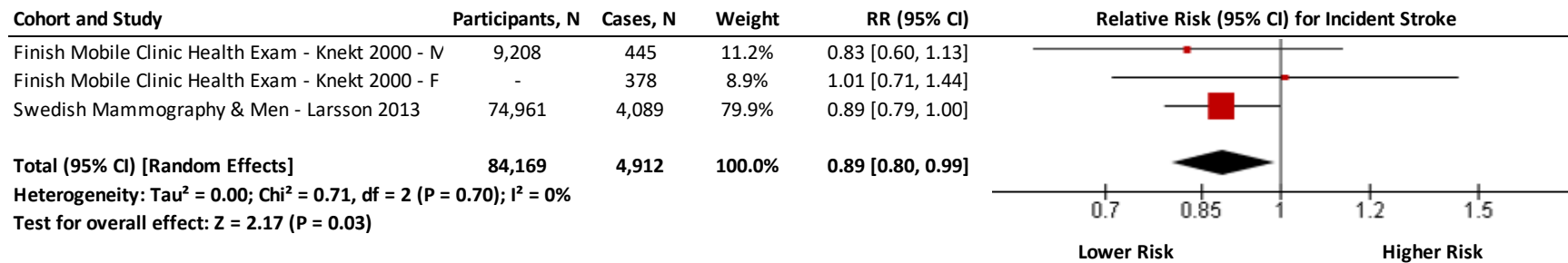
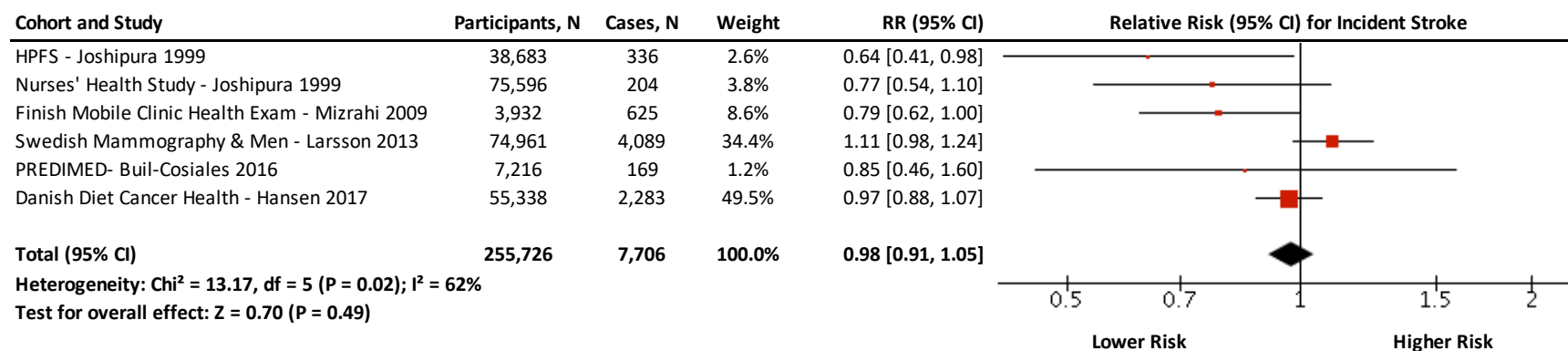


Figure S124. Relation between intake of allium vegetables and stroke incidence (highest vs. lowest level of intake). All results are presented as relative risk (RR) with 95% confidence intervals (95% CI). Pooled risk estimate is represented by the black diamond using (A) fixed effects and (B) random effects models. Inter-study heterogeneity was assessed using the Cochran Q statistic (χ^2) at a significance level of $p < 0.10$, and quantified by I^2 , with values $\geq 50\%$ indicating substantial heterogeneity.

CRUCIFEROUS VEGETABLES AND STROKE INCIDENCE

A. Fixed Effects



B. Random Effects

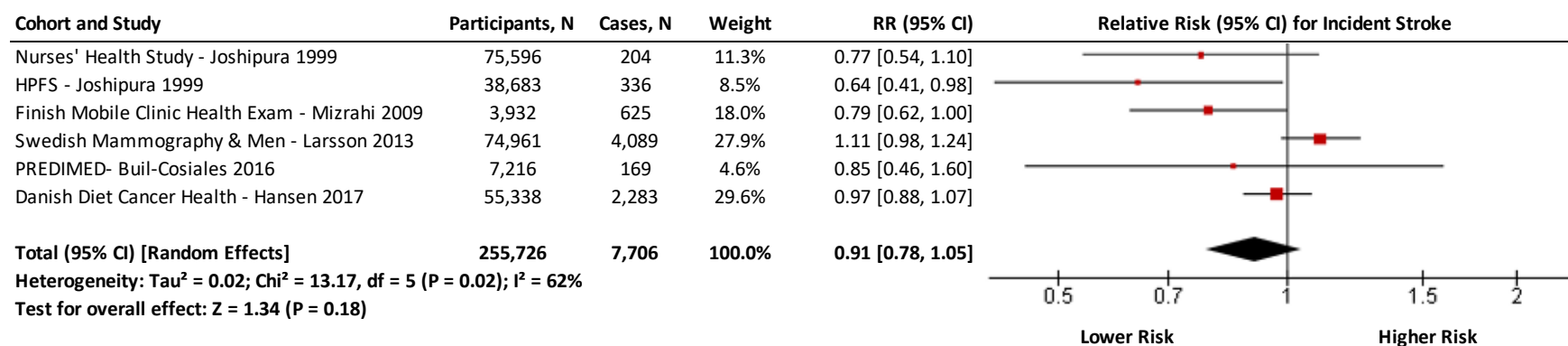
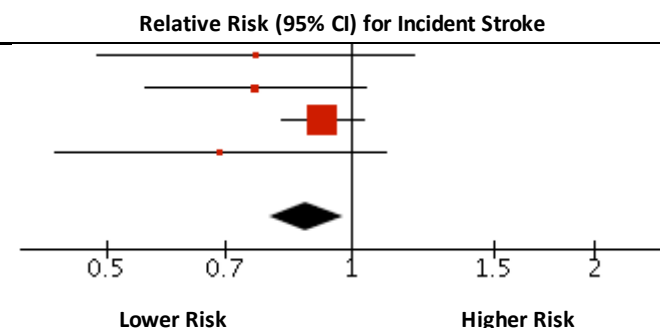


Figure S125. Relation between intake of cruciferous vegetables and stroke incidence (highest vs. lowest level of intake). All results are presented as relative risk (RR) with 95% confidence intervals (95% CI). Pooled risk estimate is represented by the black diamond using (A) fixed effects and (B) random effects models. Inter-study heterogeneity was assessed using the Cochran Q statistic (χ^2) at a significance level of $p < 0.10$, and quantified by I^2 , with values $\geq 50\%$ indicating substantial heterogeneity.

GREEN LEAFY VEGETABLES AND STROKE INCIDENCE

A. Fixed Effects

Cohort and Study	Participants, N	Cases, N	Weight	RR (95% CI)
HPFS - Joshipura 1999	38,683	336	5.4%	0.76 [0.49, 1.20]
Nurses' Health Study - Joshipura 1999	75,596	204	11.1%	0.76 [0.56, 1.04]
Swedish Mammography & Men - Larsson 2013	74,961	4,089	78.7%	0.92 [0.82, 1.04]
PREDIMED- Buil-Cosiales 2016	7,216	169	4.9%	0.69 [0.43, 1.11]
Total (95% CI)	196,456	4,798	100.0%	0.88 [0.79, 0.98]
Heterogeneity: $\chi^2 = 2.82$, $df = 3$ ($P = 0.42$); $I^2 = 0\%$				
Test for overall effect: $Z = 2.36$ ($P = 0.02$)				



B. Random Effects

Cohort and Study	Participants, N	Cases, N	Weight	RR (95% CI)
Nurses' Health Study - Joshipura 1999	75,596	204	11.1%	0.76 [0.56, 1.04]
HPFS - Joshipura 1999	38,683	336	5.4%	0.76 [0.49, 1.20]
Swedish Mammography & Men - Larsson 2013	74,961	4,089	78.7%	0.92 [0.82, 1.04]
PREDIMED- Buil-Cosiales 2016	7,216	169	4.9%	0.69 [0.43, 1.11]
Total (95% CI) [Random Effects]	196,456	4,798	100.0%	0.88 [0.79, 0.98]
Heterogeneity: $\tau^2 = 0.00$; $\chi^2 = 2.82$, $df = 3$ ($P = 0.42$); $I^2 = 0\%$				
Test for overall effect: $Z = 2.36$ ($P = 0.02$)				

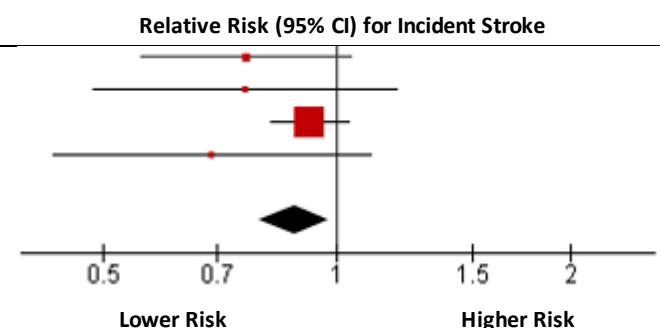


Figure S126. Relation between intake of green leafy vegetables and stroke incidence (highest vs. lowest level of intake). All results are presented as relative risk (RR) with 95% confidence intervals (95% CI). Pooled risk estimate is represented by the black diamond using (A) fixed effects and (B) random effects models. Inter-study heterogeneity was assessed using the Cochran Q statistic (χ^2) at a significance level of $p < 0.10$, and quantified by I^2 , with values $\geq 50\%$ indicating substantial heterogeneity.

TOMATOES AND STROKE INCIDENCE

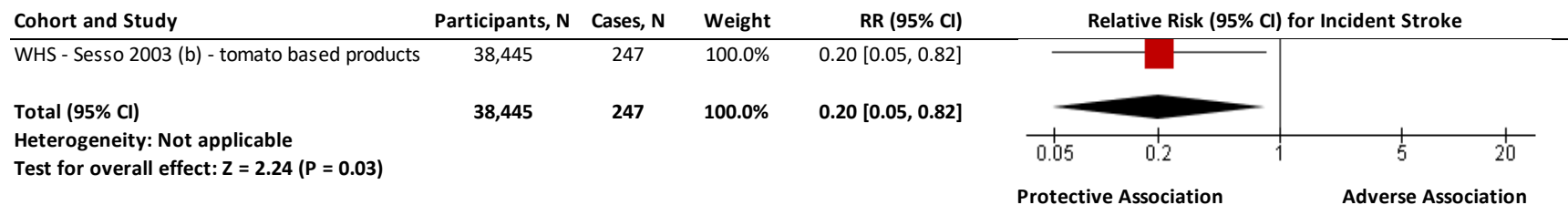
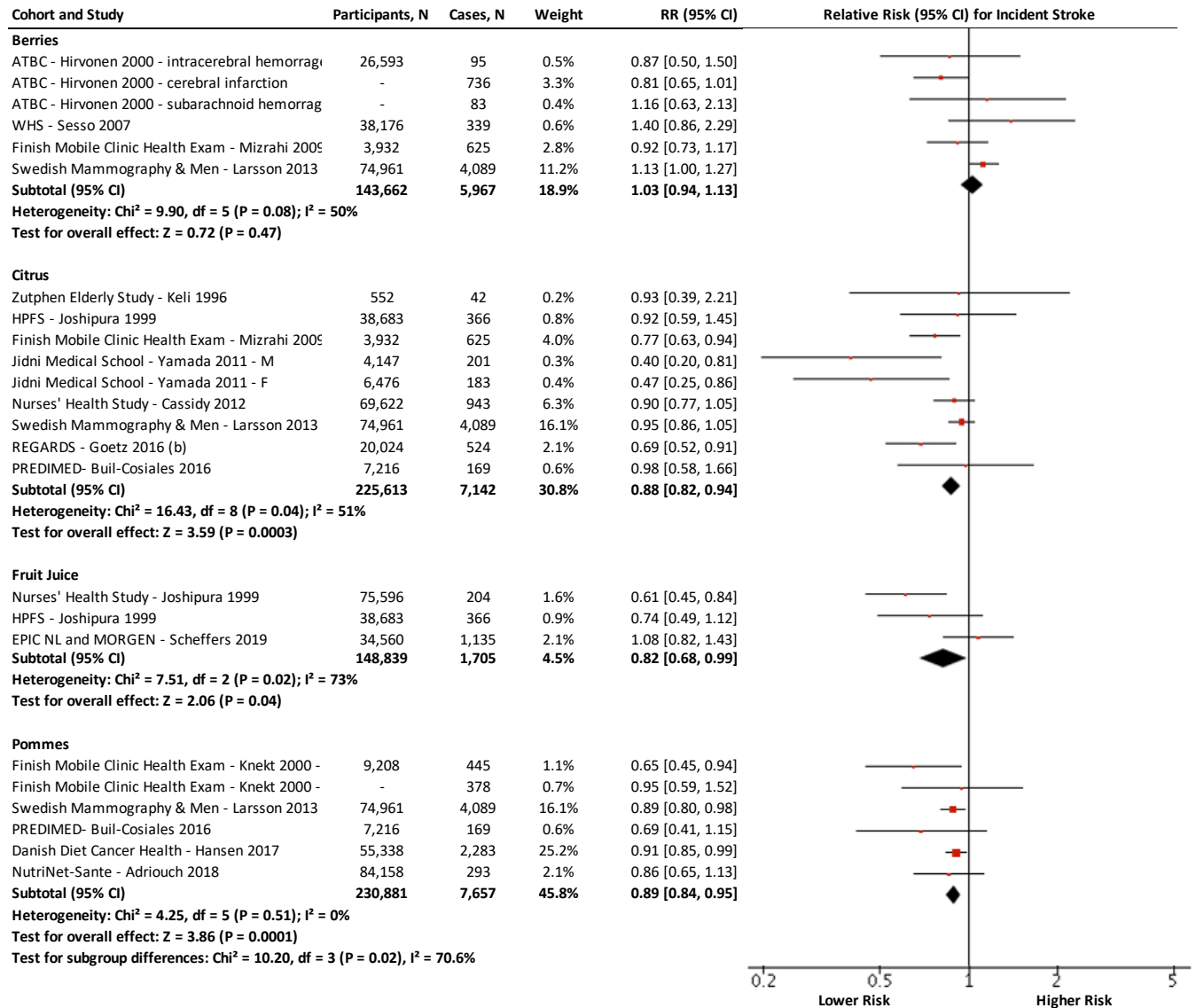


Figure S127. Relation between intake of tomatoes and stroke incidence (highest vs. lowest level of intake). All results are presented as relative risk (RR) with 95% confidence intervals (95% CI). Pooled risk estimate is represented by the black diamond. Inter-study heterogeneity was assessed using the Cochran Q statistic (χ^2) at a significance level of $p < 0.10$, and quantified by I, with values $\geq 50\%$ indicating substantial heterogeneity.

A. Fixed Effects



B. Random Effects

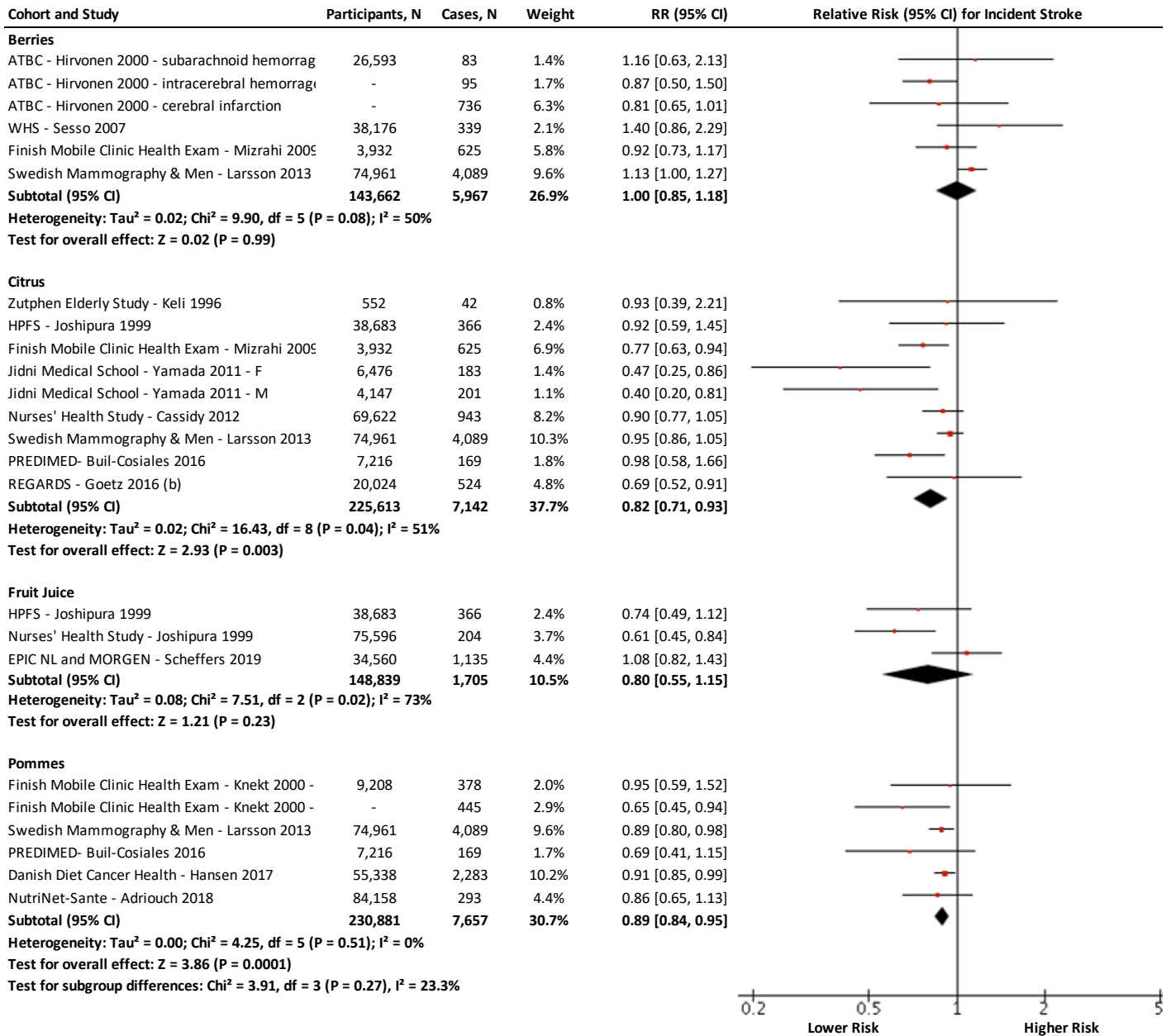
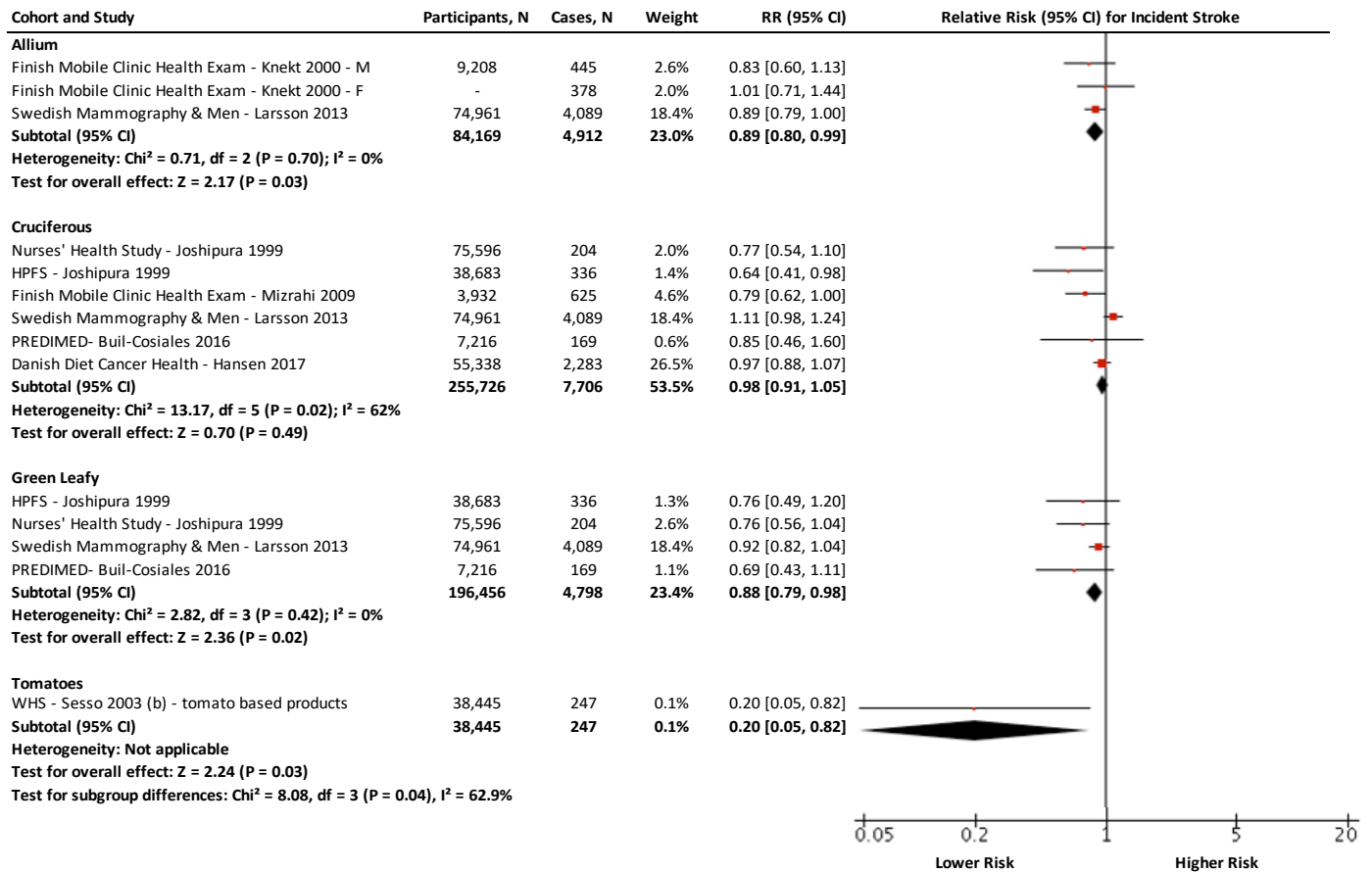


Figure S128. Relation between sources of fruit and stroke incidence (highest vs. lowest level of intake). All results are presented as relative risk (RR) with 95% confidence intervals (95% CI). Pooled risk estimate is represented by the black diamond using (A) fixed effects and (B) random effects models. Inter-study heterogeneity was assessed using the Cochran Q statistic (Chi²) at a significance level of p<0.10, and quantified by I², with values ≥ 50% indicating substantial heterogeneity.

A. Fixed Effects



B. Random Effects

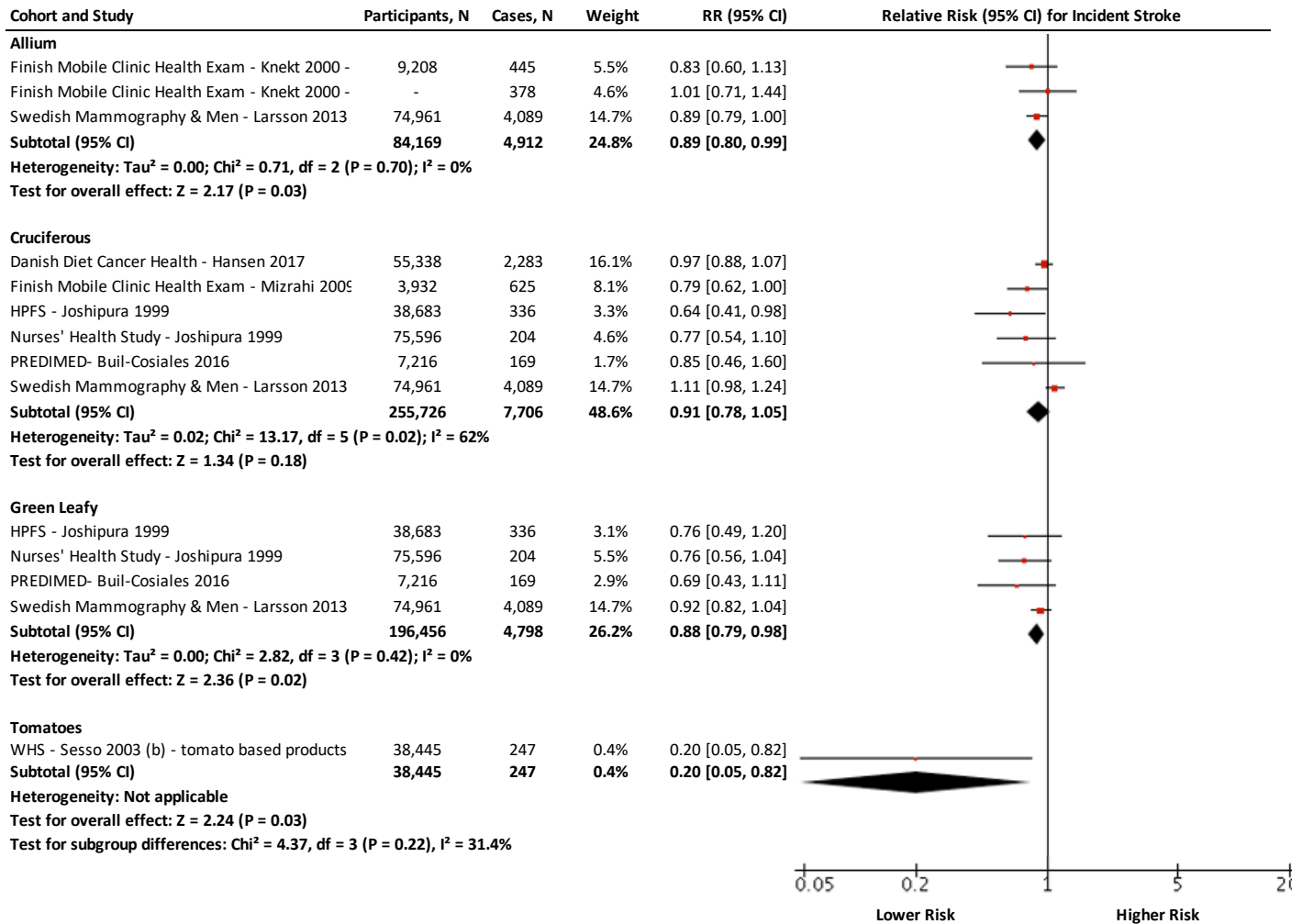
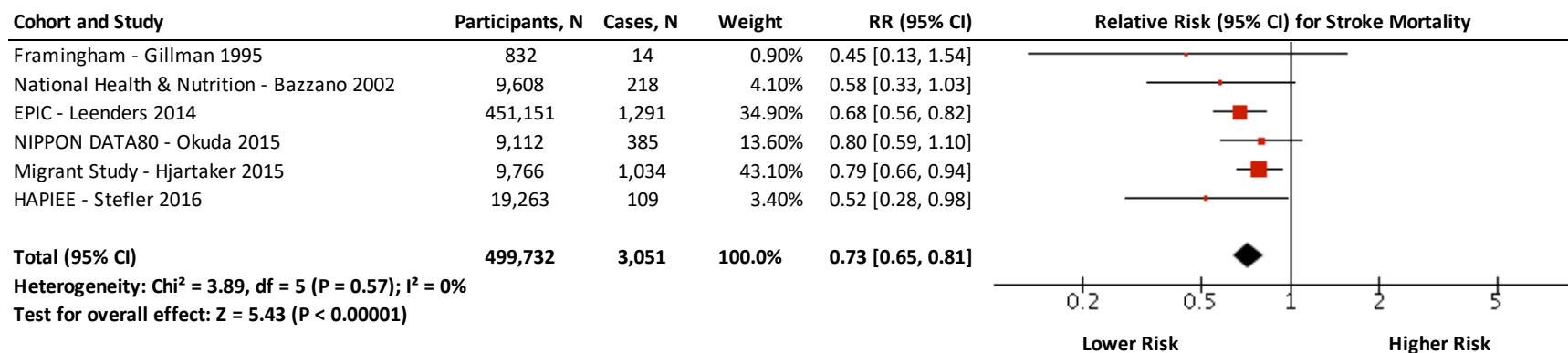


Figure S129. Relation between sources of vegetables and stroke incidence (highest vs. lowest level of intake). All results are presented as relative risk (RR) with 95% confidence intervals (95% CI). Pooled risk estimate is represented by the black diamond using (A) fixed effects and (B) random effects models. Inter-study heterogeneity was assessed using the Cochran Q statistic (Chi²) at a significance level of p<0.10, and quantified by I², with values ≥ 50% indicating substantial heterogeneity.

TOTAL FRUIT AND VEGETABLES AND STROKE MORTALITY

A. Fixed Effects



B. Random Effects

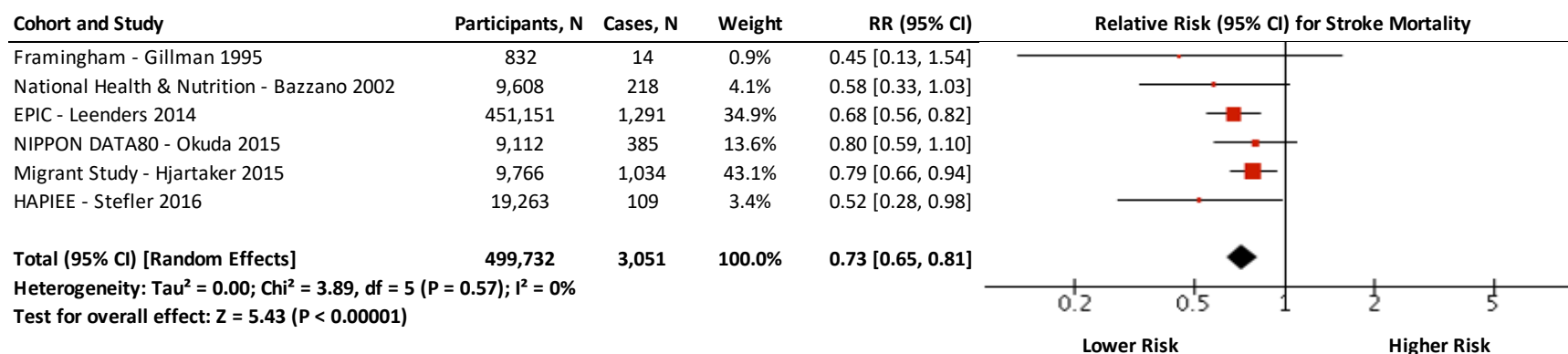
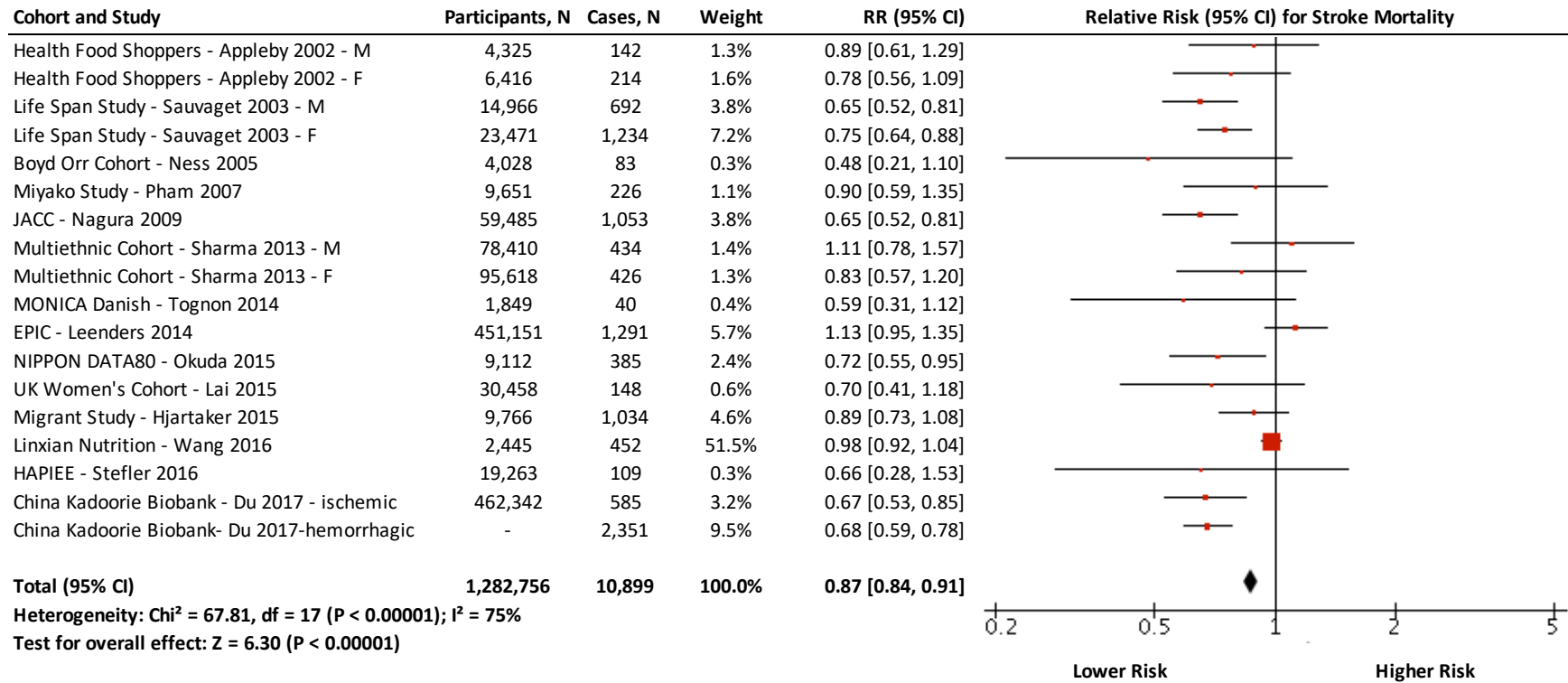


Figure S130. Relation between total fruit and vegetables intake and stroke mortality (highest vs. lowest level of intake). All results are presented as relative risk (RR) with 95% confidence intervals (95% CI). Pooled risk estimate is represented by the black diamond using (A) fixed effects and (B) random effects models. Inter-study heterogeneity was assessed using the Cochran Q statistic (χ^2) at a significance level of $p < 0.10$, and quantified by I^2 , with values $\geq 50\%$ indicating substantial heterogeneity.

FRUIT AND STROKE MORTALITY

A. Fixed Effects



B. Random Effects

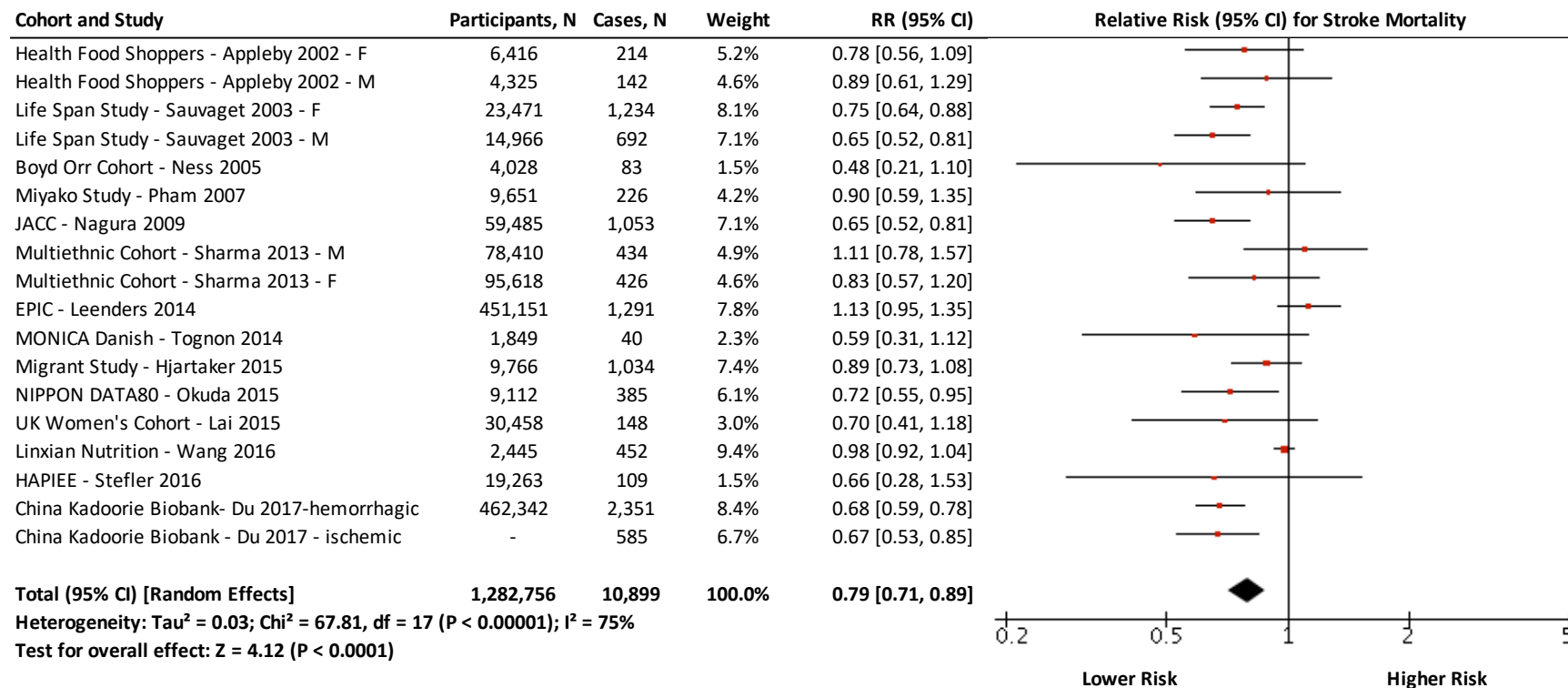
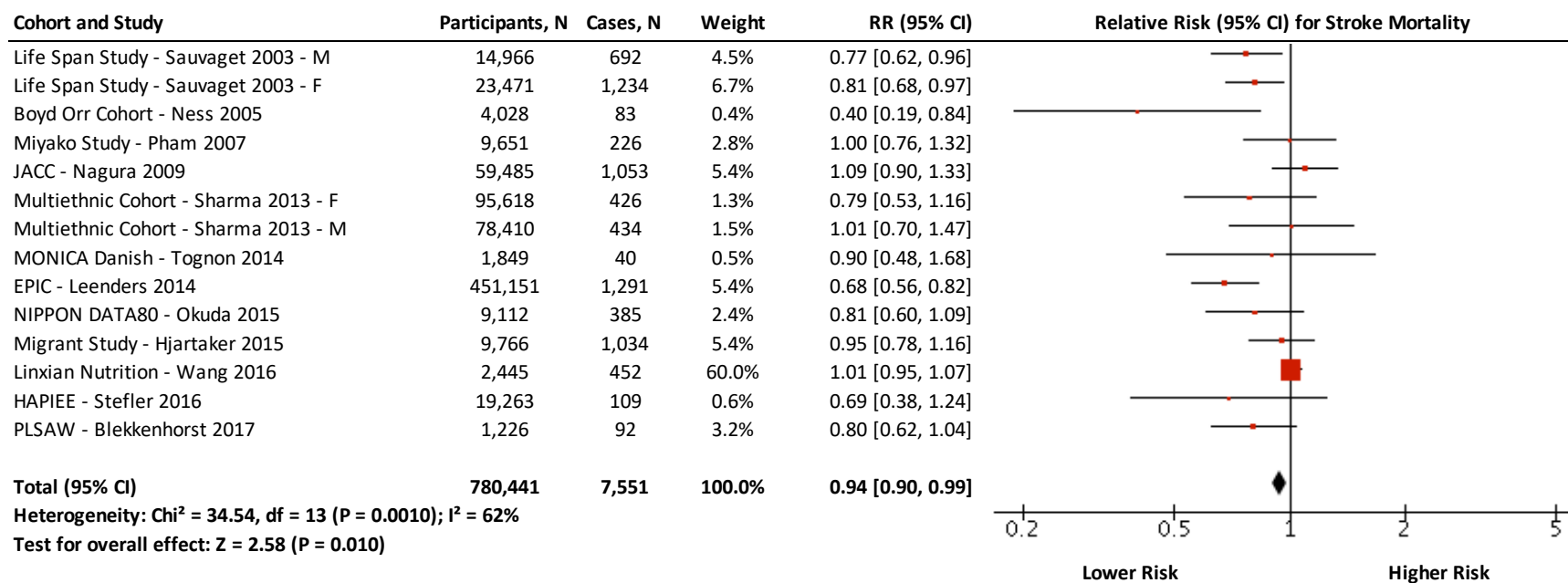


Figure S131. Relation between fruit intake and stroke mortality (highest vs. lowest level of intake). All results are presented as relative risk (RR) with 95% confidence intervals (95% CI). Pooled risk estimate is represented by the black diamond using (A) fixed effects and (B) random effects models. Inter-study heterogeneity was assessed using the Cochran Q statistic (Chi²) at a significance level of $p < 0.10$, and quantified by I², with values $\geq 50\%$ indicating substantial heterogeneity.

VEGETABLES AND STROKE MORTALITY

A. Fixed Effects



B. Random Effects

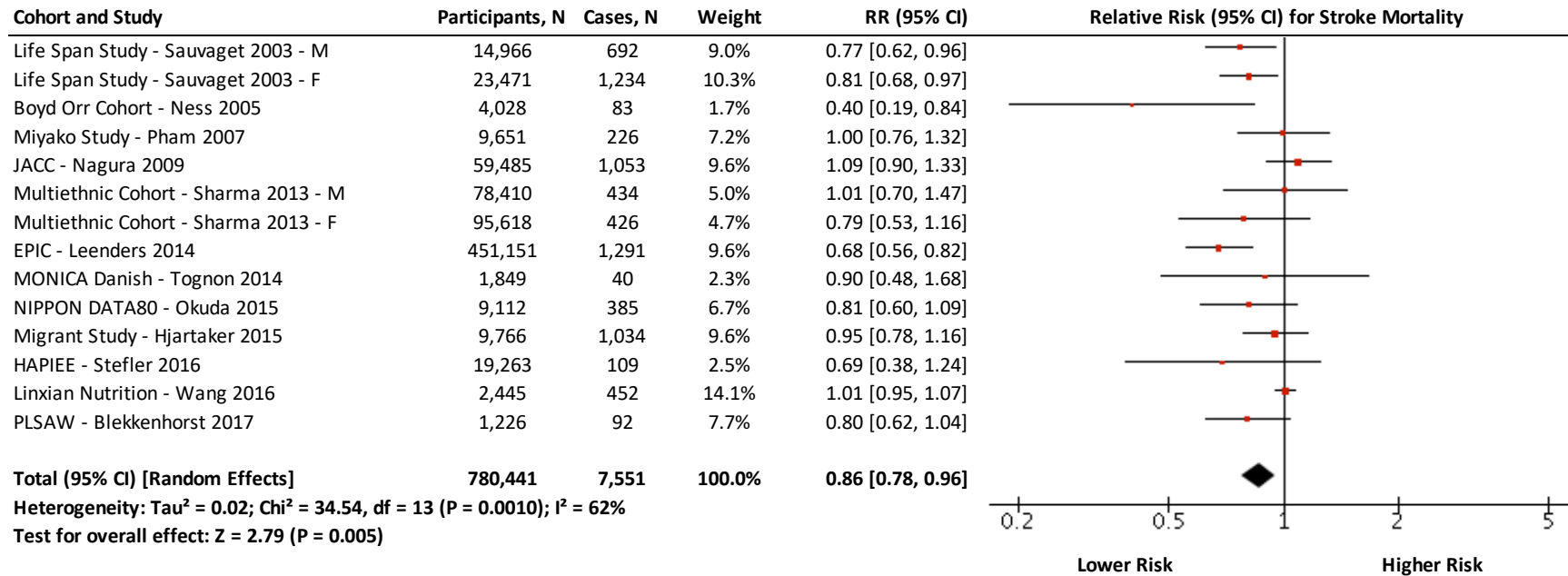


Figure S132. Relation between intake of vegetables and stroke mortality (highest vs. lowest level of intake). All results are presented as relative risk (RR) with 95% confidence intervals (95% CI). Pooled risk estimate is represented by the black diamond using (A) fixed effects and (B) random effects models. Inter-study heterogeneity was assessed using the Cochran Q statistic (χ^2) at a significance level of $p < 0.10$, and quantified by I^2 , with values $\geq 50\%$ indicating substantial heterogeneity.

BANANAS AND STROKE MORTALITY

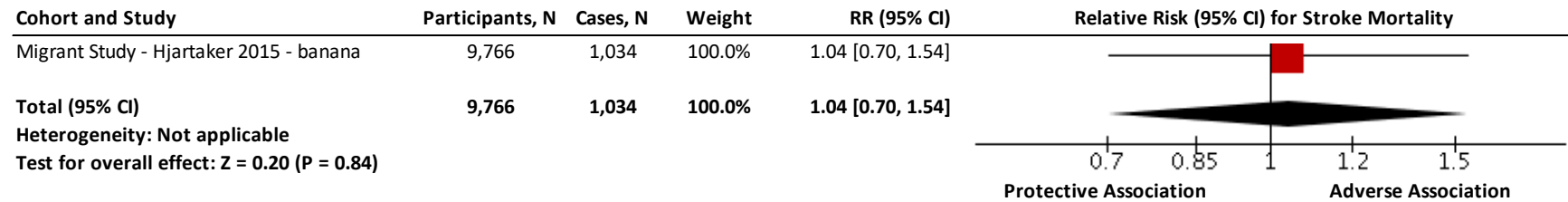
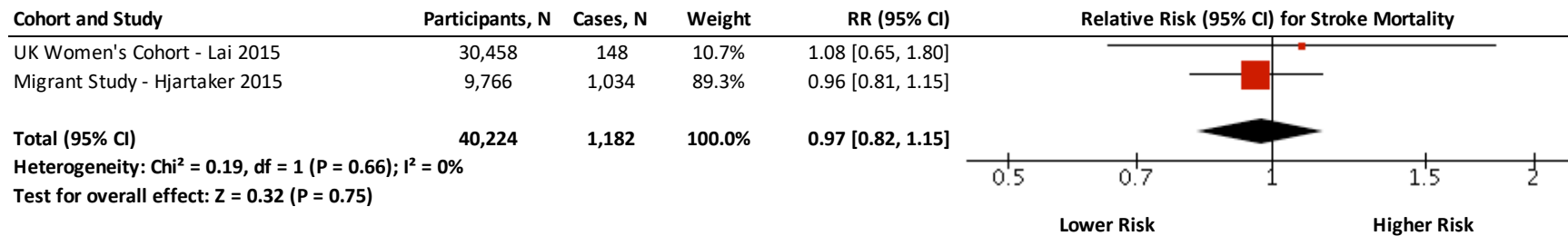


Figure S133. Relation between intake of bananas and stroke mortality (highest vs. lowest level of intake). All results are presented as relative risk (RR) with 95% confidence intervals (95% CI). Pooled risk estimate is represented by the black diamond. Inter-study heterogeneity was assessed using the Cochran Q statistic (χ^2) at a significance level of $p < 0.10$, and quantified by I^2 , with values $\geq 50\%$ indicating substantial heterogeneity.

BERRIES AND STROKE MORTALITY

A. Fixed Effects



B. Random Effects

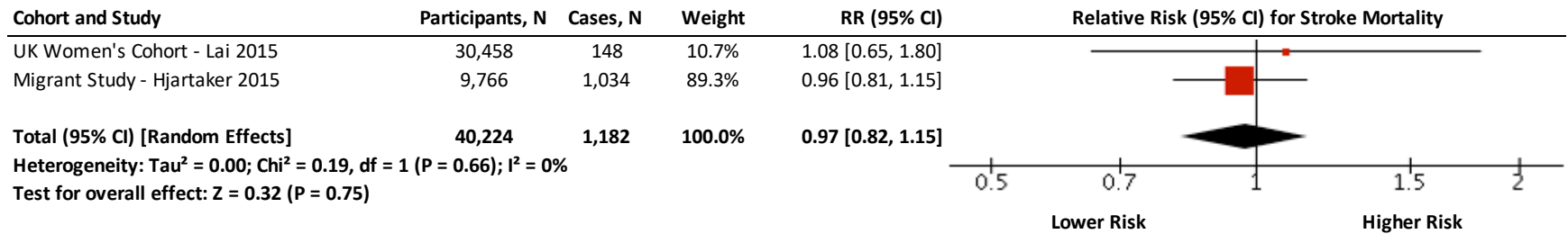
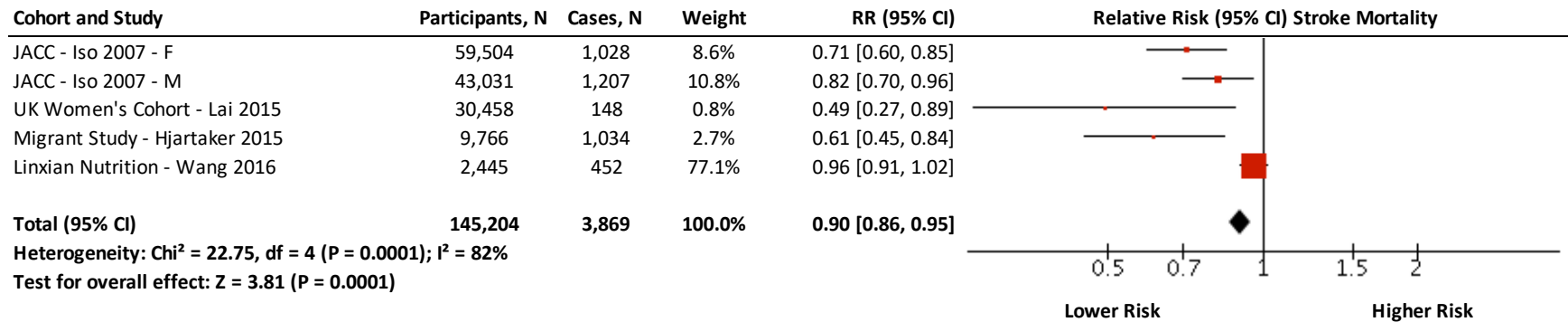


Figure S134. Relation between intake of berries and stroke mortality (highest vs. lowest level of intake). All results are presented as relative risk (RR) with 95% confidence intervals (95% CI). Pooled risk estimate is represented by the black diamond. Inter-study heterogeneity was assessed using the Cochran Q statistic (χ^2) at a significance level of $p < 0.10$, and quantified by I^2 , with values $\geq 50\%$ indicating substantial heterogeneity.

CITRUS FRUIT AND STROKE MORTALITY

A. Fixed Effects



B. Random Effects

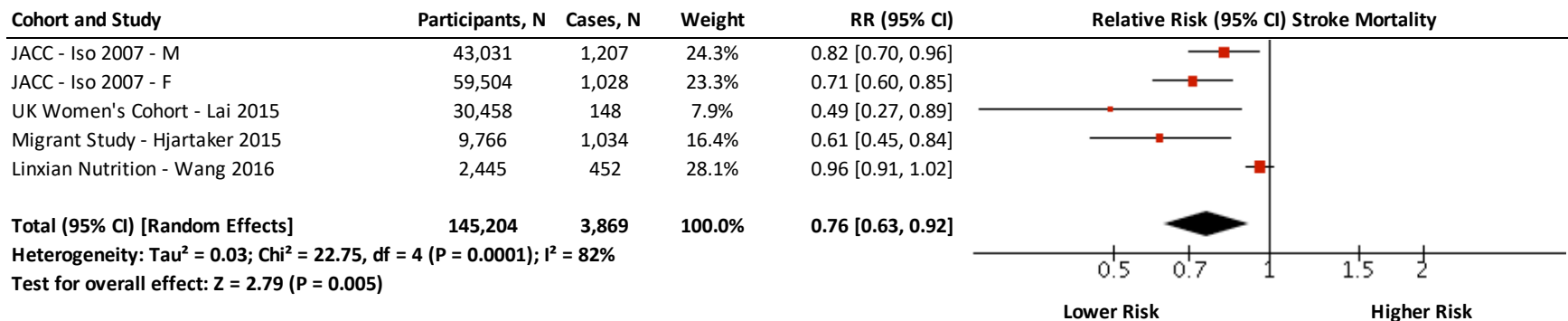


Figure S135. Relation between intake of citrus fruit and stroke mortality (highest vs. lowest level of intake). All results are presented as relative risk (RR) with 95% confidence intervals (95% CI). Pooled risk estimate is represented by the black diamond using (A) fixed effects and (B) random effects models. Inter-study heterogeneity was assessed using the Cochran Q statistic (χ^2) at a significance level of $p < 0.10$, and quantified by I^2 , with values $\geq 50\%$ indicating substantial heterogeneity.

DRIED FRUIT AND STROKE MORTALITY

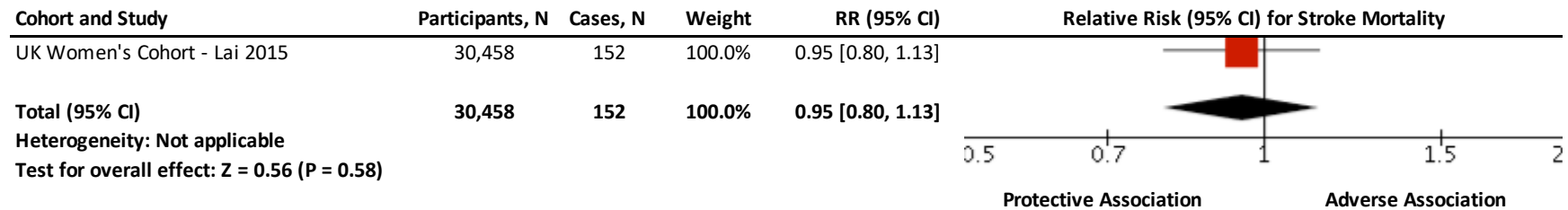
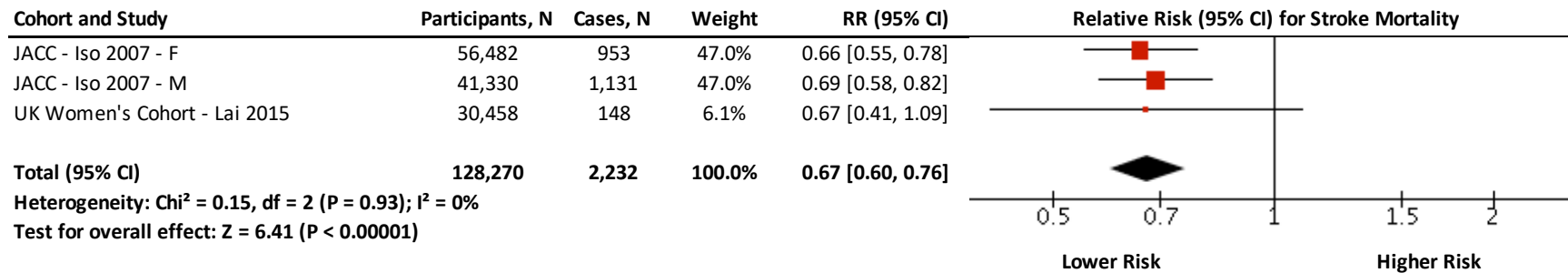


Figure S136. Relation between intake of dried fruit and stroke mortality (highest vs. lowest level of intake). All results are presented as relative risk (RR) with 95% confidence intervals (95% CI). Pooled risk estimate is represented by the black diamond. Inter-study heterogeneity was assessed using the Cochran Q statistic (χ^2) at a significance level of $p < 0.10$, and quantified by I^2 , with values $\geq 50\%$ indicating substantial heterogeneity.

FRUIT JUICE AND STROKE MORTALITY

A. Fixed Effects



B. Random Effects

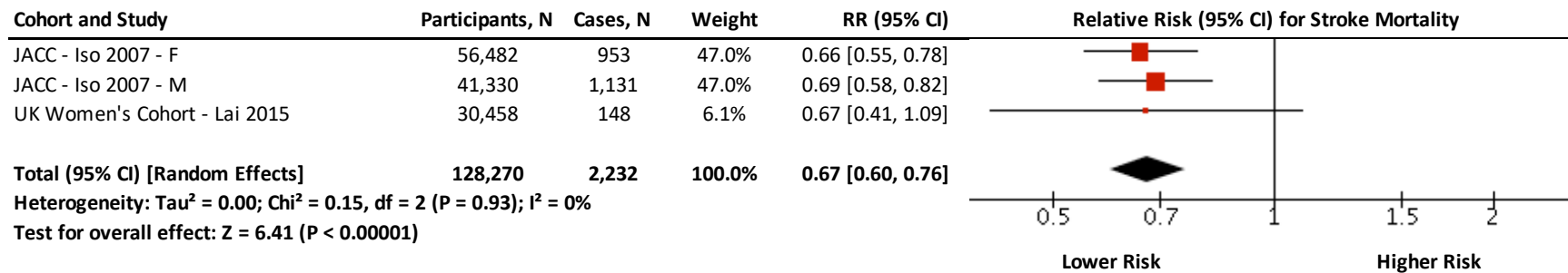
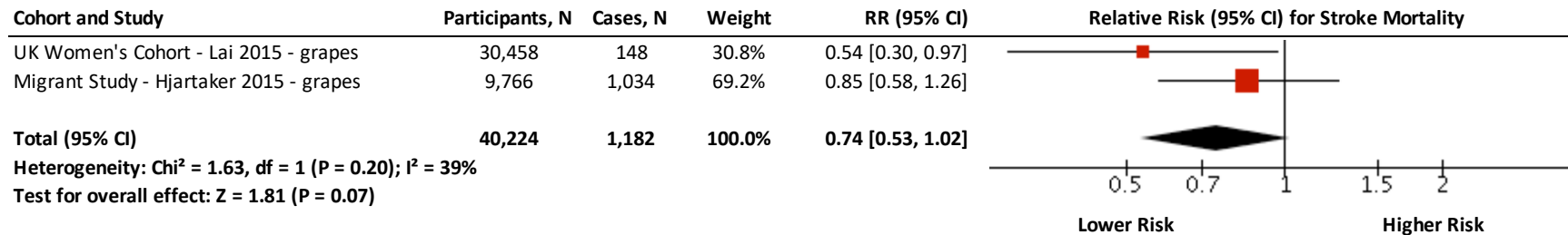


Figure S137. Relation between intake of fruit juice and stroke mortality (highest vs. lowest level of intake). All results are presented as relative risk (RR) with 95% confidence intervals (95% CI). Pooled risk estimate is represented by the black diamond using (A) fixed effects and (B) random effects models. Inter-study heterogeneity was assessed using the Cochran Q statistic (χ^2) at a significance level of $p < 0.10$, and quantified by I^2 , with values $\geq 50\%$ indicating substantial heterogeneity.

GRAPES AND STROKE MORTALITY

A. Fixed Effects



B. Random Effects

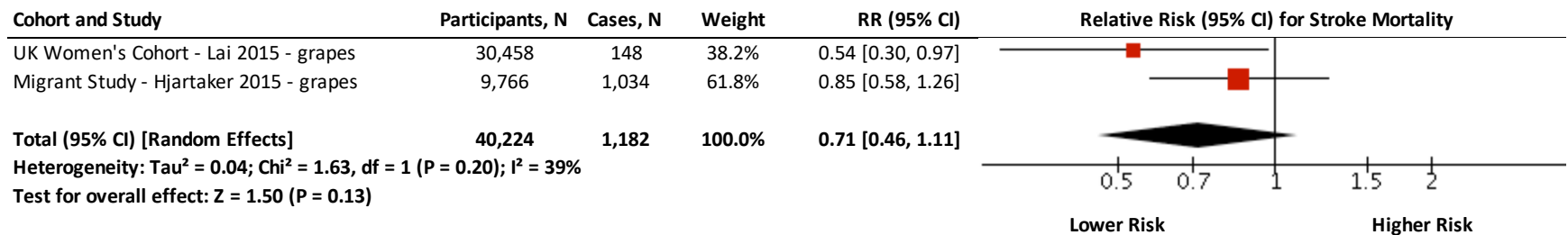
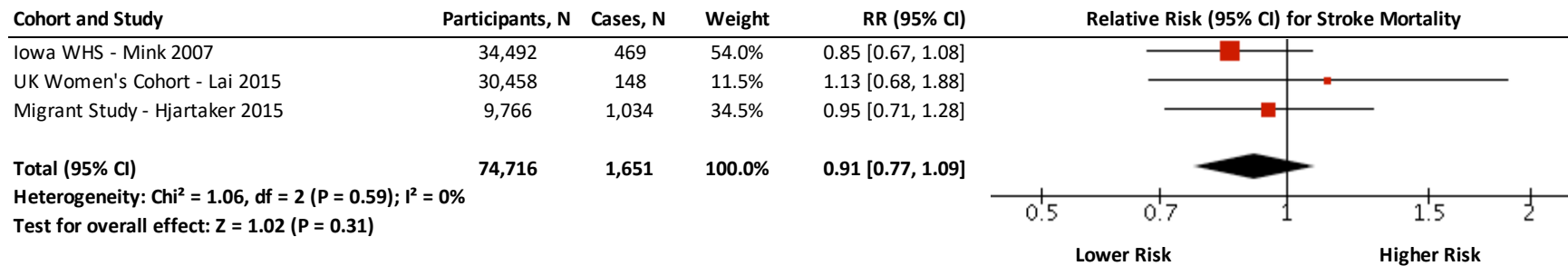


Figure S138. Relation between intake of grapes and stroke mortality (highest vs. lowest level of intake). All results are presented as relative risk (RR) with 95% confidence intervals (95% CI). Pooled risk estimate is represented by the black diamond using (A) fixed effects and (B) random effects models. Inter-study heterogeneity was assessed using the Cochran Q statistic (Chi^2) at a significance level of $p < 0.10$, and quantified by I^2 , with values $\geq 50\%$ indicating substantial heterogeneity.

POMMES AND STROKE MORTALITY

A. Fixed Effects



B. Random Effects

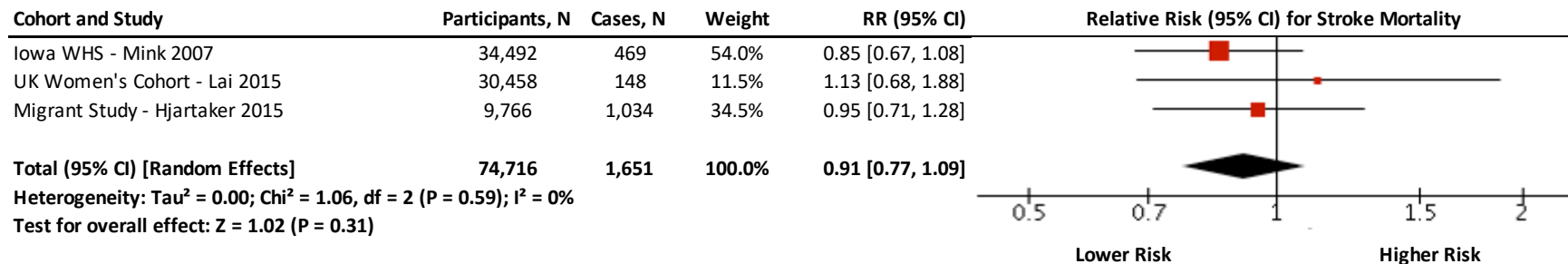
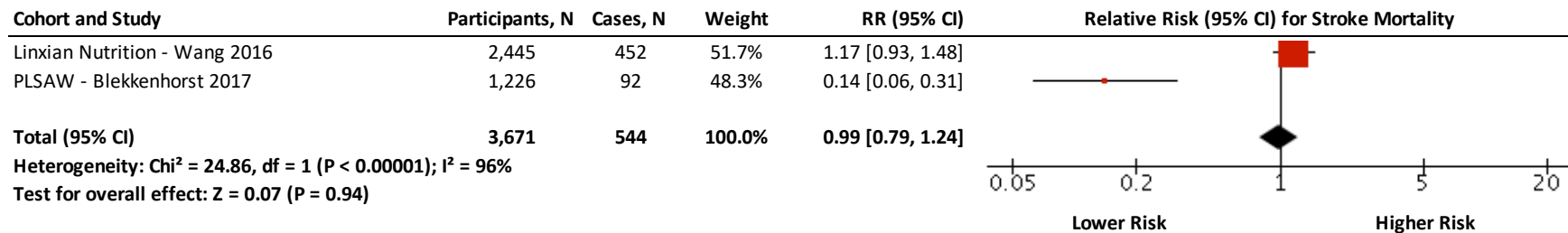


Figure S139. Relation between intake of pomes fruit and stroke mortality (highest vs. lowest level of intake). All results are presented as relative risk (RR) with 95% confidence intervals (95% CI). Pooled risk estimate is represented by the black diamond using (A) fixed effects and (B) random effects models. Inter-study heterogeneity was assessed using the Cochran Q statistic (χ^2) at a significance level of $p < 0.10$, and quantified by I^2 , with values $\geq 50\%$ indicating substantial heterogeneity.

ALLIUM AND STROKE MORTALITY

A. Fixed Effects



B. Random Effects

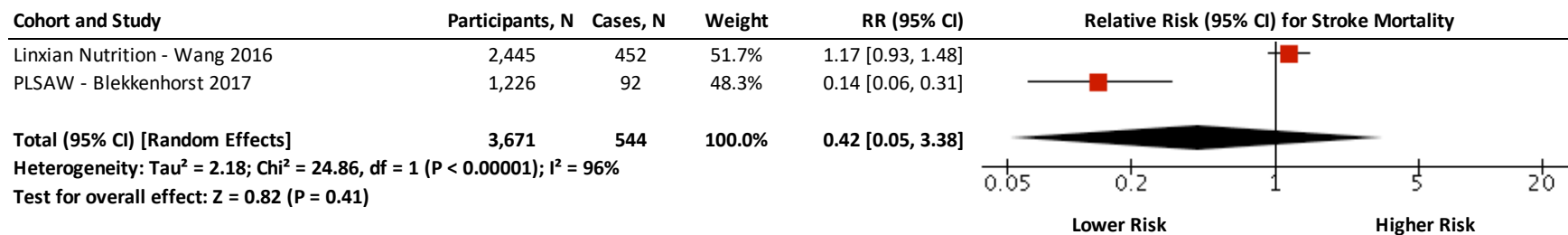


Figure S140. Relation between intake of allium vegetables and stroke mortality (highest vs. lowest level of intake). All results are presented as relative risk (RR) with 95% confidence intervals (95% CI). Pooled risk estimate is represented by the black diamond using (A) fixed effects and (B) random effects models. Inter-study heterogeneity was assessed using the Cochran Q statistic (χ^2) at a significance level of $p < 0.10$, and quantified by I^2 , with values $\geq 50\%$ indicating substantial heterogeneity.

CARROTS AND STROKE MORTALITY

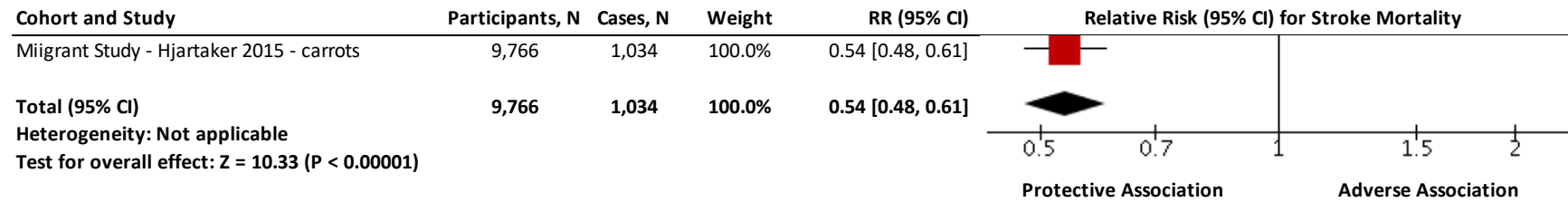
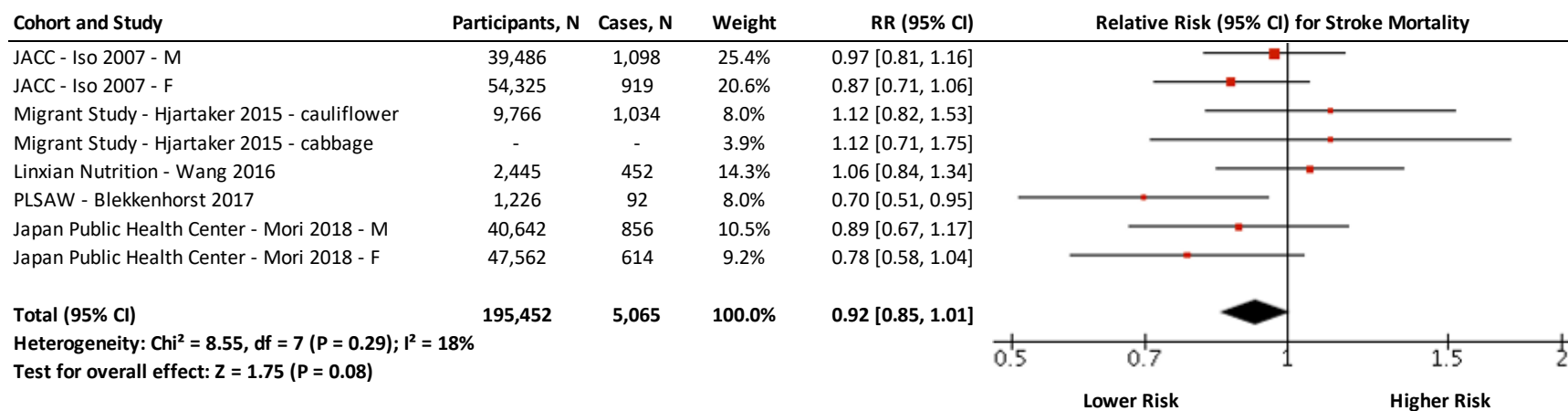


Figure S141. Relation between intake of carrots and stroke mortality (highest vs. lowest level of intake). All results are presented as relative risk (RR) with 95% confidence intervals (95% CI). Pooled risk estimate is represented by the black diamond. Inter-study heterogeneity was assessed using the Cochran Q statistic (χ^2) at a significance level of $p < 0.10$, and quantified by I^2 , with values $\geq 50\%$ indicating substantial heterogeneity.

CRUCIFEROUS VEGETABLES AND STROKE MORTALITY

A. Fixed Effects



B. Random Effects

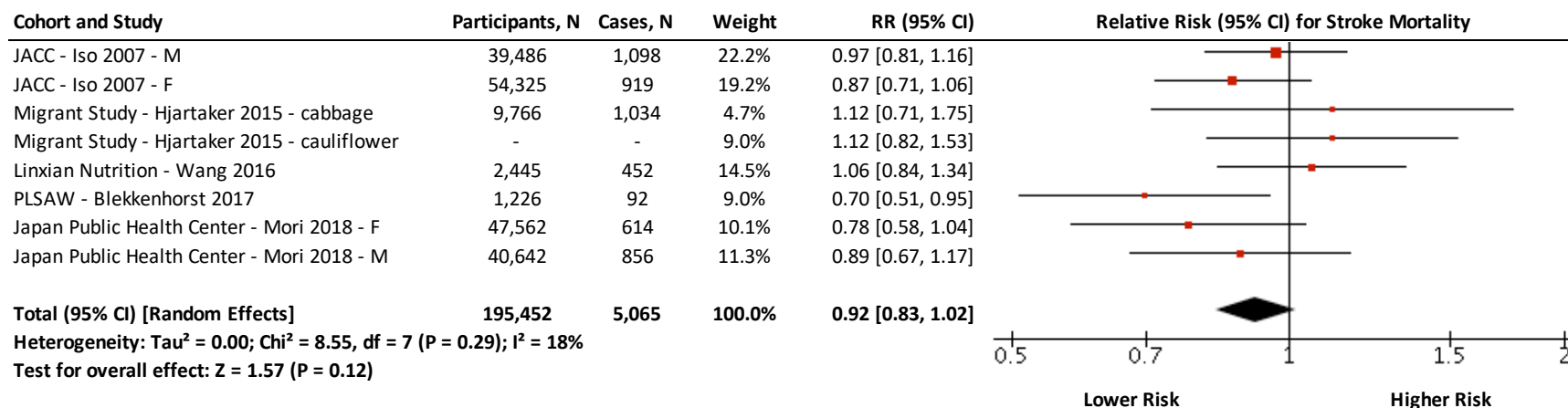
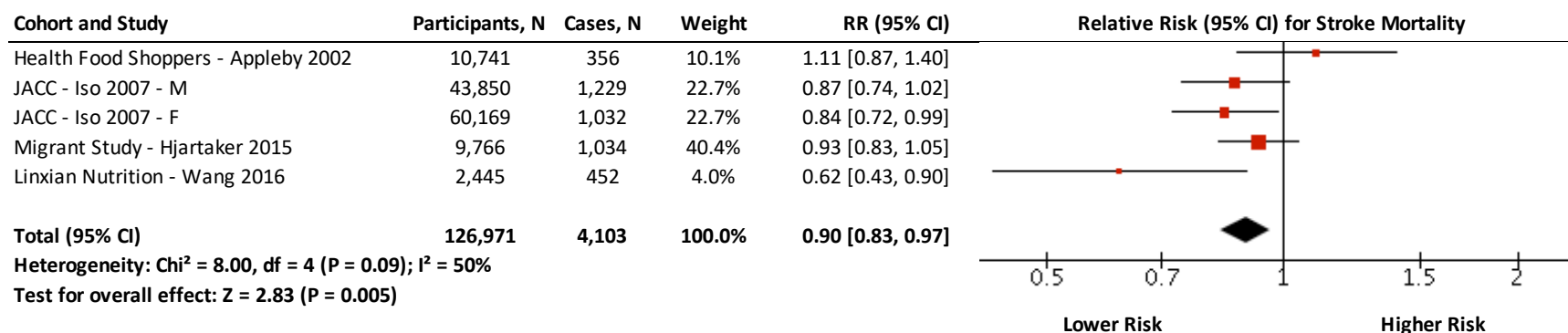


Figure S142. Relation between intake of cruciferous vegetables and stroke mortality (highest vs. lowest level of intake). All results are presented as relative risk (RR) with 95% confidence intervals (95% CI). Pooled risk estimate is represented by the black diamond using (A) fixed effects and (B) random effects models. Inter-study heterogeneity was assessed using the Cochran Q statistic (χ^2) at a significance level of $p < 0.10$, and quantified by I^2 , with values $\geq 50\%$ indicating substantial heterogeneity.

GREEN LEAFY VEGETABLES AND STROKE MORTALITY

A. Fixed Effects



B. Random Effects

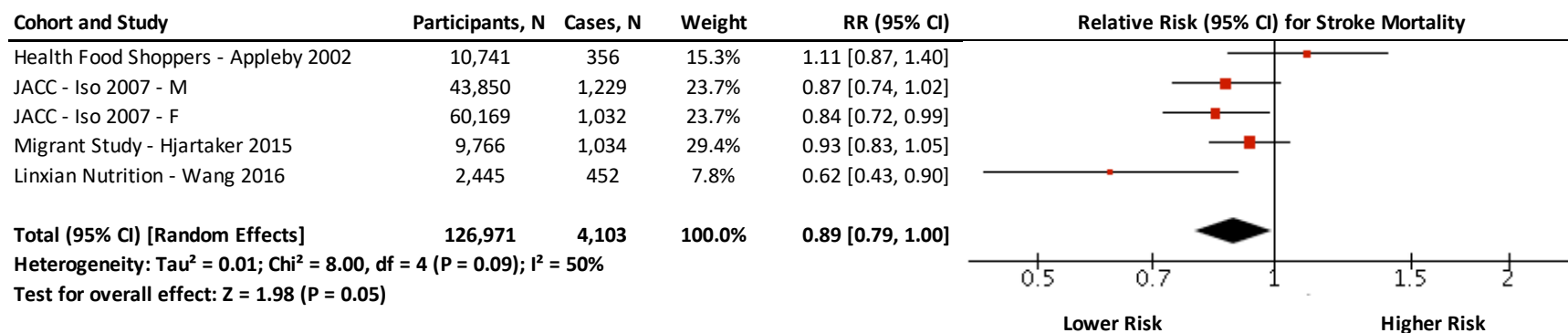
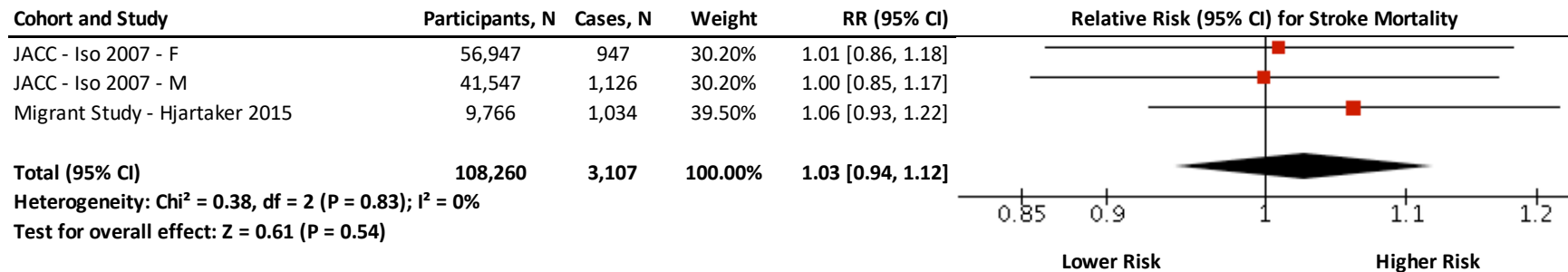


Figure S143. Relation between intake of green leafy vegetables and stroke mortality (highest vs. lowest level of intake). All results are presented as relative risk (RR) with 95% confidence intervals (95% CI). Pooled risk estimate is represented by the black diamond using (A) fixed effects and (B) random effects models. Inter-study heterogeneity was assessed using the Cochran Q statistic (χ^2) at a significance level of $p < 0.10$, and quantified by I^2 , with values $\geq 50\%$ indicating substantial heterogeneity.

TOMATOES AND STROKE MORTALITY

A. Fixed Effects



B. Random Effects

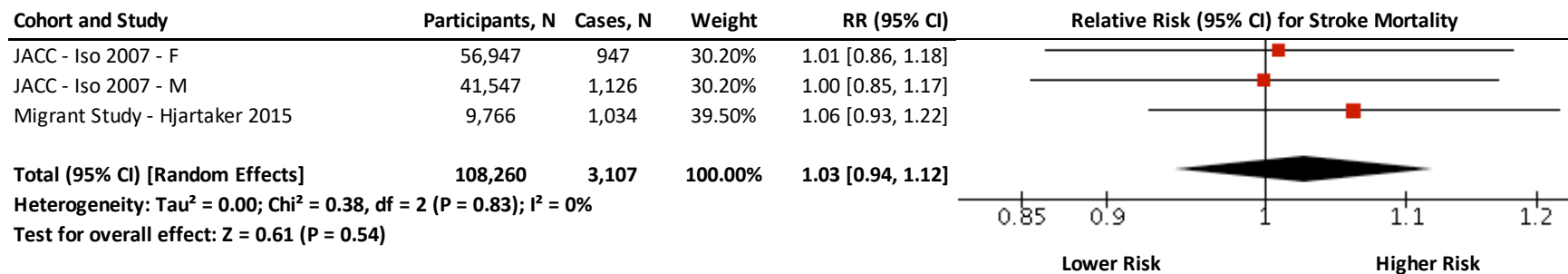
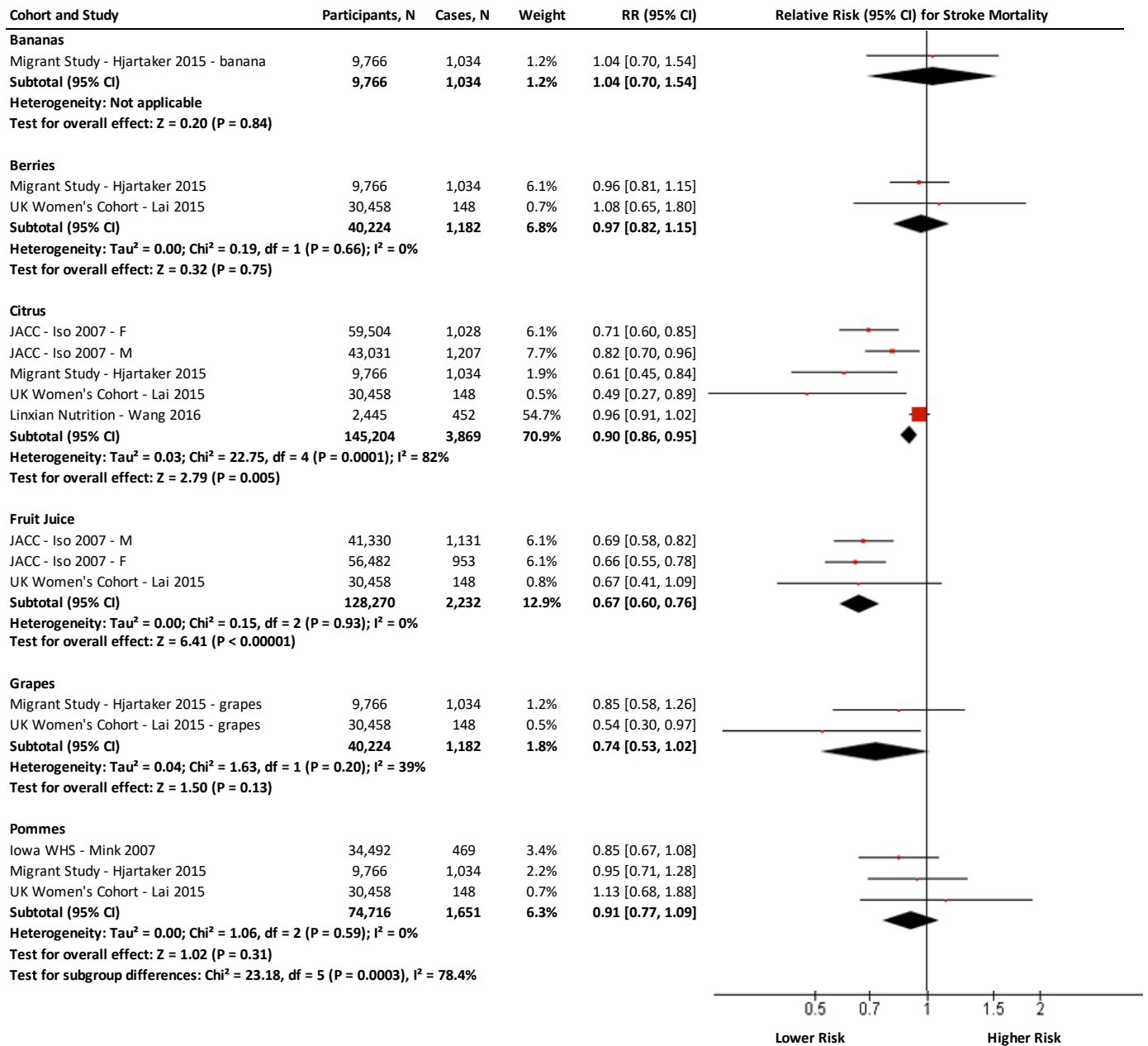


Figure S144. Relation between intake of tomatoes and stroke mortality (highest vs. lowest level of intake). All results are presented as relative risk (RR) with 95% confidence intervals (95% CI). Pooled risk estimate is represented by the black diamond using (A) fixed effects and (B) random effects models. Inter-study heterogeneity was assessed using the Cochran Q statistic (χ^2) at a significance level of $p < 0.10$, and quantified by I^2 , with values $\geq 50\%$ indicating substantial heterogeneity.

A. Fixed Effects



B. Random Effects

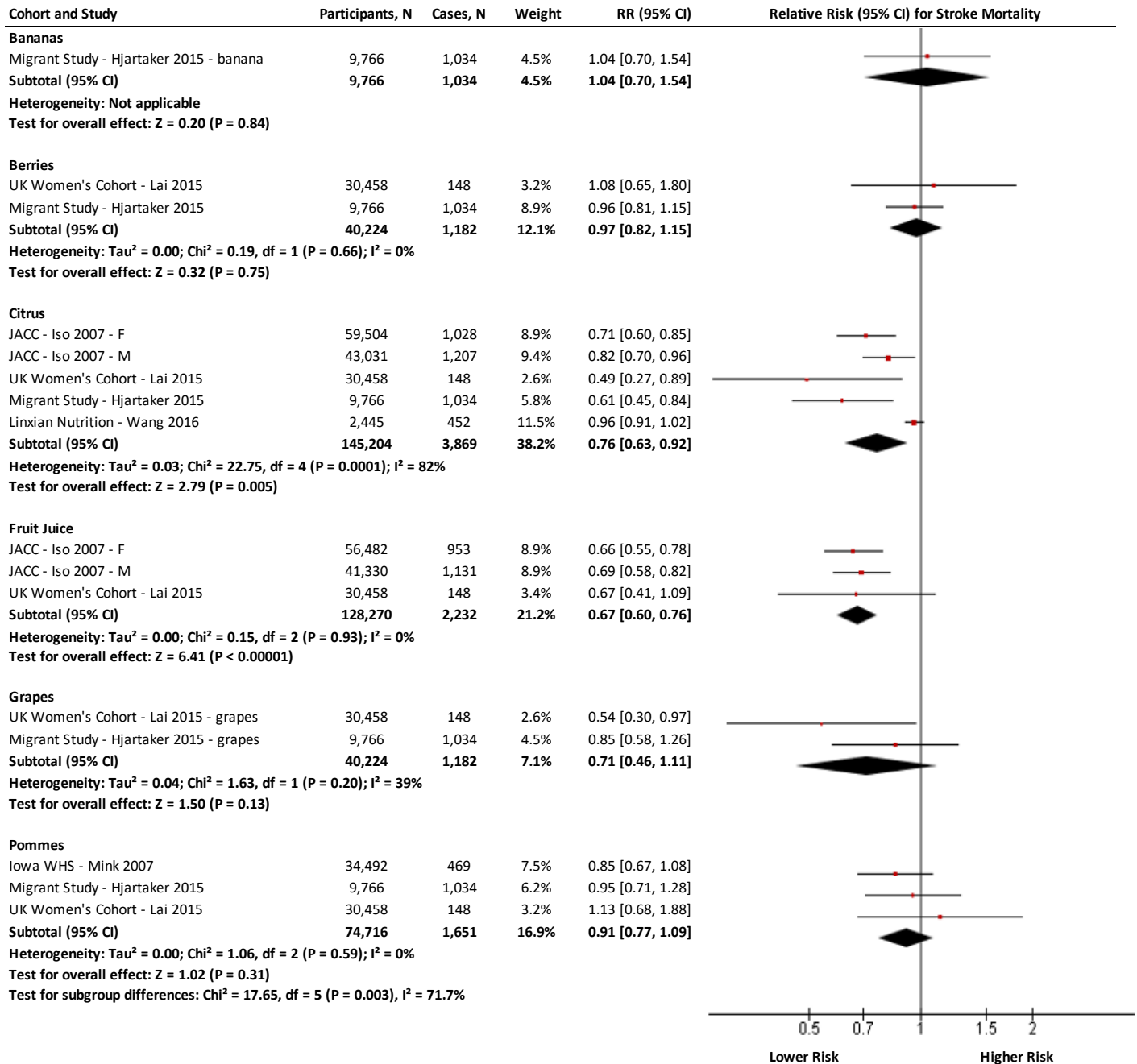
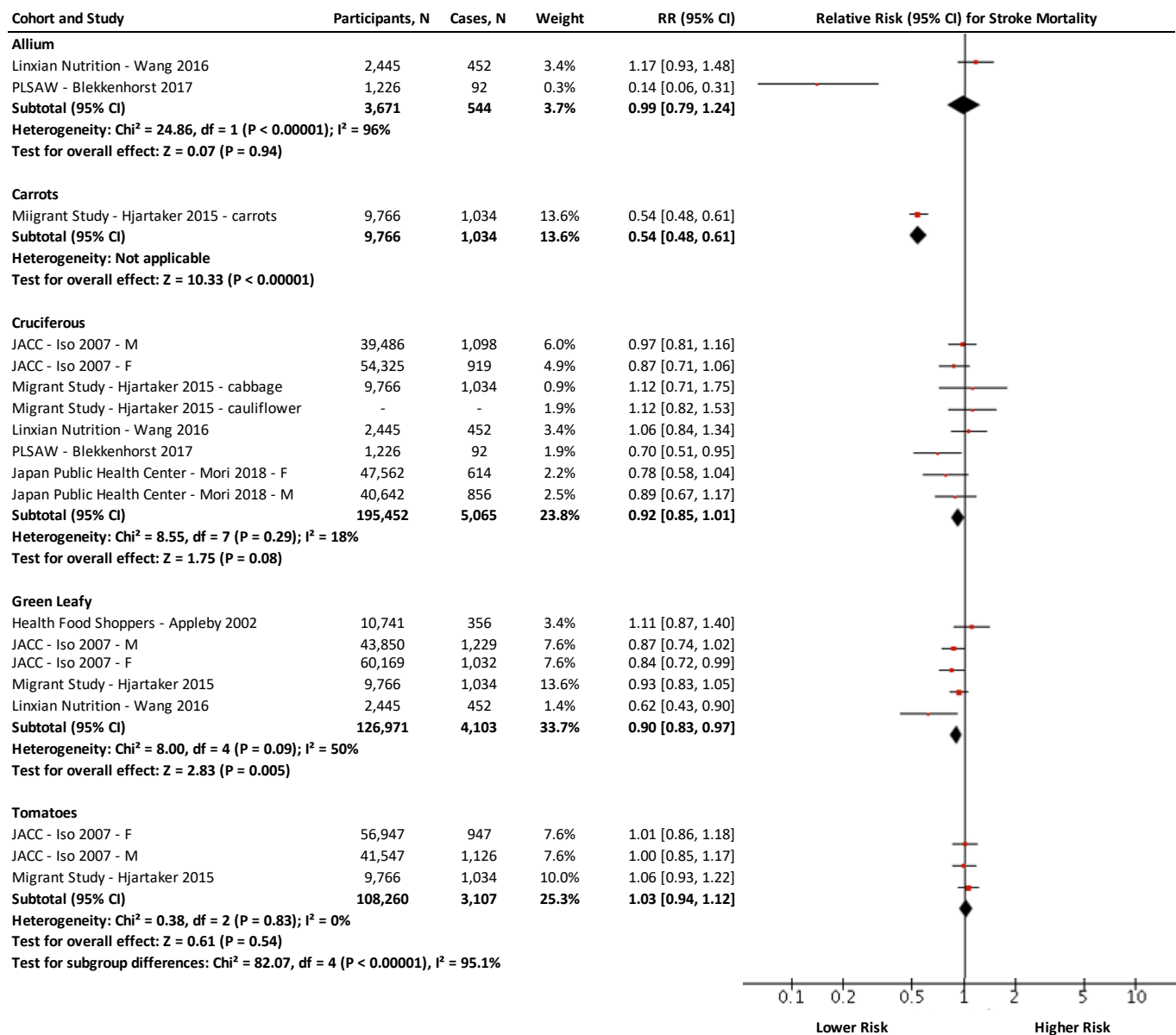


Figure S145. Relation between sources of fruit and stroke mortality (highest vs. lowest level of intake). All results are presented as relative risk (RR) with 95% confidence intervals (95% CI). Pooled risk estimate is represented by the black diamond using (A) fixed effects and (B) random effects models. Inter-study heterogeneity was assessed using the Cochran Q statistic (Chi²) at a significance level of p<0.10, and quantified by I², with values ≥ 50% indicating substantial heterogeneity.

A. Fixed Effects



B. Random Effects

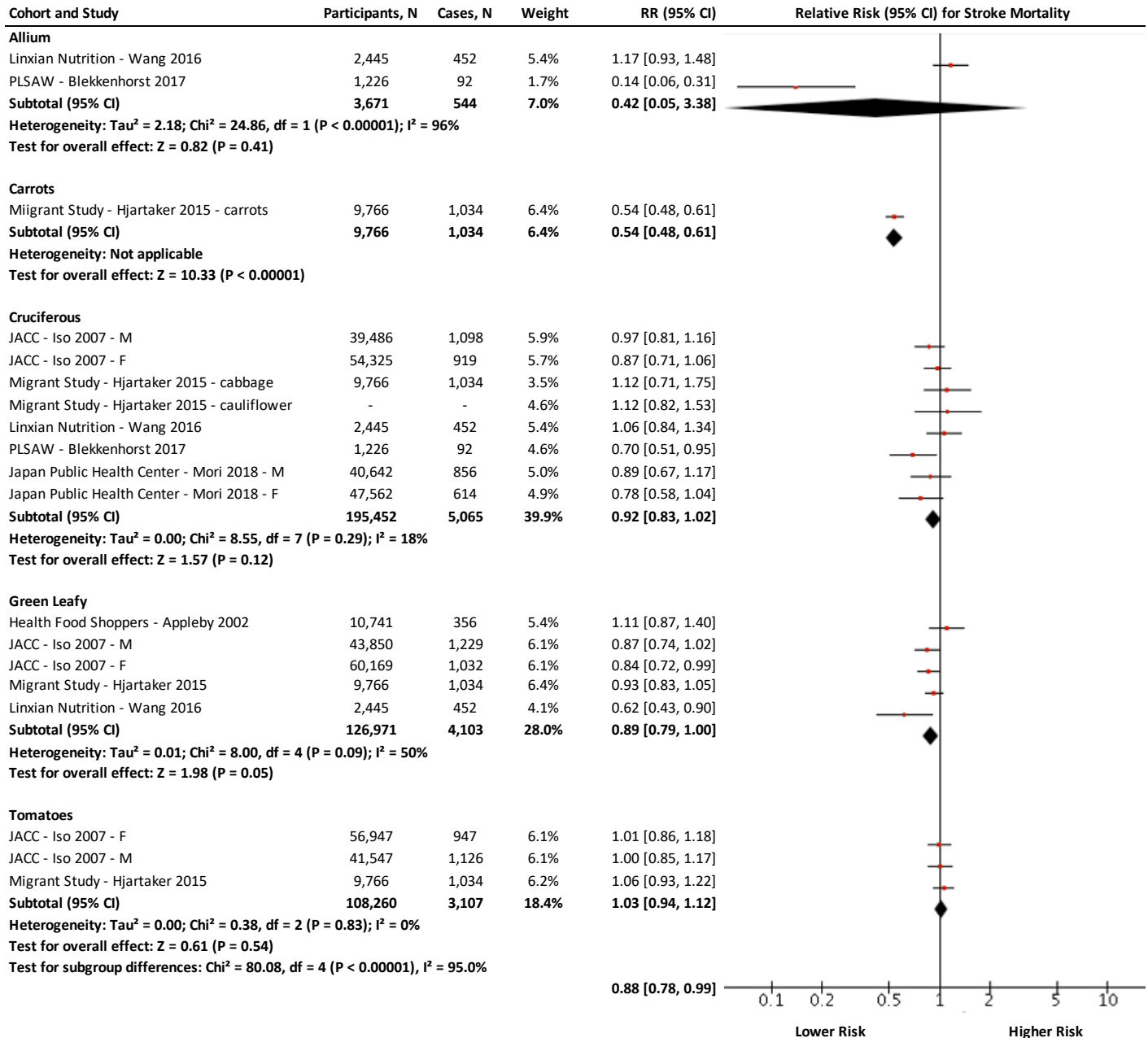


Figure S146. Relation between sources of vegetables and stroke mortality (highest vs. lowest level of intake). All results are presented as relative risk (RR) with 95% confidence intervals (95% CI). Pooled risk estimate is represented by the black diamond using (A) fixed effects and (B) random effects models. Inter-study heterogeneity was assessed using the Cochran Q statistic (χ^2) at a significance level of $p < 0.10$, and quantified by I^2 , with values $\geq 50\%$ indicating substantial heterogeneity.

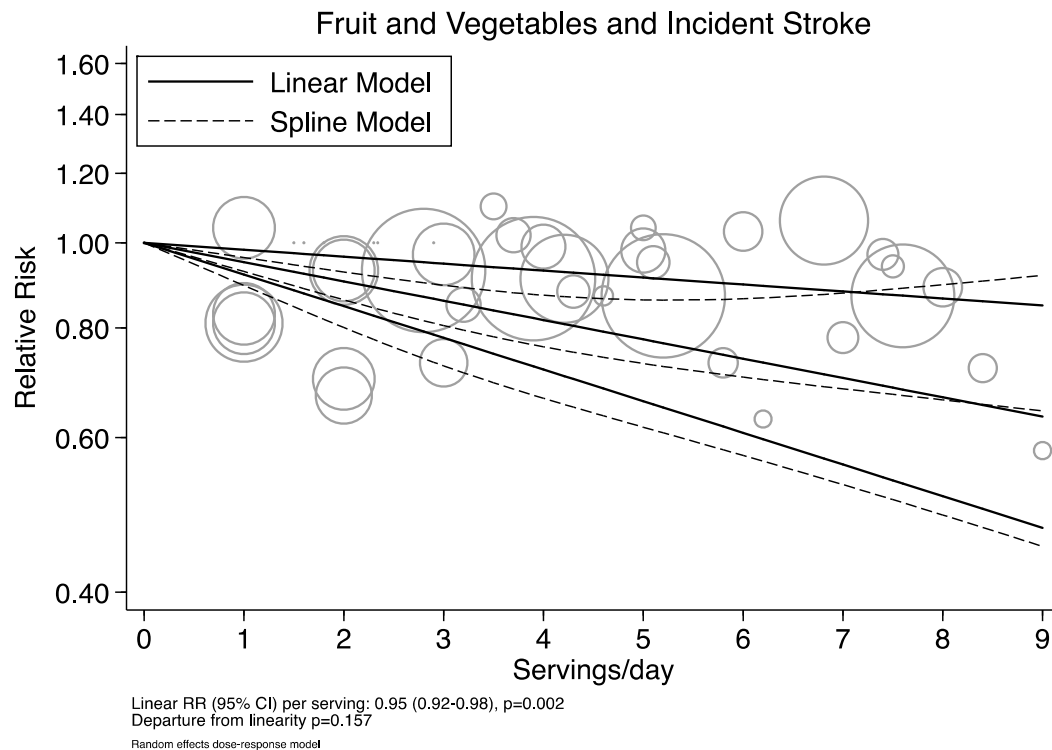


Figure S147. Linear and cubic-spline dose-response relation between increasing fruit and vegetable intake and incidence of stroke. Linear dose-response data was modeled using the Greenland and Longnecker²³ method to estimate the covariances of multivariable-adjusted relative risk. Cubic spline data were modeled with fixed-effects restricted cubic spline with 3 knots and using the Greenland and Longnecker²³ method to estimate the covariances of multivariable-adjusted relative risk. All data was kept on the original dose scale. The fitted trend for each model is represented by a central line (solid lines for linear model; dashed lines for cubic spline model) with 95% confidence intervals represented by the outer lines. Individual observations are represented by the circles, with the weight of the study in the overall analysis represented by the size of the circles.

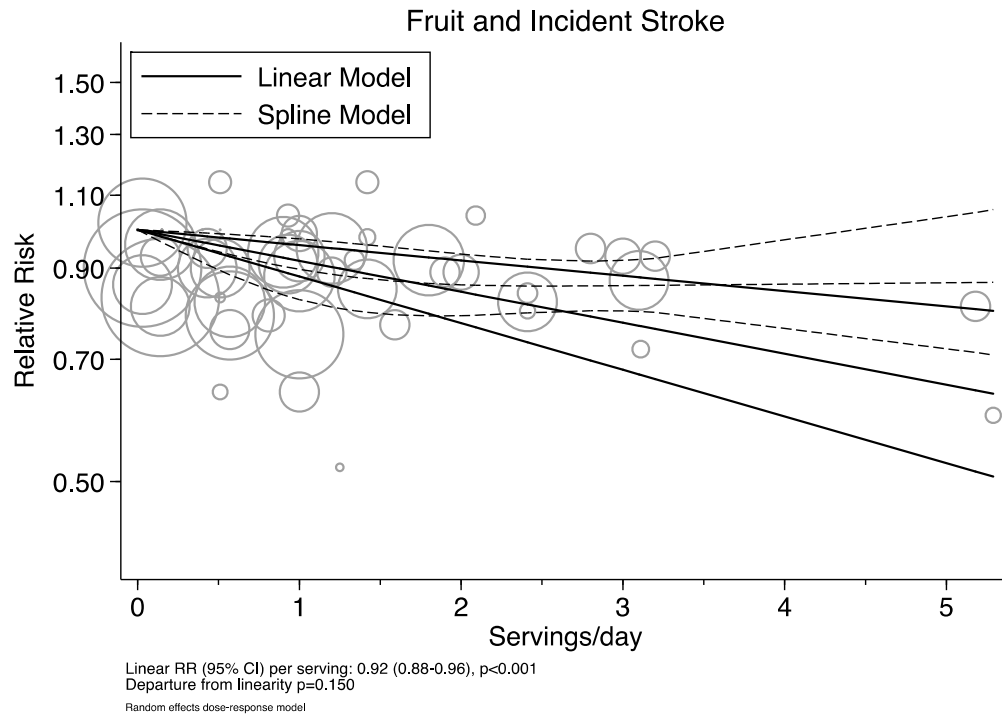


Figure S148. Linear and cubic-spline dose-response relation between increasing fruit intake and incidence of stroke. Linear dose-response data was modeled using the Greenland and Longnecker²³ method to estimate the covariances of multivariable-adjusted relative risk. Cubic spline data were modeled with fixed-effects restricted cubic spline with 3 knots and using the Greenland and Longnecker²³ method to estimate the covariances of multivariable-adjusted relative risk. All data was kept on the original dose scale. The fitted trend for each model is represented by a central line (solid lines for linear model; dashed lines for cubic spline model) with 95% confidence intervals represented by the outer lines. Individual observations are represented by the circles, with the weight of the study in the overall analysis represented by the size of the circles.

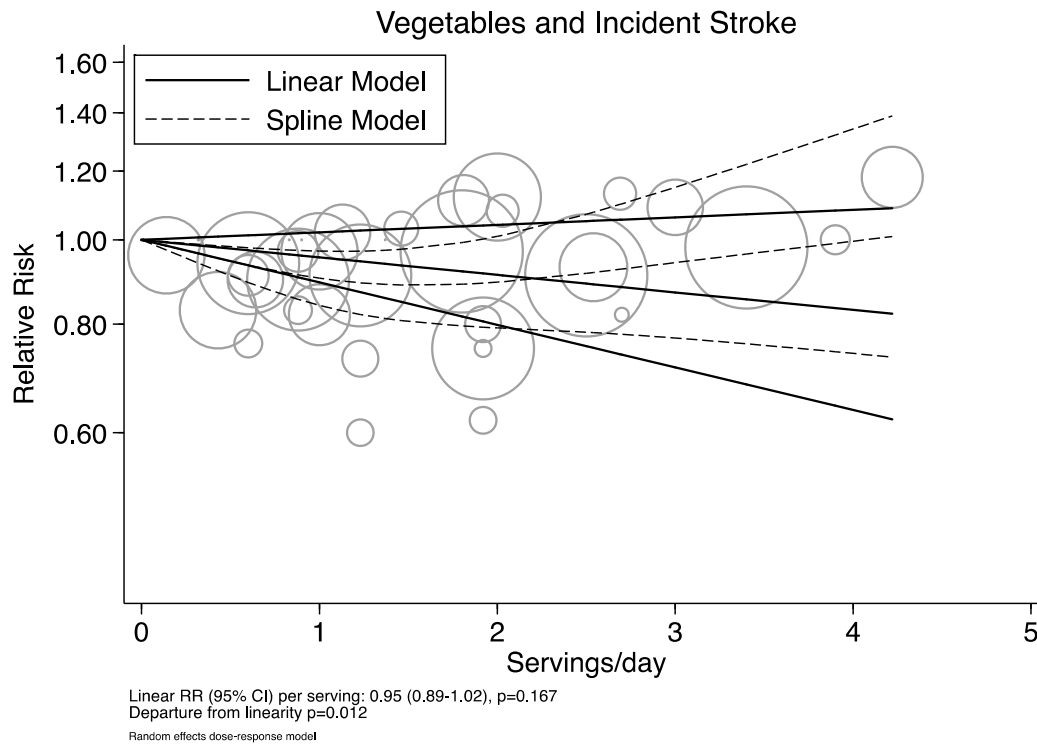


Figure S149. Linear and cubic-spline dose-response relation between increasing intake of vegetables and incidence of stroke. Linear dose-response data was modeled using the Greenland and Longnecker²³ method to estimate the covariances of multivariable-adjusted relative risk. Cubic spline data were modeled with fixed-effects restricted cubic spline with 3 knots and using the Greenland and Longnecker²³ method to estimate the covariances of multivariable-adjusted relative risk. All data was kept on the original dose scale. The fitted trend for each model is represented by a central line (solid lines for linear model; dashed lines for cubic spline model) with 95% confidence intervals represented by the outer lines. Individual observations are represented by the circles, with the weight of the study in the overall analysis represented by the size of the circles.

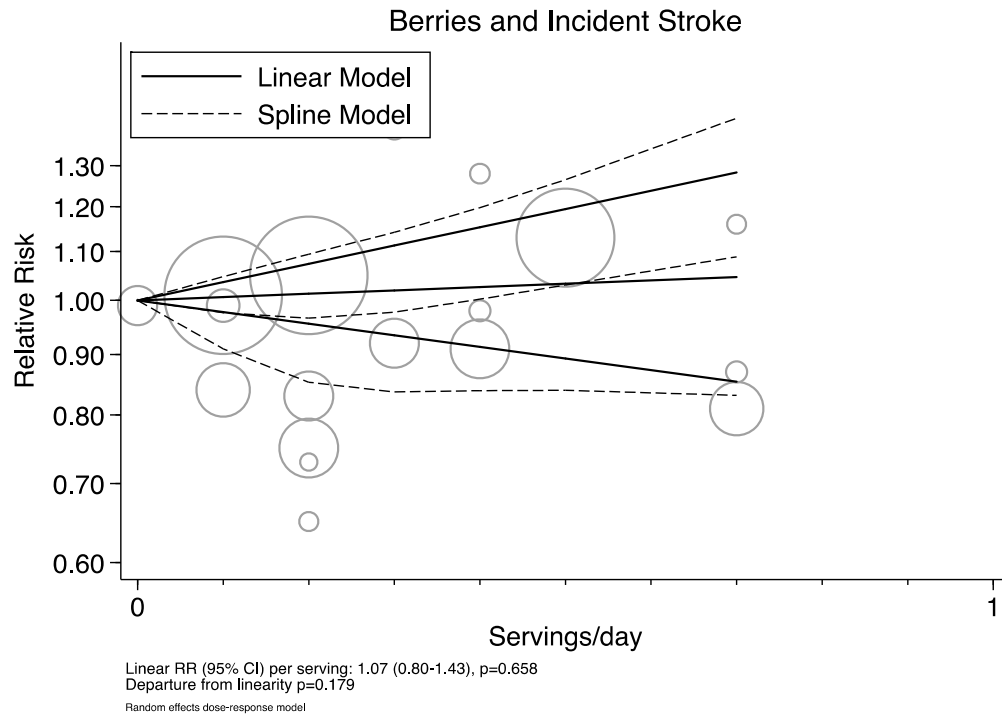


Figure S150. Linear and cubic-spline dose-response relation between increasing berries intake and incidence of stroke. Linear dose-response data was modeled using the Greenland and Longnecker²³ method to estimate the covariances of multivariable-adjusted relative risk. Cubic spline data were modeled with fixed-effects restricted cubic spline with 3 knots and using the Greenland and Longnecker²³ method to estimate the covariances of multivariable-adjusted relative risk. All data was kept on the original dose scale. The fitted trend for each model is represented by a central line (solid lines for linear model; dashed lines for cubic spline model) with 95% confidence intervals represented by the outer lines. Individual observations are represented by the circles, with the weight of the study in the overall analysis represented by the size of the circles.

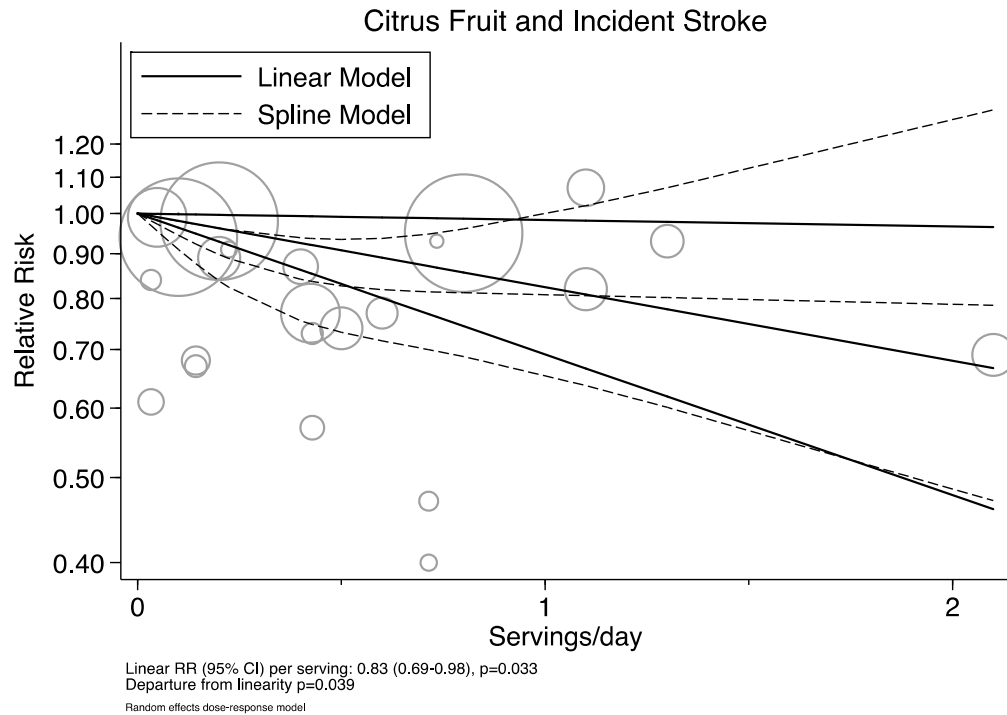


Figure S151. Linear and cubic-spline dose-response relation between increasing citrus fruit intake and incidence of stroke. Linear dose-response data was modeled using the Greenland and Longnecker²³ method to estimate the covariances of multivariable-adjusted relative risk. Cubic spline data were modeled with fixed-effects restricted cubic spline with 3 knots and using the Greenland and Longnecker²³ method to estimate the covariances of multivariable-adjusted relative risk. All data was kept on the original dose scale. The fitted trend for each model is represented by a central line (solid lines for linear model; dashed lines for cubic spline model) with 95% confidence intervals represented by the outer lines. Individual observations are represented by the circles, with the weight of the study in the overall analysis represented by the size of the circles.

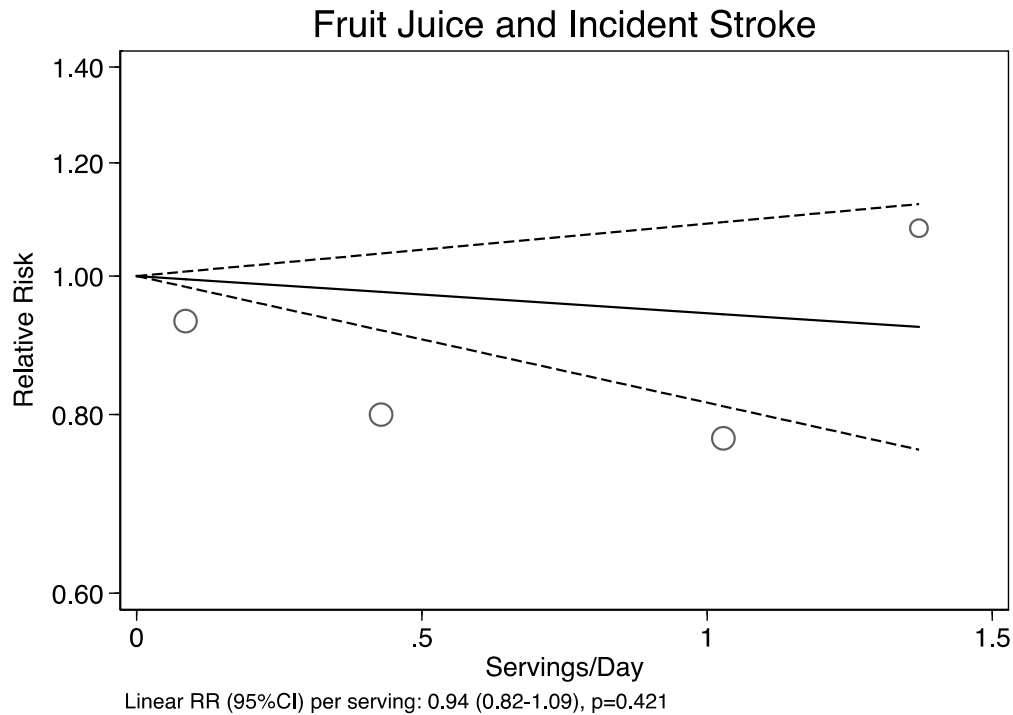


Figure S152. Linear and cubic-spline dose-response relation between increasing fruit juice intake and incidence of stroke. Linear dose-response data was modeled using the Greenland and Longnecker²³ method to estimate the covariances of multivariable-adjusted relative risk. Cubic spline data were modeled with fixed-effects restricted cubic spline with 3 knots and using the Greenland and Longnecker²³ method to estimate the covariances of multivariable-adjusted relative risk. All data was kept on the original dose scale. The fitted trend for each model is represented by a central line (solid lines for linear model; dashed lines for cubic spline model) with 95% confidence intervals represented by the outer lines. Individual observations are represented by the circles, with the weight of the study in the overall analysis represented by the size of the circles.

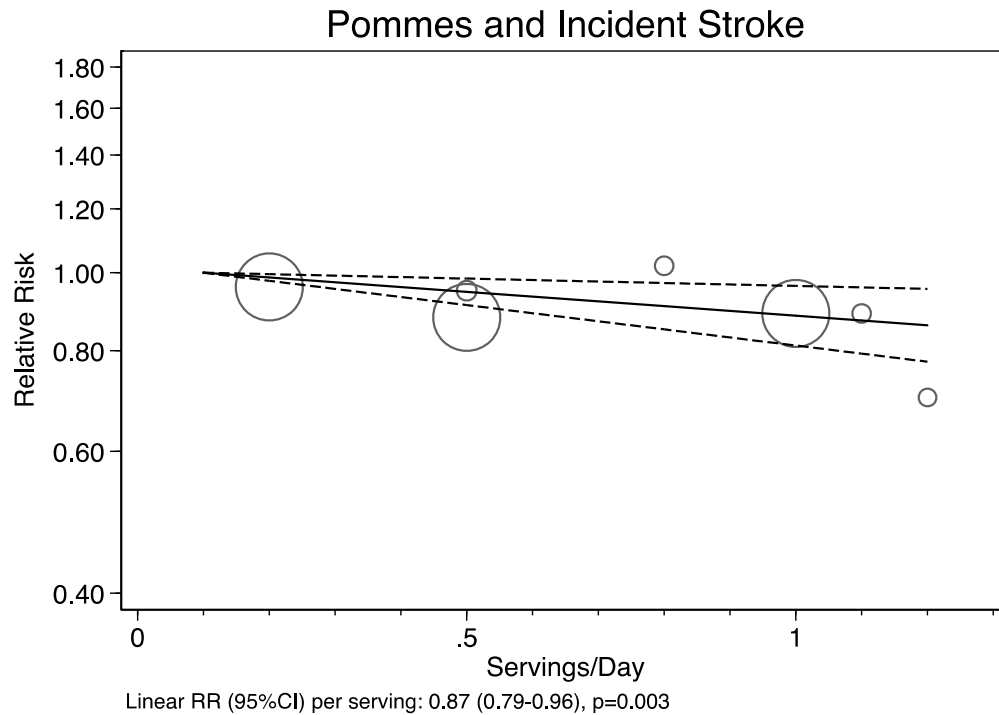


Figure S153. Linear dose-response relation between increasing pommes intake and incidence of stroke. Linear dose-response data was modeled using the Greenland and Longnecker²³ method to estimate the covariances of multivariable-adjusted relative risk, with kept on the original dose scale. Dashed lines represent the pointwise 95% confidence intervals for the fitted linear trend represented by a solid line. Individual observations are represented by the circles, with the weight of the study in the overall analysis represented by the size of the circles.

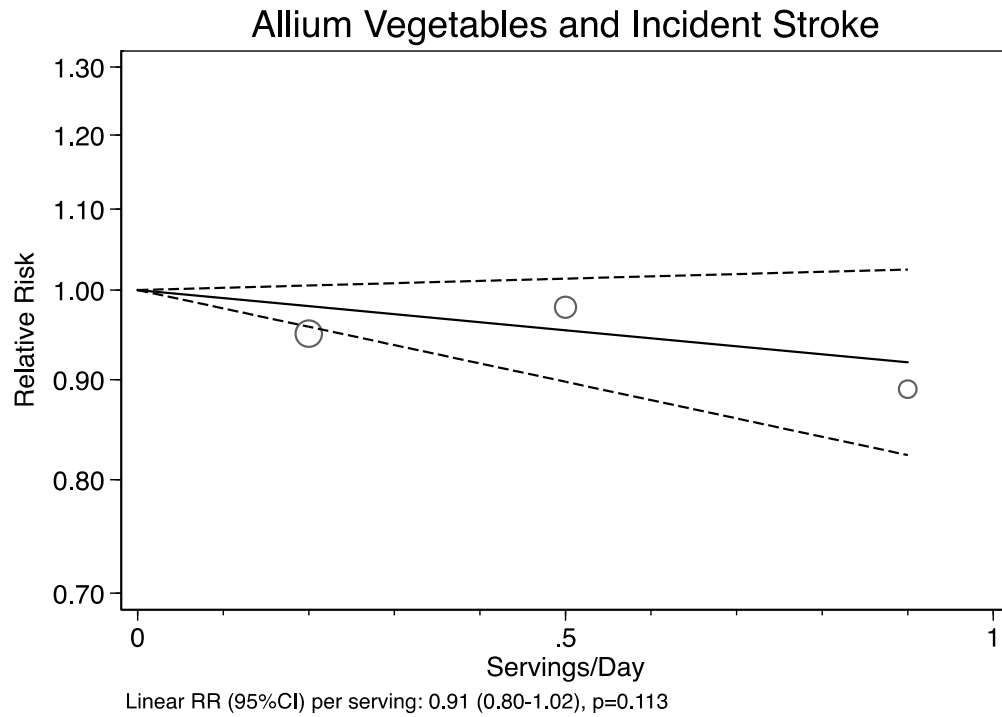


Figure S154 Linear dose-response relation between increasing intake of allium vegetables and incidence of stroke. Linear dose-response data was modeled using the Greenland and Longnecker²³ method to estimate the covariances of multivariable-adjusted relative risk, with kept on the original dose scale. Dashed lines represent the pointwise 95% confidence intervals for the fitted linear trend represented by a solid line. Individual observations are represented by the circles, with the weight of the study in the overall analysis represented by the size of the circles.

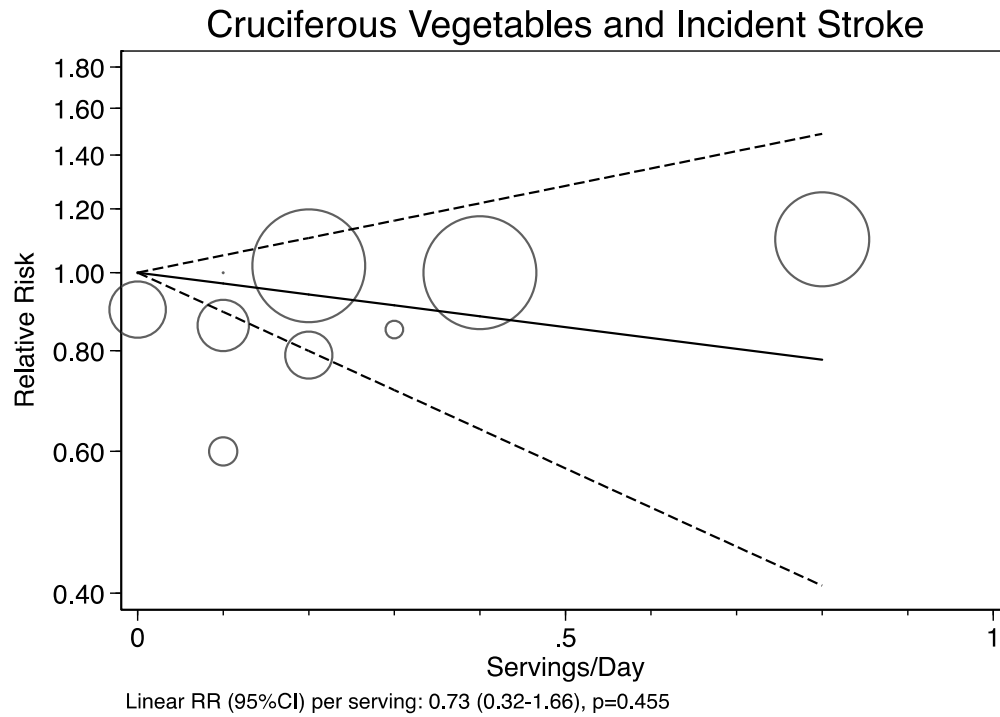


Figure S155. Linear dose-response relation between increasing intake of cruciferous vegetables and incidence of stroke. Linear dose-response data was modeled using the Greenland and Longnecker²³ method to estimate the covariances of multivariable-adjusted relative risk, with kept on the original dose scale. Dashed lines represent the pointwise 95% confidence intervals for the fitted linear trend represented by a solid line. Individual observations are represented by the circles, with the weight of the study in the overall analysis represented by the size of the circles.

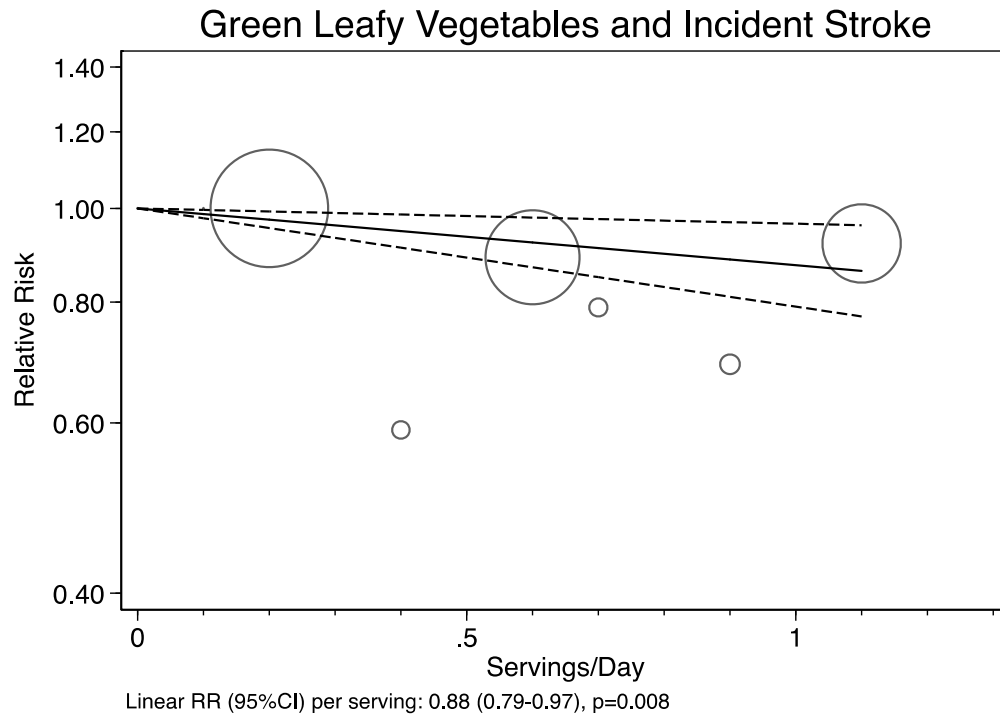


Figure S156. Linear dose-response relation between increasing intake of green leafy vegetables and incidence of stroke. Linear dose-response data was modeled using the Greenland and Longnecker²³ method to estimate the covariances of multivariable-adjusted relative risk, with kept on the original dose scale. Dashed lines represent the pointwise 95% confidence intervals for the fitted linear trend represented by a solid line. Individual observations are represented by the circles, with the weight of the study in the overall analysis represented by the size of the circles.

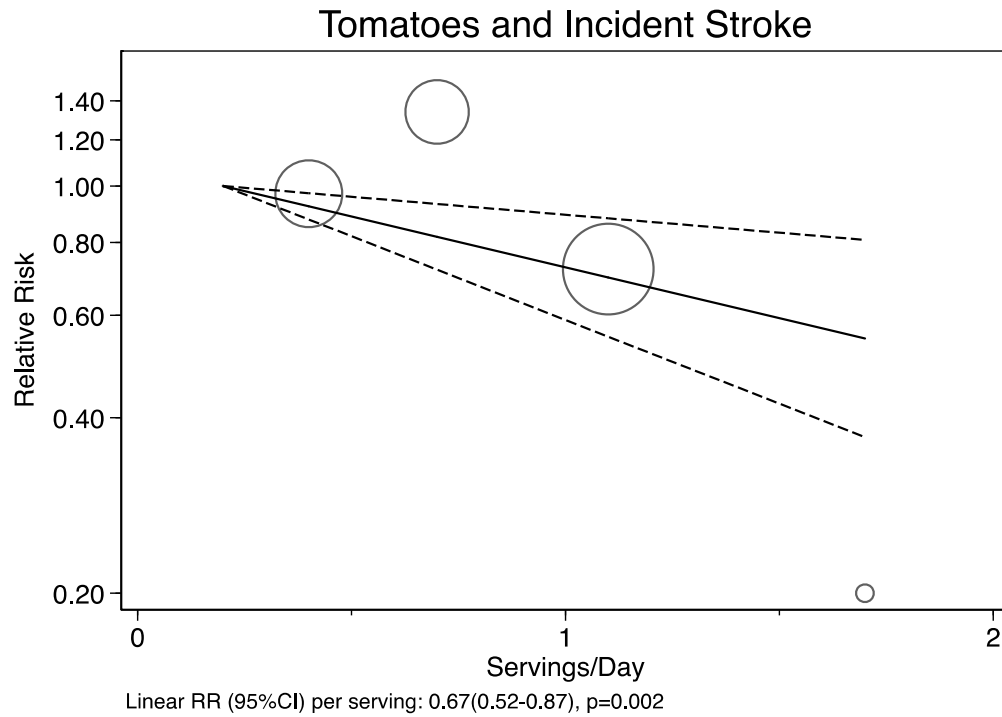


Figure S157. Linear dose-response relation between increasing tomato intake and incidence of stroke. Linear dose-response data was modeled using the Greenland and Longnecker²³ method to estimate the covariances of multivariable-adjusted relative risk, with kept on the original dose scale. Dashed lines represent the pointwise 95% confidence intervals for the fitted linear trend represented by a solid line. Individual observations are represented by the circles, with the weight of the study in the overall analysis represented by the size of the circles.

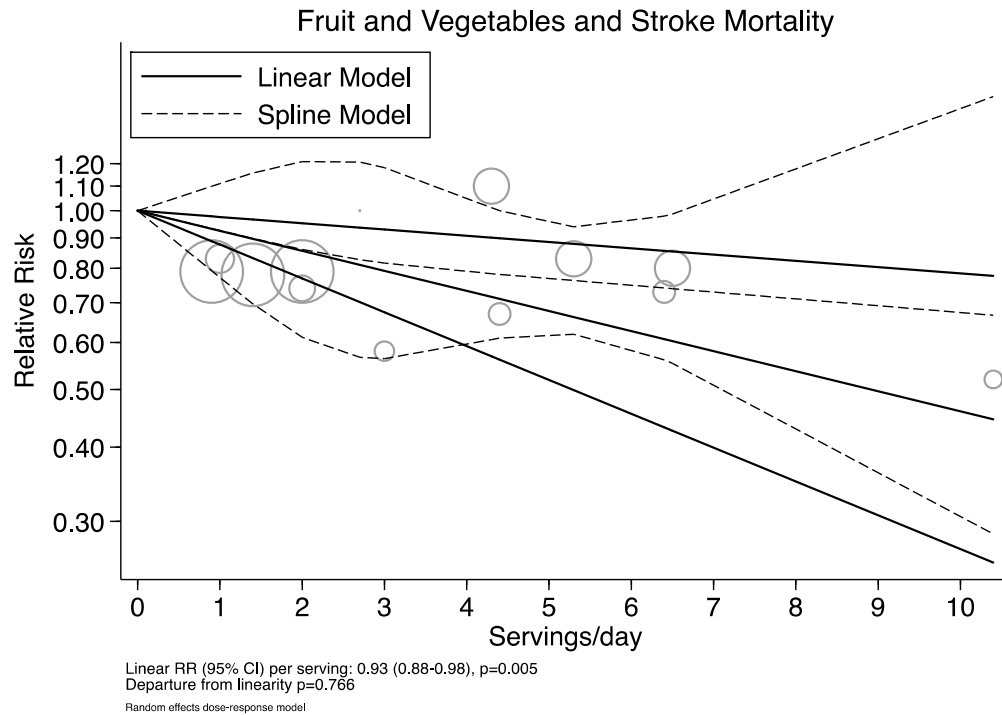


Figure S158. Linear dose-response relation between increasing fruit and vegetable intake and stroke mortality. Linear dose-response data was modeled using the Greenland and Longnecker²³ method to estimate the covariances of multivariable-adjusted relative risk, with kept on the original dose scale. Dashed lines represent the pointwise 95% confidence intervals for the fitted linear trend represented by a solid line. Individual observations are represented by the circles, with the weight of the study in the overall analysis represented by the size of the circles.

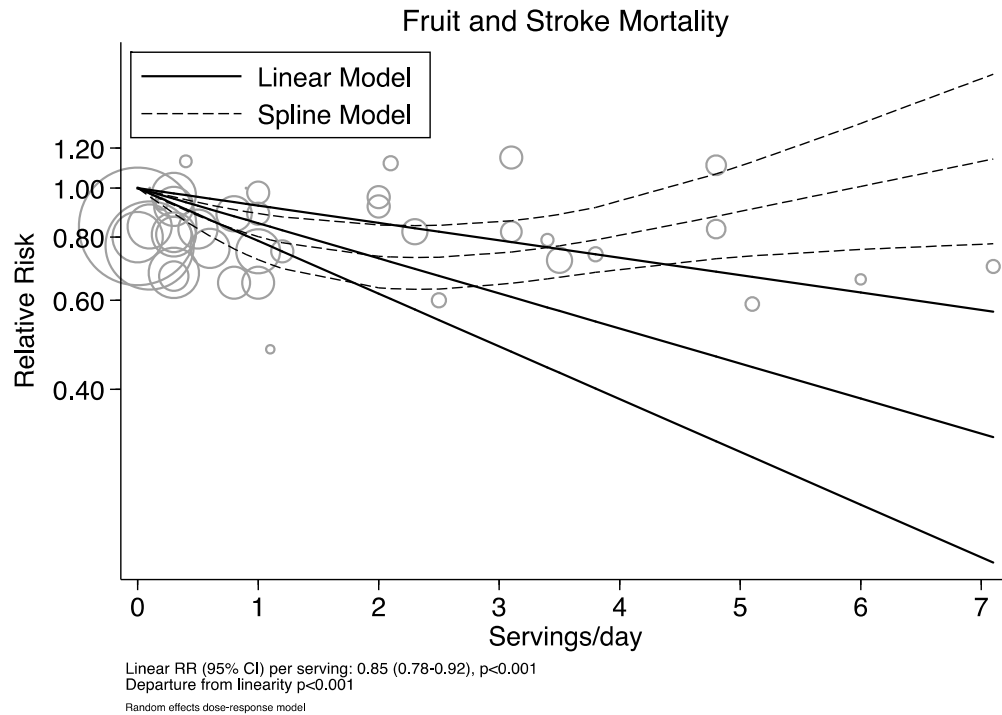


Figure S159. Linear and cubic-spline dose-response relation between increasing fruit intake and stroke mortality. Linear dose-response data was modeled using the Greenland and Longnecker²³ method to estimate the covariances of multivariable-adjusted relative risk. Cubic spline data were modeled with fixed-effects restricted cubic spline with 3 knots and using the Greenland and Longnecker²³ method to estimate the covariances of multivariable-adjusted relative risk. All data was kept on the original dose scale. The fitted trend for each model is represented by a central line (solid lines for linear model; dashed lines for cubic spline model) with 95% confidence intervals represented by the outer lines. Individual observations are represented by the circles, with the weight of the study in the overall analysis represented by the size of the circles.

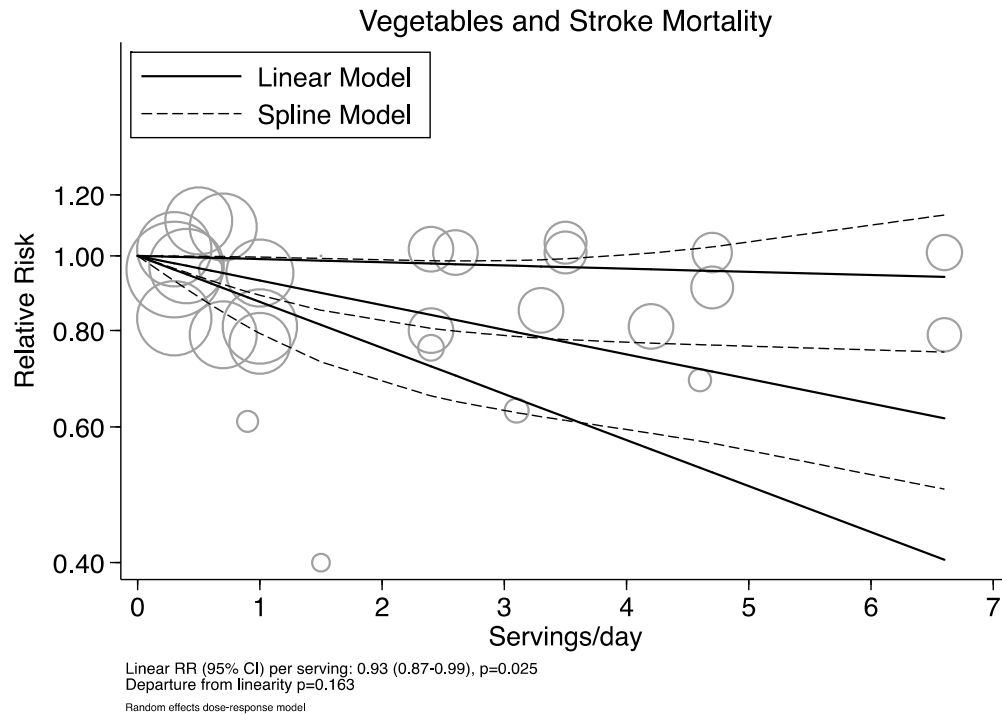


Figure S160. Linear and cubic-spline dose-response relation between increasing intake of vegetables and stroke mortality. Linear dose-response data was modeled using the Greenland and Longnecker²³ method to estimate the covariances of multivariable-adjusted relative risk. Cubic spline data were modeled with fixed-effects restricted cubic spline with 3 knots and using the Greenland and Longnecker²³ method to estimate the covariances of multivariable-adjusted relative risk. All data was kept on the original dose scale. The fitted trend for each model is represented by a central line (solid lines for linear model; dashed lines for cubic spline model) with 95% confidence intervals represented by the outer lines. Individual observations are represented by the circles, with the weight of the study in the overall analysis represented by the size of the circles.

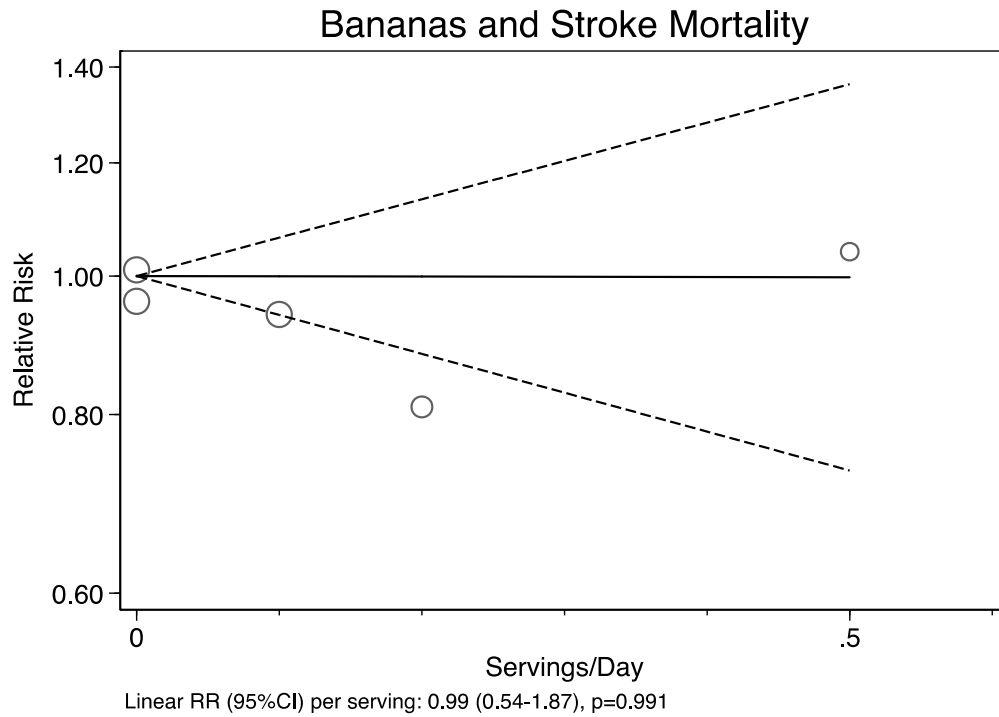


Figure S161 Linear dose-response relation between increasing banana intake and stroke mortality. Linear dose-response data was modeled using the Greenland and Longnecker²³ method to estimate the covariances of multivariable-adjusted relative risk, with kept on the original dose scale. Dashed lines represent the pointwise 95% confidence intervals for the fitted linear trend represented by a solid line. Individual observations are represented by the circles, with the weight of the study in the overall analysis represented by the size of the circles.

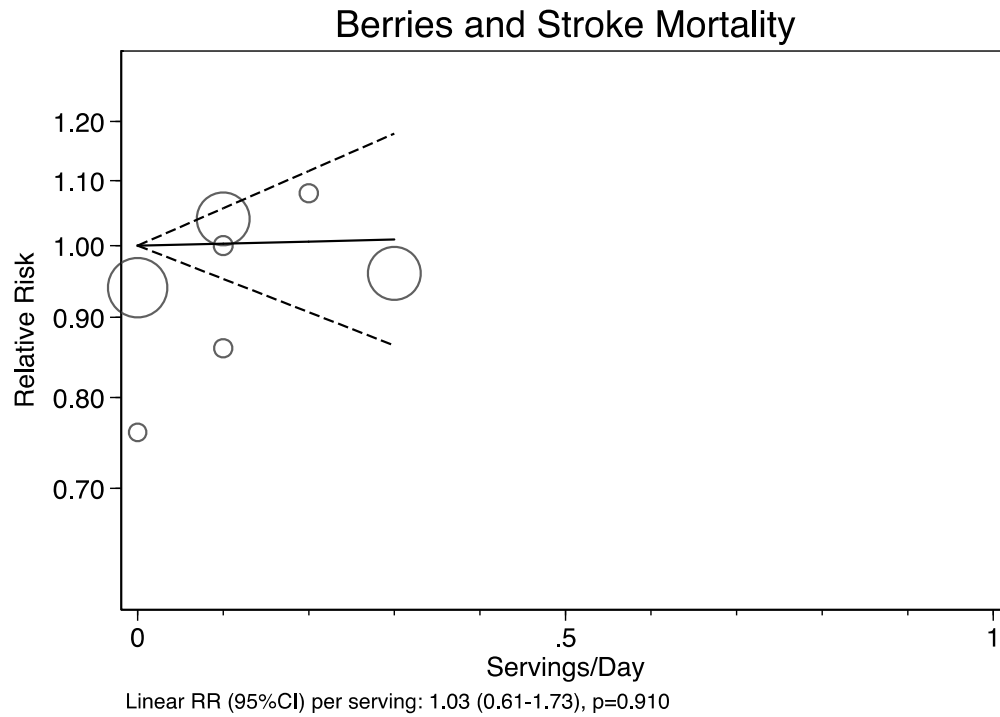


Figure S162. Linear dose-response relation between increasing berries intake and stroke mortality. Linear dose-response data was modeled using the Greenland and Longnecker²³ method to estimate the covariances of multivariable-adjusted relative risk, with kept on the original dose scale. Dashed lines represent the pointwise 95% confidence intervals for the fitted linear trend represented by a solid line. Individual observations are represented by the circles, with the weight of the study in the overall analysis represented by the size of the circles.

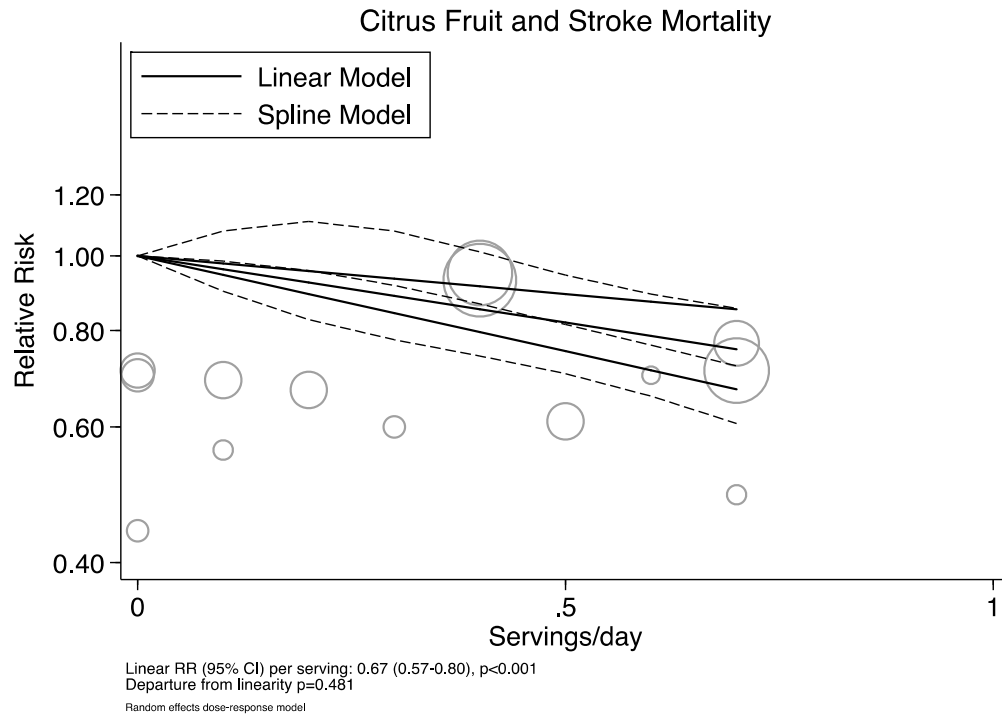


Figure S163. Linear and cubic-spline dose-response relation between increasing citrus fruit intake and stroke mortality. Linear dose-response data was modeled using the Greenland and Longnecker²³ method to estimate the covariances of multivariable-adjusted relative risk. Cubic spline data were modeled with fixed-effects restricted cubic spline with 3 knots and using the Greenland and Longnecker²³ method to estimate the covariances of multivariable-adjusted relative risk. All data was kept on the original dose scale. The fitted trend for each model is represented by a central line (solid lines for linear model; dashed lines for cubic spline model) with 95% confidence intervals represented by the outer lines. Individual observations are represented by the circles, with the weight of the study in the overall analysis represented by the size of the circles.

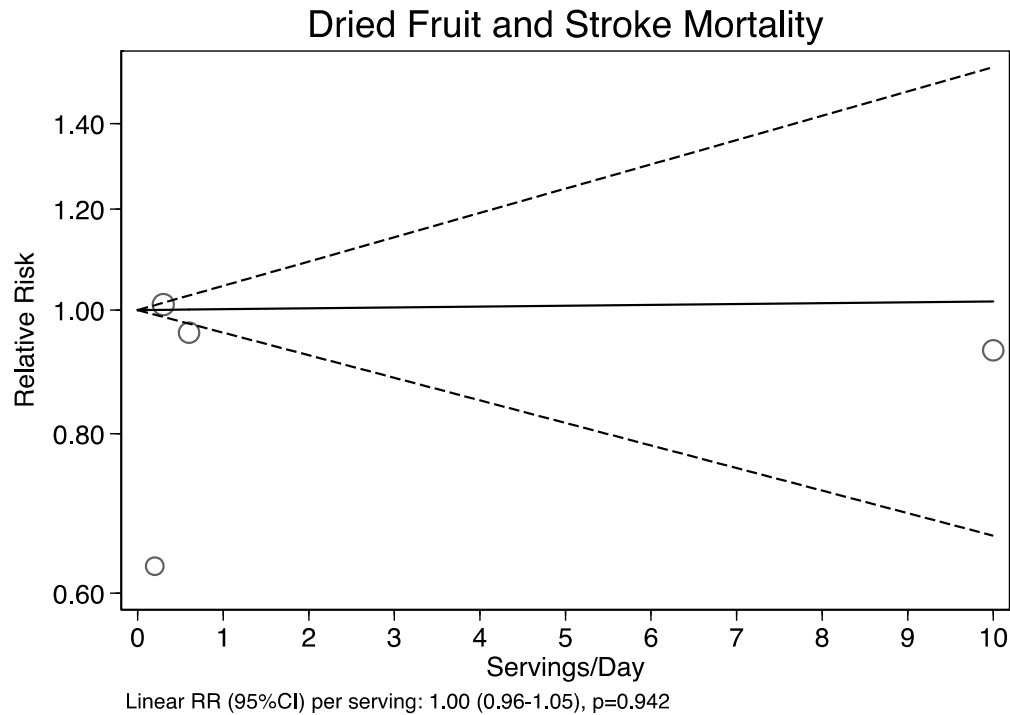


Figure S164. Linear and cubic-spline dose-response relation between increasing dried fruit intake and stroke mortality. Linear dose-response data was modeled using the Greenland and Longnecker²³ method to estimate the covariances of multivariable-adjusted relative risk. Cubic spline data were modeled with fixed-effects restricted cubic spline with 3 knots and using the Greenland and Longnecker²³ method to estimate the covariances of multivariable-adjusted relative risk. All data was kept on the original dose scale. The fitted trend for each model is represented by a central line (solid lines for linear model; dashed lines for cubic spline model) with 95% confidence intervals represented by the outer lines. Individual observations are represented by the circles, with the weight of the study in the overall analysis represented by the size of the circles.

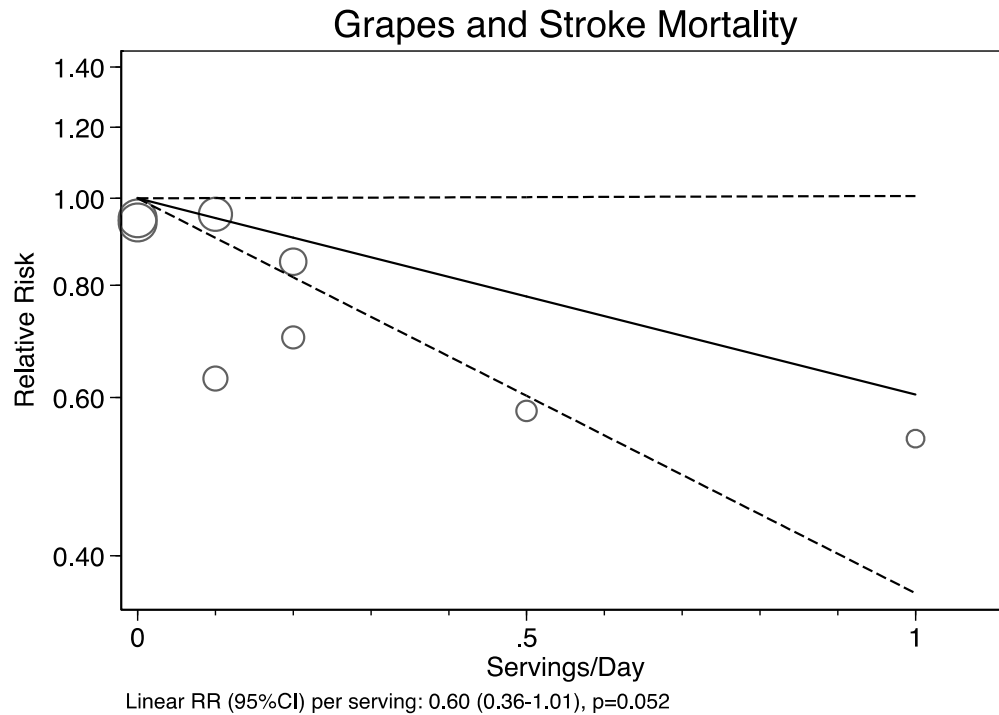


Figure S165. Linear dose-response relation between increasing grapes intake and stroke mortality. Linear dose-response data was modeled using the Greenland and Longnecker²³ method to estimate the covariances of multivariable-adjusted relative risk, with kept on the original dose scale. Dashed lines represent the pointwise 95% confidence intervals for the fitted linear trend represented by a solid line. Individual observations are represented by the circles, with the weight of the study in the overall analysis represented by the size of the circles.

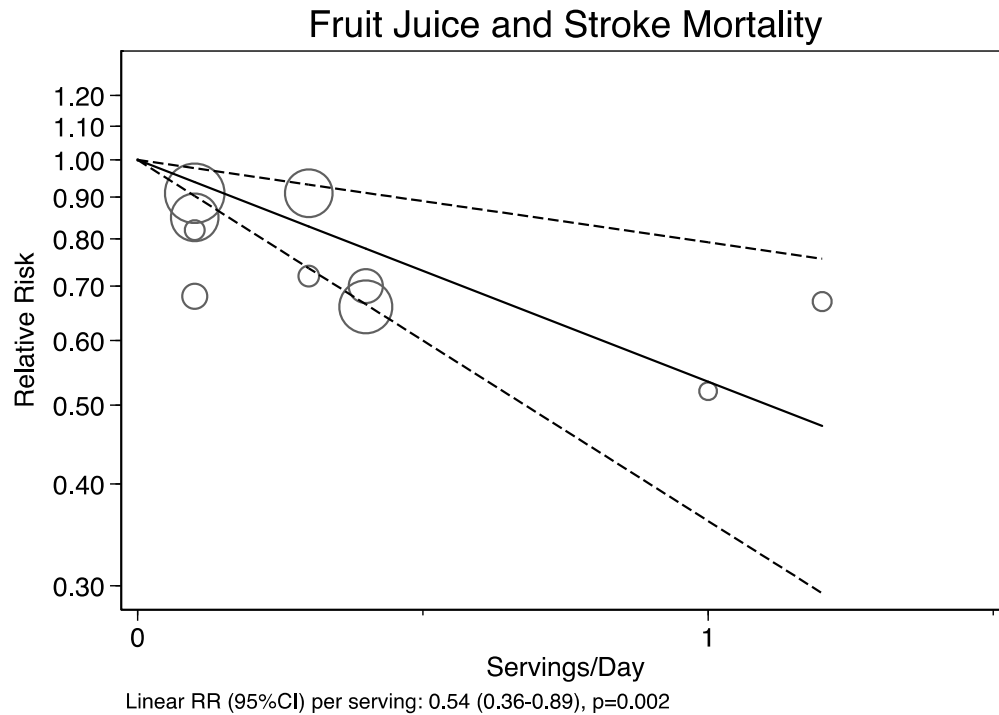


Figure S166. Linear dose-response relation between increasing fruit juice intake and stroke mortality. Linear dose-response data was modeled using the Greenland and Longnecker²³ method to estimate the covariances of multivariable-adjusted relative risk, with kept on the original dose scale. Dashed lines represent the pointwise 95% confidence intervals for the fitted linear trend represented by a solid line. Individual observations are represented by the circles, with the weight of the study in the overall analysis represented by the size of the circles.

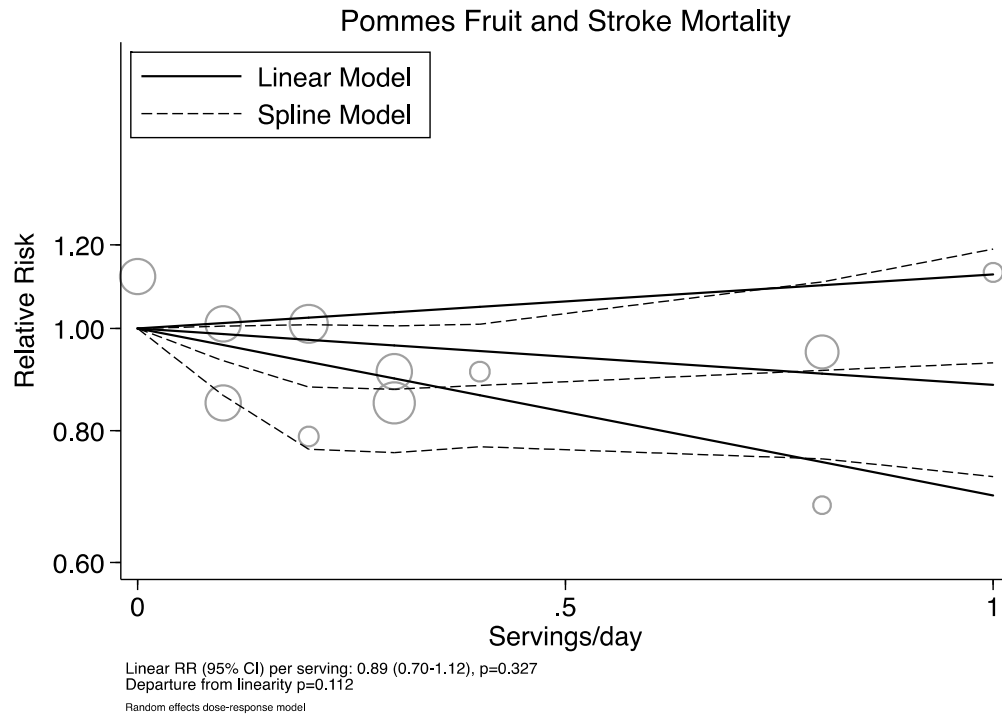


Figure S167. Linear and cubic-spline dose-response relation between increasing pomme fruit intake and stroke mortality. Linear dose-response data was modeled using the Greenland and Longnecker²³ method to estimate the covariances of multivariable-adjusted relative risk. Cubic spline data were modeled with fixed-effects restricted cubic spline with 3 knots and using the Greenland and Longnecker²³ method to estimate the covariances of multivariable-adjusted relative risk. All data was kept on the original dose scale. The fitted trend for each model is represented by a central line (solid lines for linear model; dashed lines for cubic spline model) with 95% confidence intervals represented by the outer lines. Individual observations are represented by the circles, with the weight of the study in the overall analysis represented by the size of the circles.

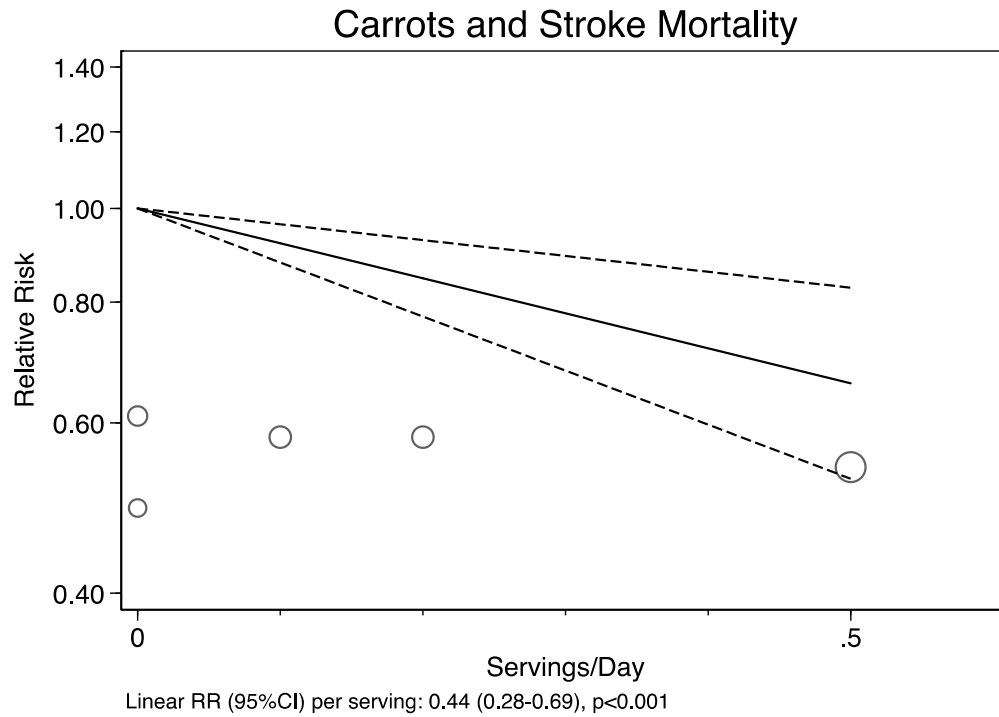


Figure S168. Linear dose-response relation between increasing intake of carrots and stroke mortality. Linear dose-response data was modeled using the Greenland and Longnecker²³ method to estimate the covariances of multivariable-adjusted relative risk, with kept on the original dose scale. Dashed lines represent the pointwise 95% confidence intervals for the fitted linear trend represented by a solid line. Individual observations are represented by the circles, with the weight of the study in the overall analysis represented by the size of the circles.

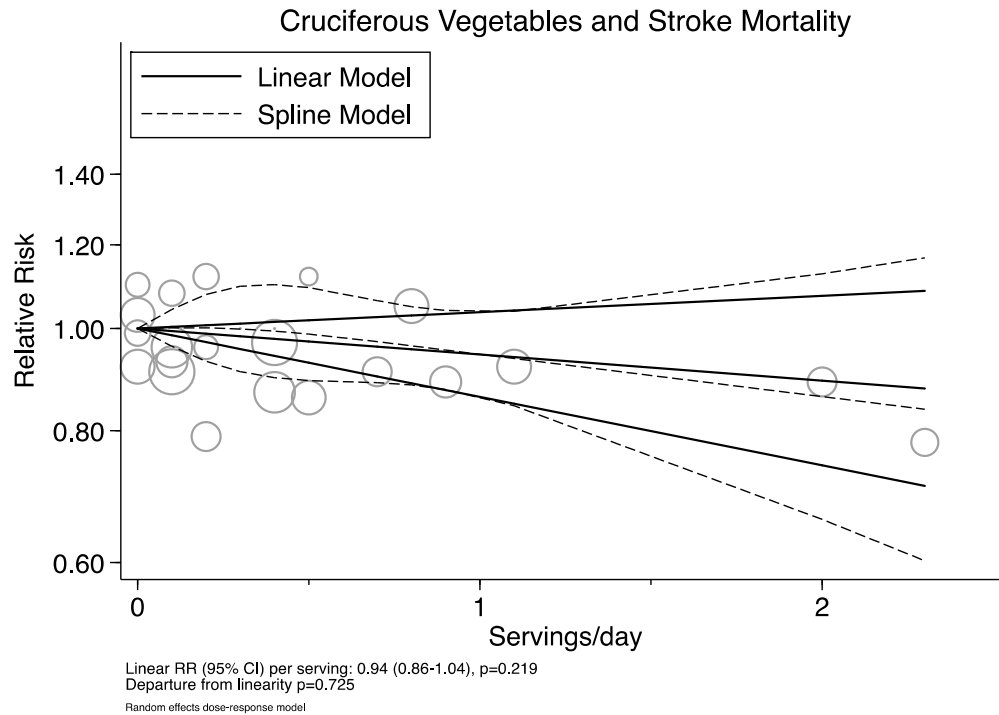


Figure S169. Linear and cubic-spline dose-response relation between increasing cruciferous vegetable intake and stroke mortality. Linear dose-response data was modeled using the Greenland and Longnecker²³ method to estimate the covariances of multivariable-adjusted relative risk. Cubic spline data were modeled with fixed-effects restricted cubic spline with 3 knots and using the Greenland and Longnecker²³ method to estimate the covariances of multivariable-adjusted relative risk. All data was kept on the original dose scale. The fitted trend for each model is represented by a central line (solid lines for linear model; dashed lines for cubic spline model) with 95% confidence intervals represented by the outer lines. Individual observations are represented by the circles, with the weight of the study in the overall analysis represented by the size of the circles.

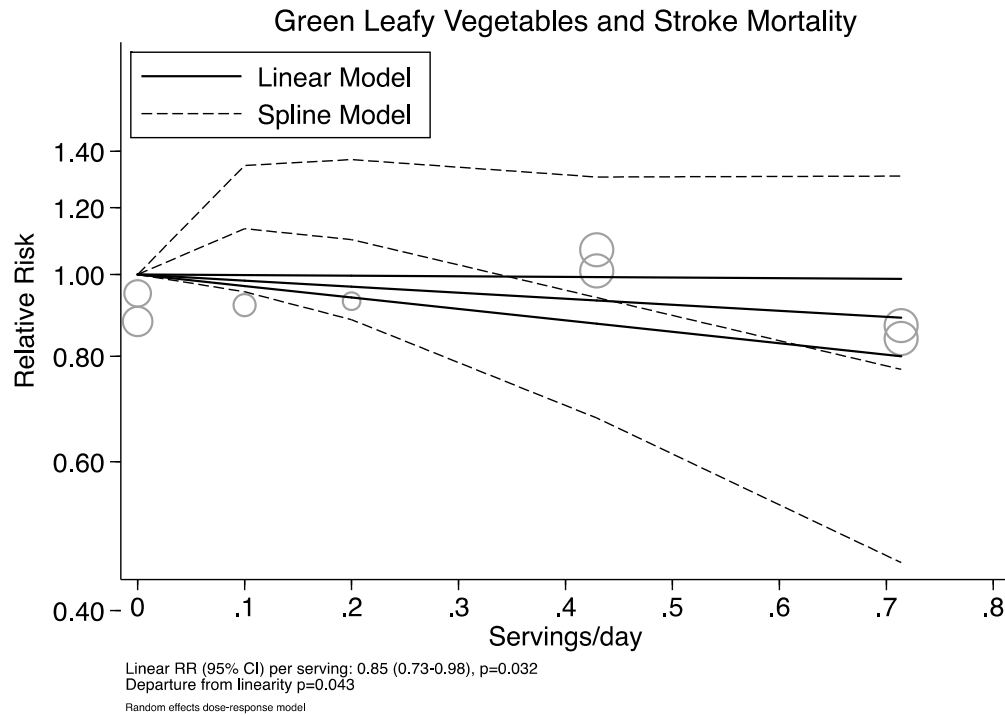


Figure S170. Linear and cubic-spline dose-response relation between increasing green leafy vegetable intake and stroke mortality. Linear dose-response data was modeled using the Greenland and Longnecker²³ method to estimate the covariances of multivariable-adjusted relative risk. Cubic spline data were modeled with fixed-effects restricted cubic spline with 3 knots and using the Greenland and Longnecker²³ method to estimate the covariances of multivariable-adjusted relative risk. All data was kept on the original dose scale. The fitted trend for each model is represented by a central line (solid lines for linear model; dashed lines for cubic spline model) with 95% confidence intervals represented by the outer lines. Individual observations are represented by the circles, with the weight of the study in the overall analysis represented by the size of the circles.

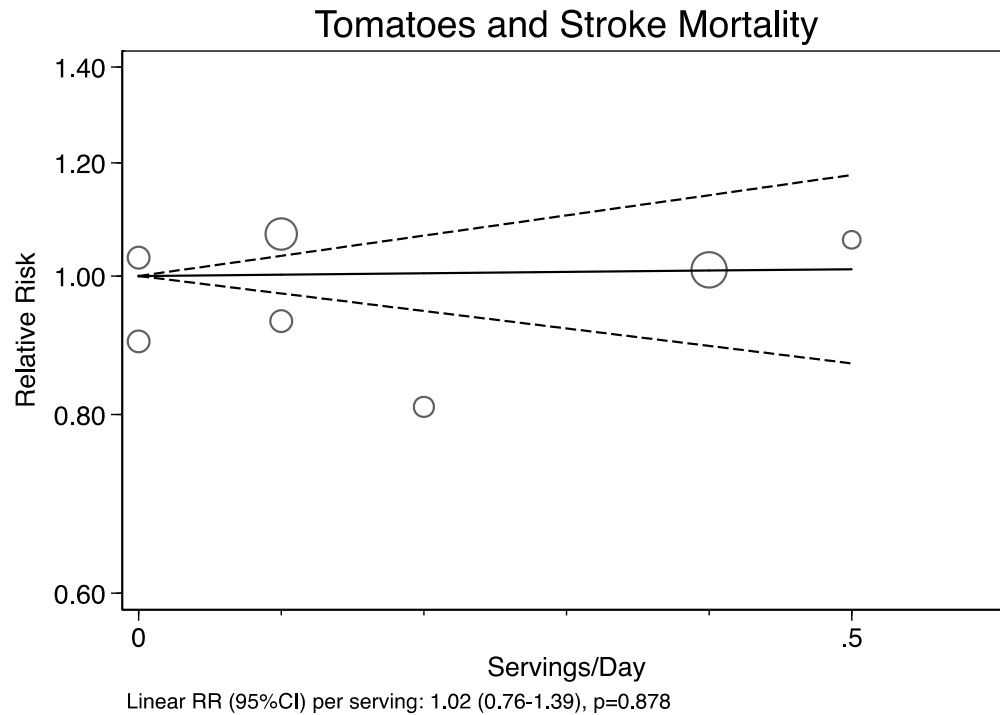


Figure S171. Linear dose-response relation between increasing intake of tomatoes and stroke mortality. Linear dose-response data was modeled using the Greenland and Longnecker²³ method to estimate the covariances of multivariable-adjusted relative risk, with kept on the original dose scale. Dashed lines represent the pointwise 95% confidence intervals for the fitted linear trend represented by a solid line. Individual observations are represented by the circles, with the weight of the study in the overall analysis represented by the size of the circles.

TOTAL FRUIT AND VEGETABLES AND CARDIOVASCULAR DISEASE INCIDENCE

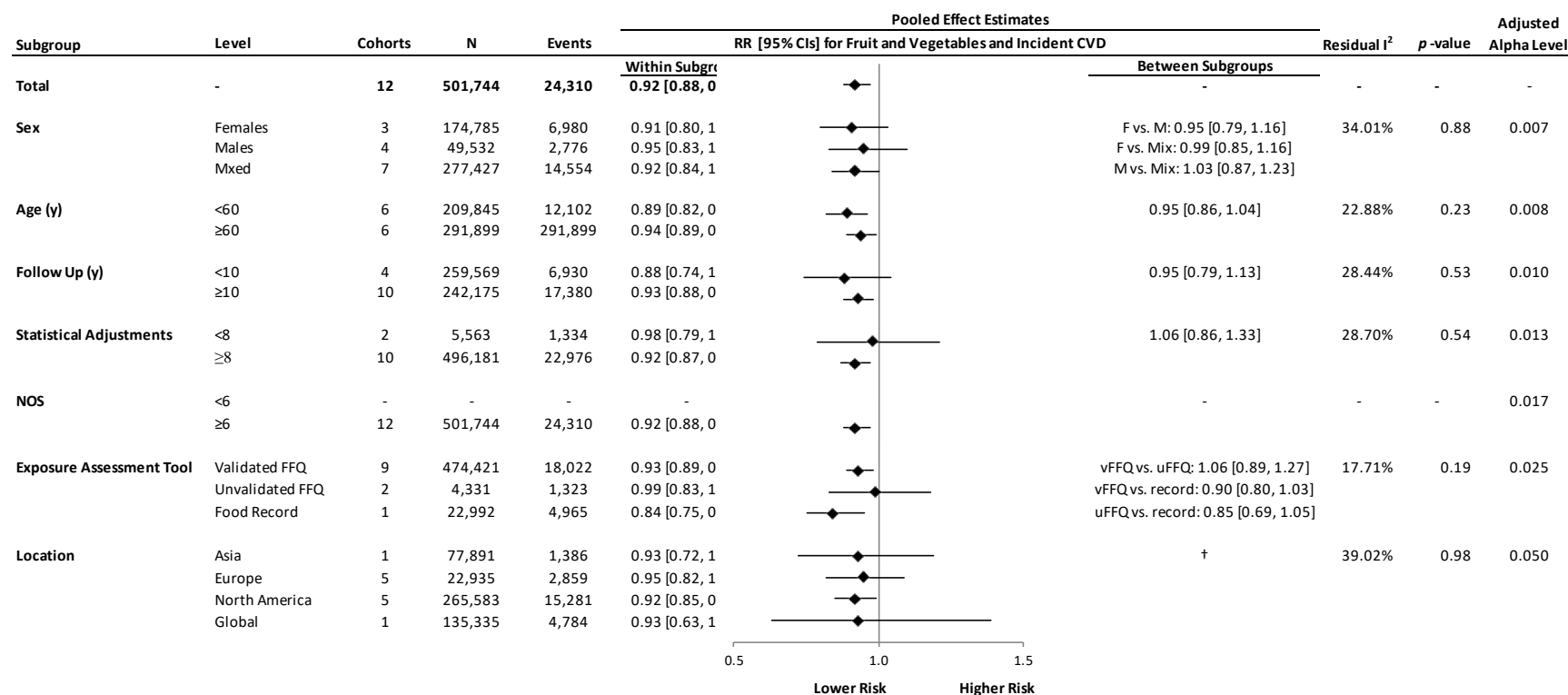


Figure S172. Categorical subgroup analyses of total fruit and vegetable intake and cardiovascular disease incidence. Point estimates for within subgroup level are the pooled effect estimates and are represented by a black diamond. The residual I² value indicates the inter-study heterogeneity unexplained by the subgroup. CVD – cardiovascular disease; FFQ – food frequency questionnaire; NOS – Newcastle-Ottawa Scale; RR – relative risk; 95% CIs – 95% confidence intervals. † Europe vs. Asia 0.98 [0.74, 1.31]; Europe vs. Global 0.99 [0.64, 1.51]; Europe vs. North America 0.97 [0.83, 1.14]; Asia vs. Global 0.99 [0.62, 1.60]; Asia vs. North America 1.00 [0.78, 1.32]; Global vs. North America 1.02 [0.68, 1.53];

FRUIT AND CARDIOVASCULAR DISEASE INCIDENCE

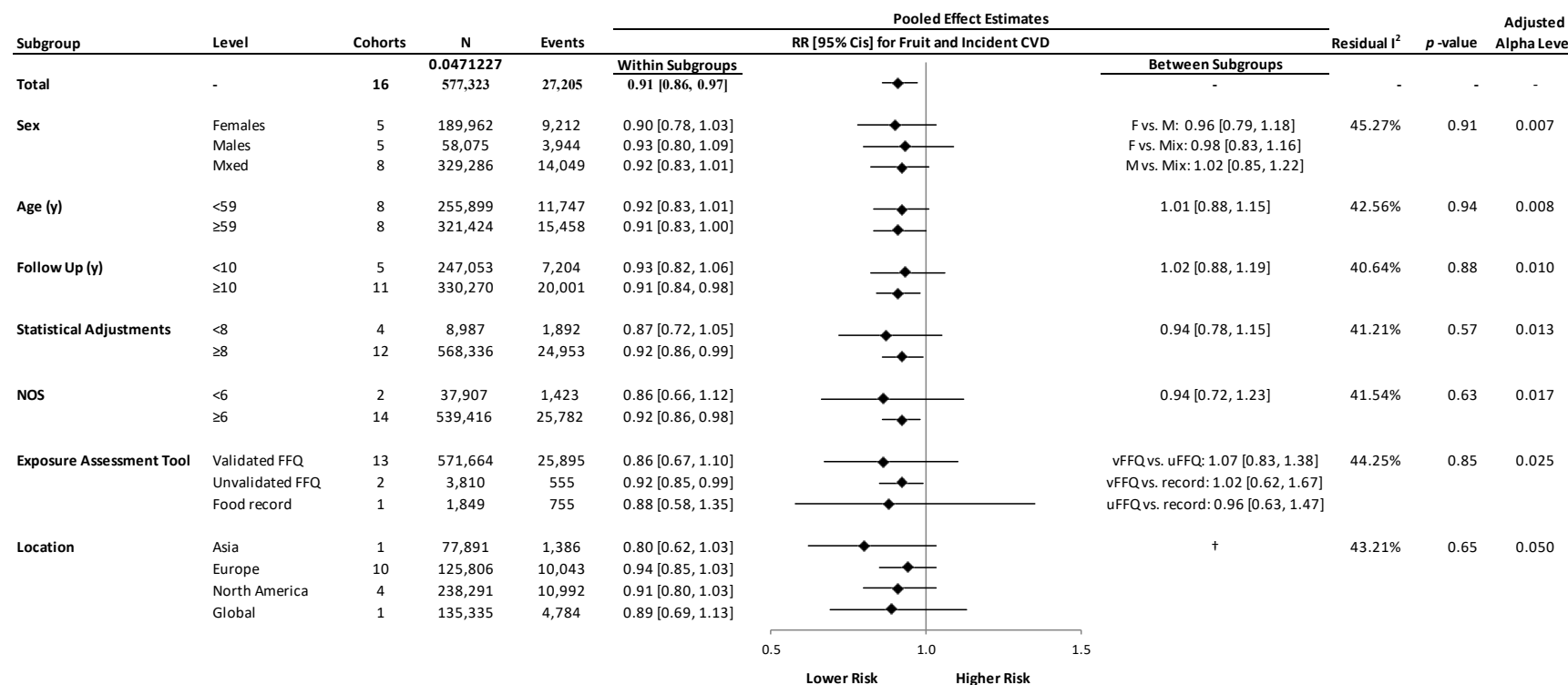


Figure S173. Categorical subgroup analyses of fruit intake and cardiovascular disease incidence. Point estimates for within subgroup level are the pooled effect estimates and are represented by a black diamond. The residual I² value indicates the inter-study heterogeneity unexplained by the subgroup. CVD – cardiovascular disease; FFQ – food frequency questionnaire; NOS – Newcastle-Ottawa Scale; RR – relative risk; 95% CIs – 95% confidence intervals.

† Europe vs. Asia 0.85 [0.65, 1.12]; Europe vs. Global 0.94 [0.73, 1.23]; Europe vs. North America 0.96 [0.82, 1.13]; Asia vs. Global 0.90 [0.63, 1.29]; Asia vs. North America 0.88 [0.67, 1.18]; Global vs. North America 0.98 [0.74, 1.29]

VEGETABLES AND CARDIOVASCULAR DISEASE INCIDENCE

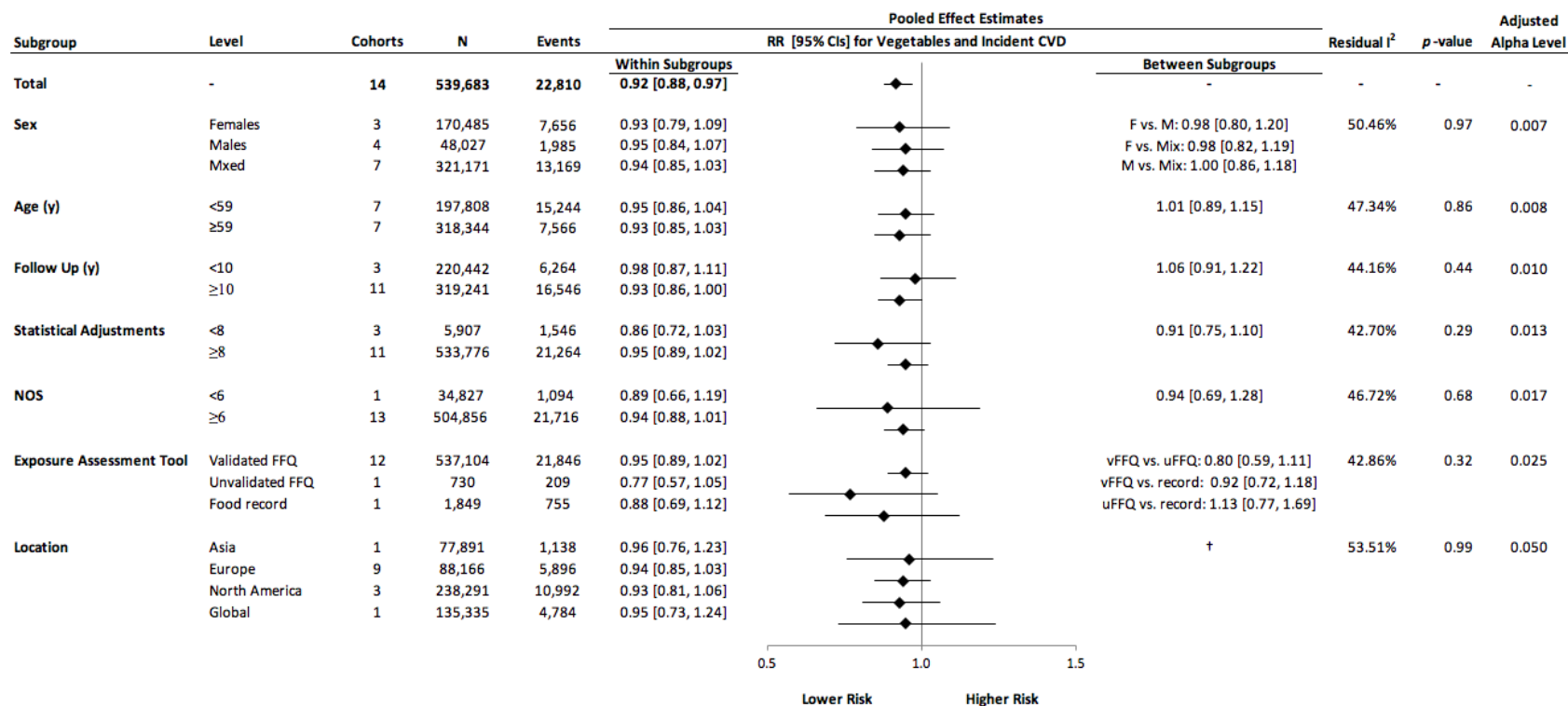


Figure S174. Categorical subgroup analyses of intake of vegetables and cardiovascular disease incidence. Point estimates for within subgroup level are the pooled effect estimates and are represented by a black diamond. The residual I² value indicates the inter-study heterogeneity unexplained by the subgroup. CVD – cardiovascular disease; FFQ – food frequency questionnaire; NOS – Newcastle-Ottawa Scale; RR – relative risk; 95% CIs – 95% confidence intervals.
 † Europe vs. Asia 1.03 [0.79, 1.33]; Europe vs. Global 1.01 [0.76, 1.34]; Europe vs. NA 0.99 [0.84, 1.16]; Asia vs. Global 1.01 [0.71, 1.45]; Asia vs. NA 1.04 [0.79, 1.37]; Global vs. NA 1.03 [0.76, 1.38]

TOTAL FRUIT AND VEGETABLES AND CARDIOVASCULAR DISEASE MORTALITY

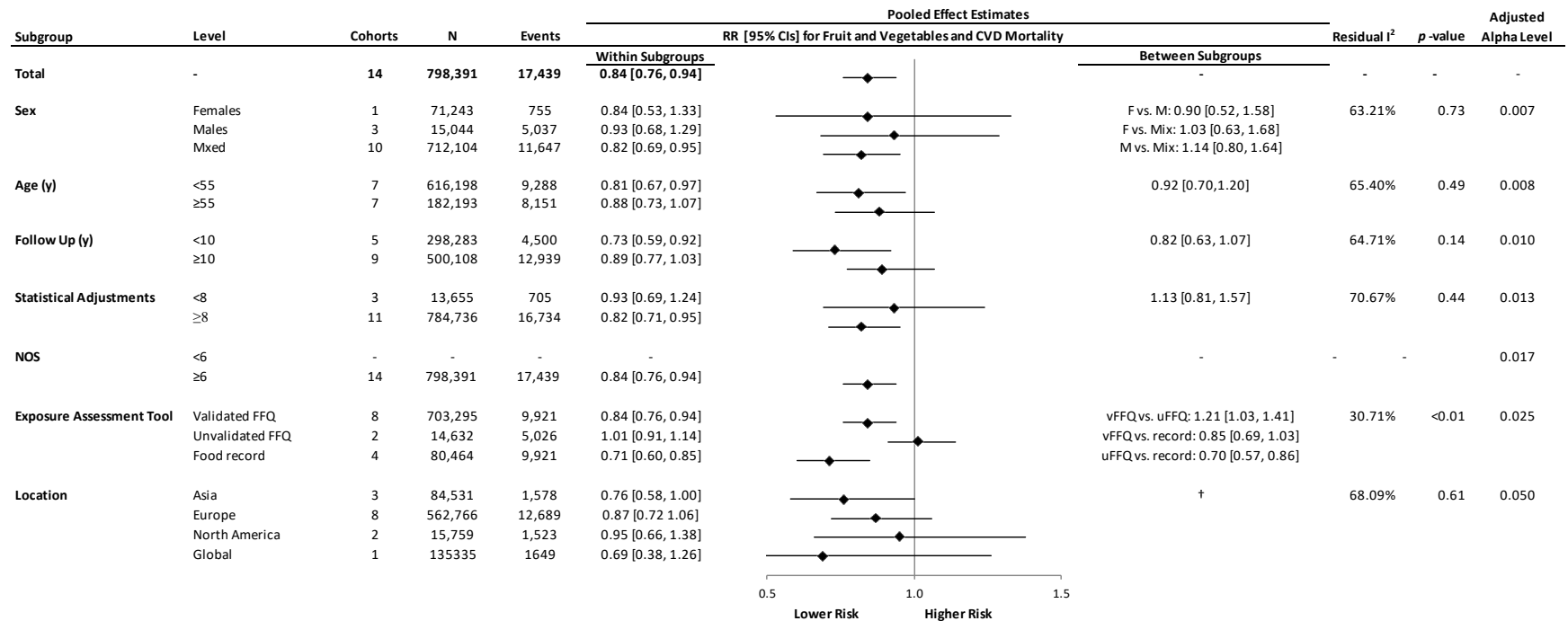


Figure S175. Categorical subgroup analyses of total fruit and vegetable intake and cardiovascular disease mortality. Point estimates for within subgroup level are the pooled effect estimates and are represented by a black diamond. The residual I² value indicates the inter-study heterogeneity unexplained by the subgroup. CVD – cardiovascular disease; FFQ – food frequency questionnaire; NOS – Newcastle-Ottawa Scale; RR – relative risk; 95% CIs – 95% confidence intervals. † Europe vs. Asia 0.87 [0.63, 1.22]; Europe vs. Global 0.79 [0.42, 1.49]; Europe vs. North America 1.09 [0.72, 1.66]; Asia vs. Global 1.10 [0.57, 2.13]; Asia vs. North America 0.80 [0.50, 1.27]; Global vs. North America 0.73 [0.36, 1.47]

FRUIT AND CARDIOVASCULAR DISEASE MORTALITY

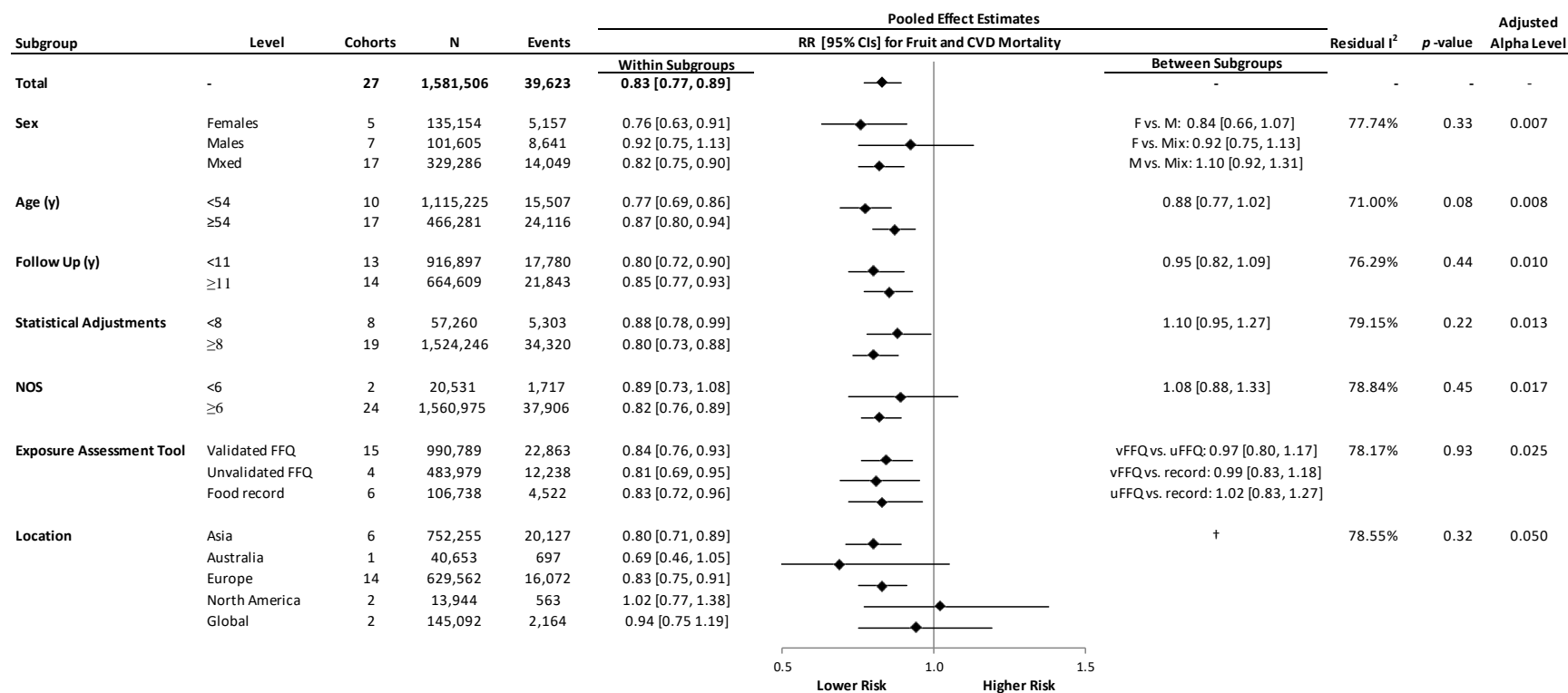


Figure S176. Categorical subgroup analyses of fruit intake and cardiovascular disease mortality. Point estimates for within subgroup level are the pooled effect estimates and are represented by a black diamond. The residual I² value indicates the inter-study heterogeneity unexplained by the subgroup. CVD – cardiovascular disease; FFQ – food frequency questionnaire; NOS – Newcastle-Ottawa Scale; RR – relative risk; 95% CIs – 95% confidence intervals.

† Europe vs. Asia 0.96 [0.83, 1.13]; Europe vs. Australia 0.84 [0.55, 1.28]; Europe vs. Global 1.14 [0.89, 1.47]; Europe vs. North America 1.25 [0.92, 1.70]; Asia vs. Australia 1.15 [0.75, 1.77]; Asia vs. Global 0.85 [0.65, 1.10]; Asia vs. North America 0.77 [0.56, 1.06]; Australia vs. Global 0.73 [0.46, 1.18]; Australia vs. North America 0.67 [0.41, 1.12]; Global vs. North America 0.92 [0.63, 1.33]

VEGETABLES AND CARDIOVASCULAR DISEASE MORTALITY

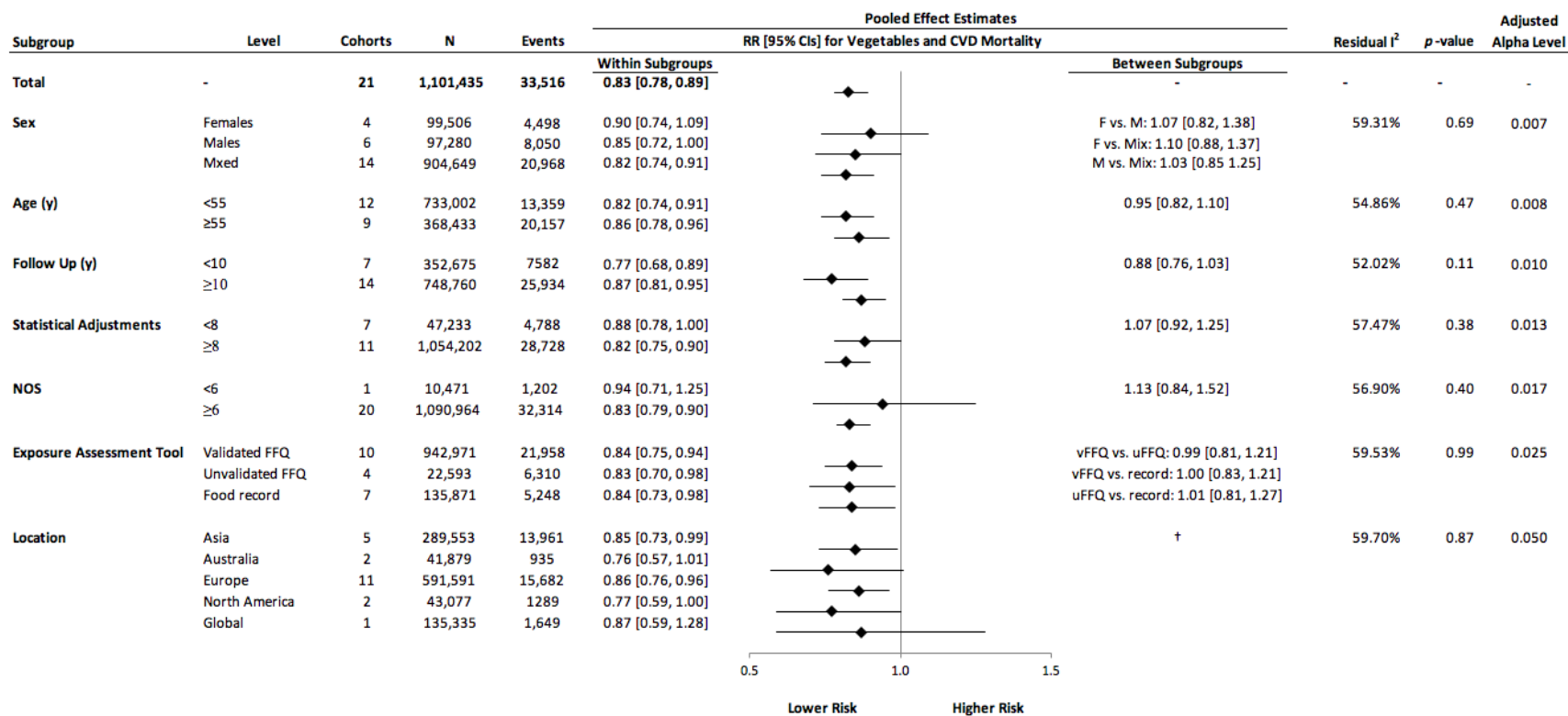


Figure S177. Categorical subgroup analyses of intake of vegetables and cardiovascular disease mortality. Point estimates for within subgroup level are the pooled effect estimates and are represented by a black diamond. The residual I² value indicates the inter-study heterogeneity unexplained by the subgroup. CVD – cardiovascular disease; FFQ – food frequency questionnaire; NOS – Newcastle-Ottawa Scale; RR – relative risk; 95% CIs – 95% confidence intervals.
 † Europe vs. Asia 0.99 [0.82, 1.19]; Europe vs. Australia 0.88 [0.65, 1.20]; Europe vs. Global 1.01 [0.68, 1.52]; Europe vs. North America 0.90 [0.67, 1.20]; Asia vs. Australia 1.12 [0.81, 1.56]; Asia vs. Global 0.98 [0.64, 1.48]; Asia vs. North America 1.11 [0.81, 1.50]; Australia vs. Global 0.87 [0.54, 1.41]; Australia vs. North America 0.98 [0.66, 1.46]; Global vs. North America 1.13 [0.71, 1.81]

TOTAL FRUIT AND VEGETABLES AND CORONARY HEART DISEASE INCIDENCE

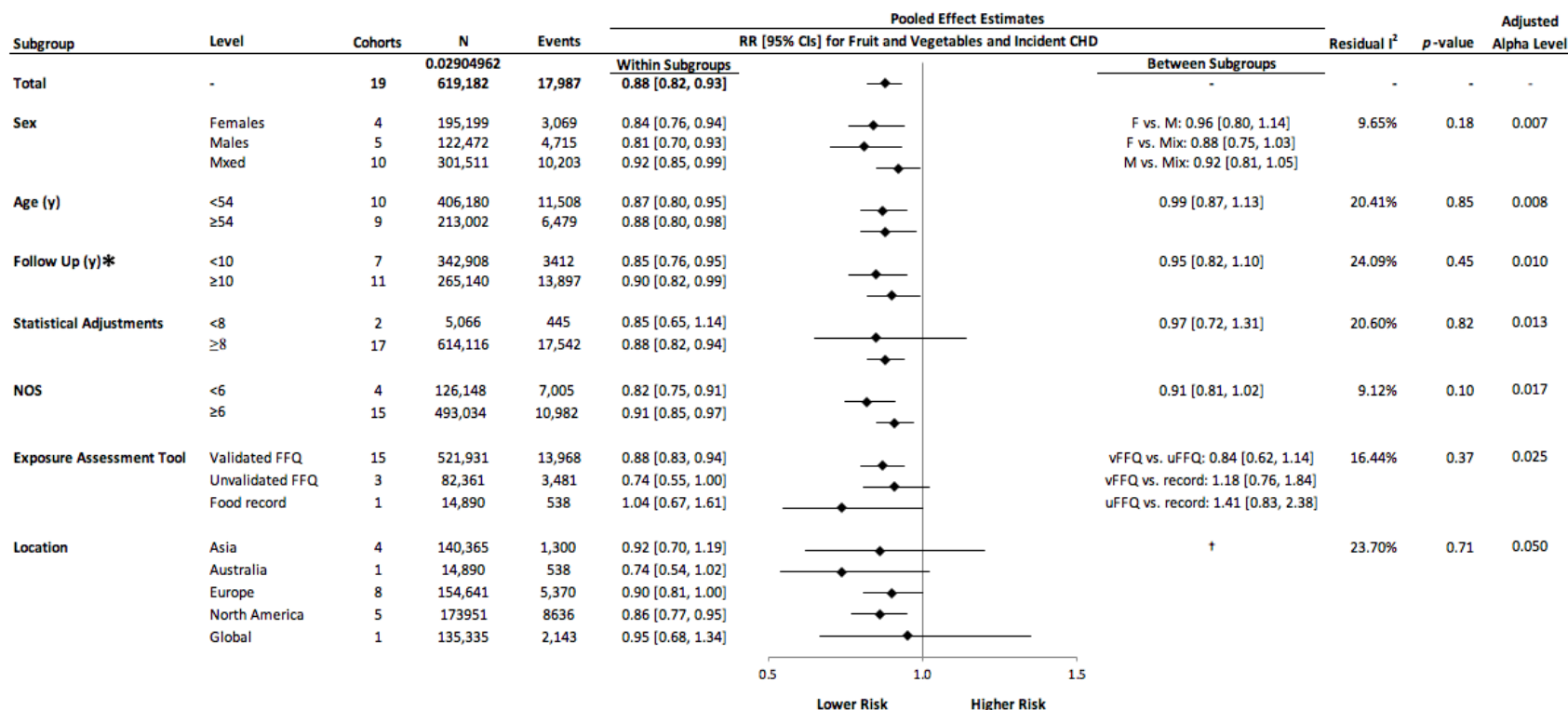


Figure S178. Categorical subgroup analyses of total fruit and vegetable intake and incident coronary heart disease. Point estimates for within subgroup level are the pooled effect estimates and are represented by a black diamond. The residual I² value indicates the inter-study heterogeneity unexplained by the subgroup. CHD – coronary heart disease; FFQ – food frequency questionnaire; NOS – Newcastle-Ottawa Scale; RR – relative risk; 95% CIs – 95% confidence intervals. * Follow-up years includes 17 cohorts as Bingham et al. 2008 (EPIC Norfolk) did not report follow-up time. † Europe vs. Asia 1.02 [0.77, 1.35]; Europe vs. Australia 0.82 [0.59, 1.14]; Europe vs. Global 1.06 [0.74, 1.51]; Europe vs. North America 0.95 [0.83, 1.10]; Asia vs. Australia 1.24 [0.82, 1.87]; Asia vs. Global 0.96 [0.63, 1.48]; Asia vs. North America 1.07 [0.81, 1.42]; Australia vs. Global 0.78 [0.49, 1.24]; Australia vs. North America 0.86 [0.62, 1.21]; Global vs. North America 1.11 [0.78, 1.58]

FRUIT AND CORONARY HEART DISEASE INCIDENCE

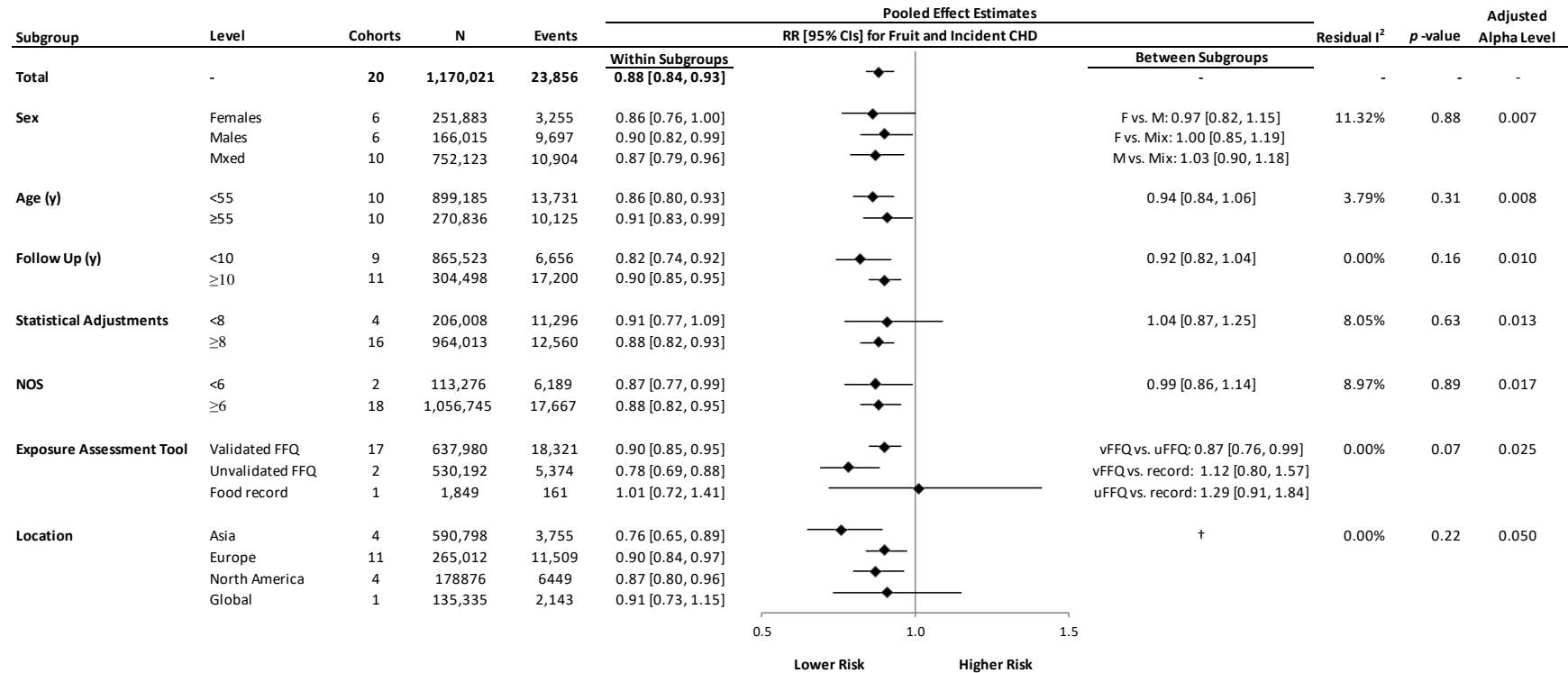


Figure S179. Categorical subgroup analyses of fruit intake and incident coronary heart disease. Point estimates for within subgroup level are the pooled effect estimates and are represented by a black diamond. The residual I² value indicates the inter-study heterogeneity unexplained by the subgroup. CHD – coronary heart disease; FFQ – food frequency questionnaire; NOS – Newcastle-Ottawa Scale; RR – relative risk; 95% CIs – 95% confidence intervals. † Europe vs. Asia 0.84 [0.71, 0.99]; Europe vs. Global 1.01 [0.79, 1.29]; Europe vs. North America 0.96 [0.85, 1.08]; Asia vs. Global 0.83 [0.63, 1.10]; Asia vs. North America 0.87 [0.73, 1.04]; Global vs. North America 1.05 [0.82, 1.34]

VEGETABLE AND CORONARY HEART DISEASE INCIDENCE

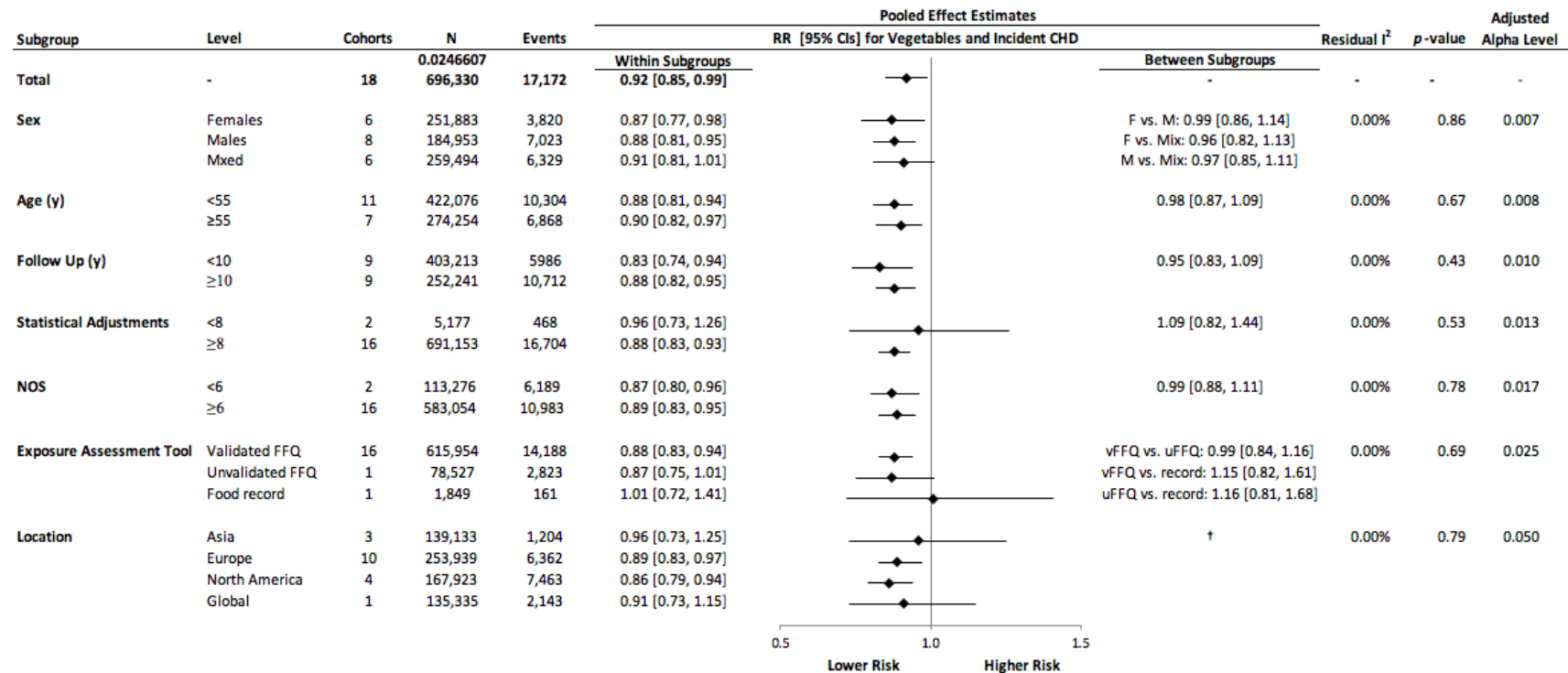


Figure S180. Categorical subgroup analyses of intake of vegetables and incident coronary heart disease. Point estimates for within subgroup level are the pooled effect estimates and are represented by a black diamond. The residual I² value indicates the inter-study heterogeneity unexplained by the subgroup. CHD – coronary heart disease; FFQ – food frequency questionnaire; NOS – Newcastle-Ottawa Scale; RR – relative risk; 95% CIs – 95% confidence intervals.

† Europe vs. Asia 1.07 [0.81, 1.41]; Europe vs. Global 1.02 [0.80, 1.30]; Europe vs. NA 0.96 [0.85, 1.08]; Asia vs. Global 1.05 [0.74, 1.49]; Asia vs. NA 1.11 [0.84, 1.48]; Global vs. NA 1.07 [0.83, 1.37]

CITRUS FRUIT AND CORONARY HEART DISEASE INCIDENCE

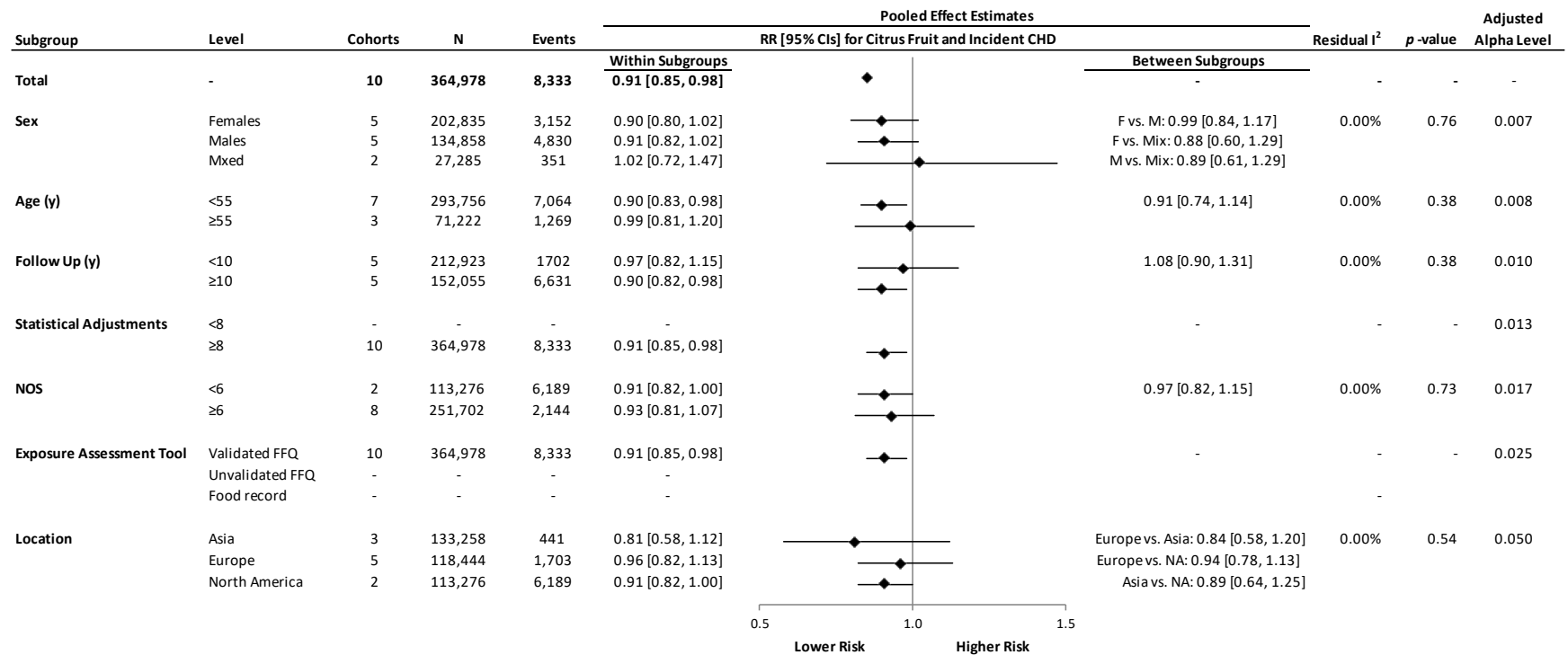


Figure S181. Categorical subgroup analyses of citrus fruit intake and incident coronary heart disease. Point estimates for within subgroup level are the pooled effect estimates and are represented by a black diamond. The residual I² value indicates the inter-study heterogeneity unexplained by the subgroup. CHD – coronary heart disease; FFQ – food frequency questionnaire; NOS – Newcastle-Ottawa Scale; RR – relative risk; 95% CIs – 95% confidence intervals.

FRUIT AND CORONARY HEART DISEASE MORTALITY

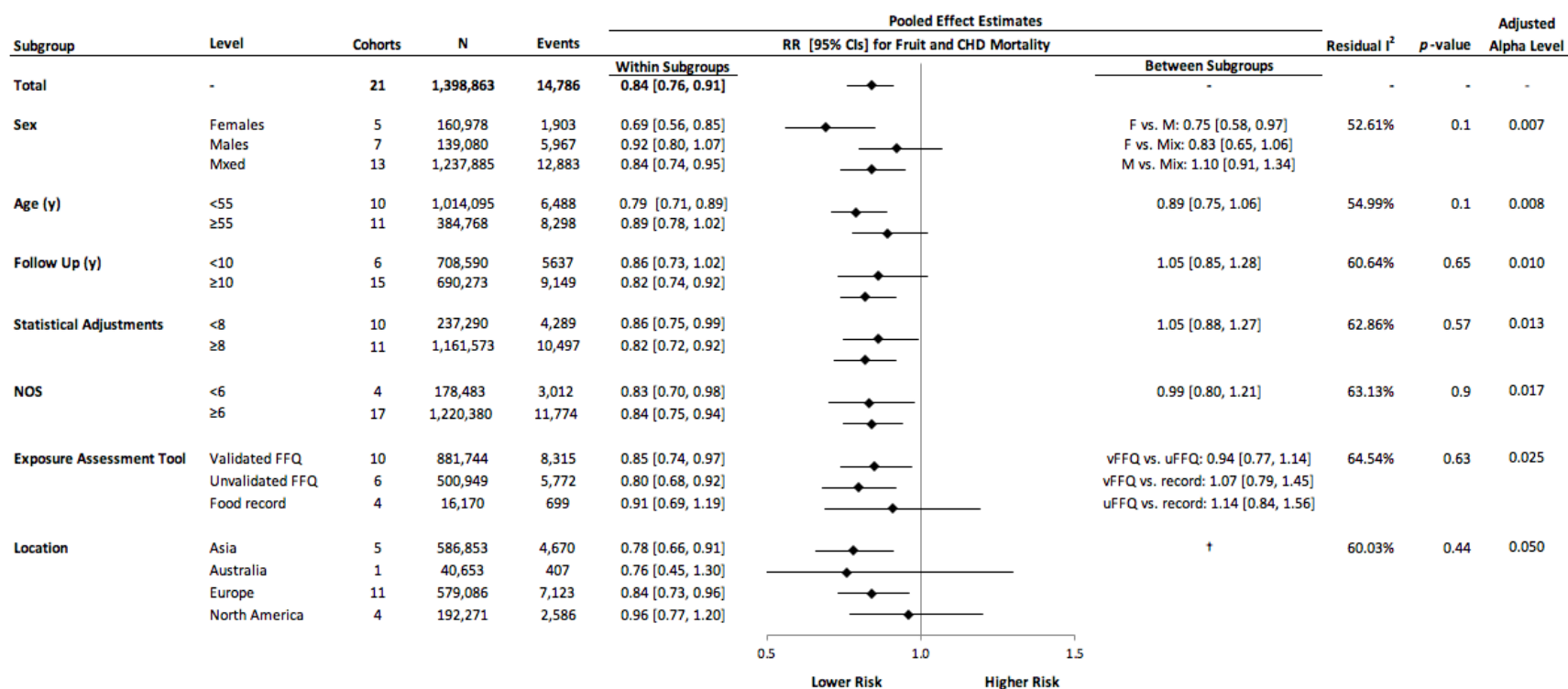


Figure S182. Categorical subgroup analyses of fruit intake and coronary heart disease mortality. Point estimates for within subgroup level are the pooled effect estimates and are represented by a black diamond. The residual I² value indicates the inter-study heterogeneity unexplained by the subgroup. CHD – coronary heart disease; FFQ – food frequency questionnaire; NOS – Newcastle-Ottawa Scale; RR – relative risk; 95% CIs – 95% confidence intervals.

† Europe vs. Asia 0.93 [0.76, 1.14]; Europe vs. Australia 0.91 [0.53, 1.57]; Europe vs. North America 1.15 [0.89, 1.47]; Asia vs. Australia 1.01 [0.59, 1.77]; Asia vs. North America 0.81 [0.62, 1.06]; Australia vs. North America 0.80 [0.45, 1.41]

VEGETABLES AND CORONARY HEART DISEASE MORTALITY

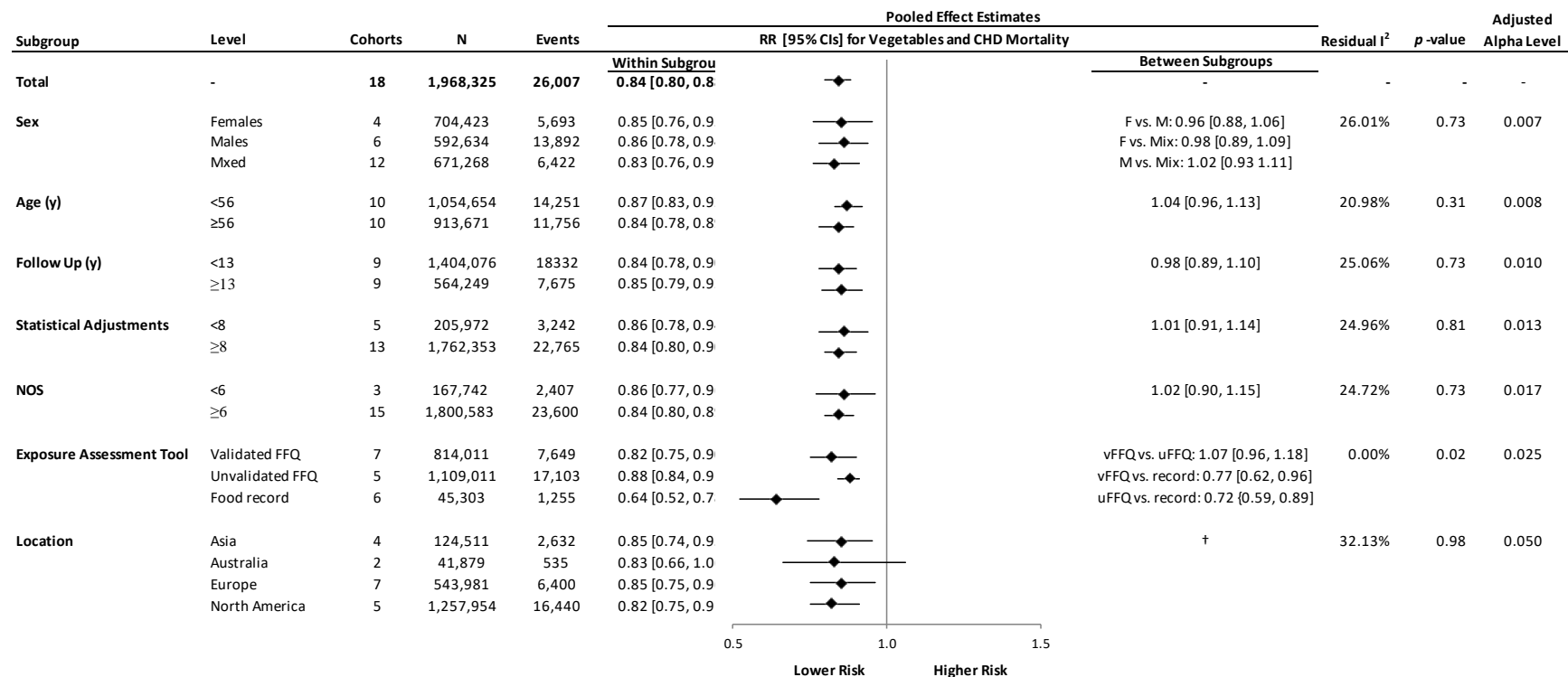


Figure S183. Categorical subgroup analyses of intake of vegetables and coronary heart disease mortality. Point estimates for within subgroup level are the pooled effect estimates and are represented by a black diamond. The residual I² value indicates the inter-study heterogeneity unexplained by the subgroup. CHD – coronary heart disease; FFQ – food frequency questionnaire; NOS – Newcastle-Ottawa Scale; RR – relative risk; 95% CIs – 95% confidence intervals.

† Europe vs. Asia 0.98 [0.83, 1.17]; Europe vs. Australia 0.98 [0.75, 1.28]; Europe vs. North America 0.97 [0.83, 1.14]; Asia vs. Australia 1.01 [0.77, 1.32]; Asia vs. North America 1.02 [0.87, 1.19]; Australia vs. North America 1.01 [0.78, 1.30]

TOTAL FRUIT AND VEGETABLES AND STROKE INCIDENCE

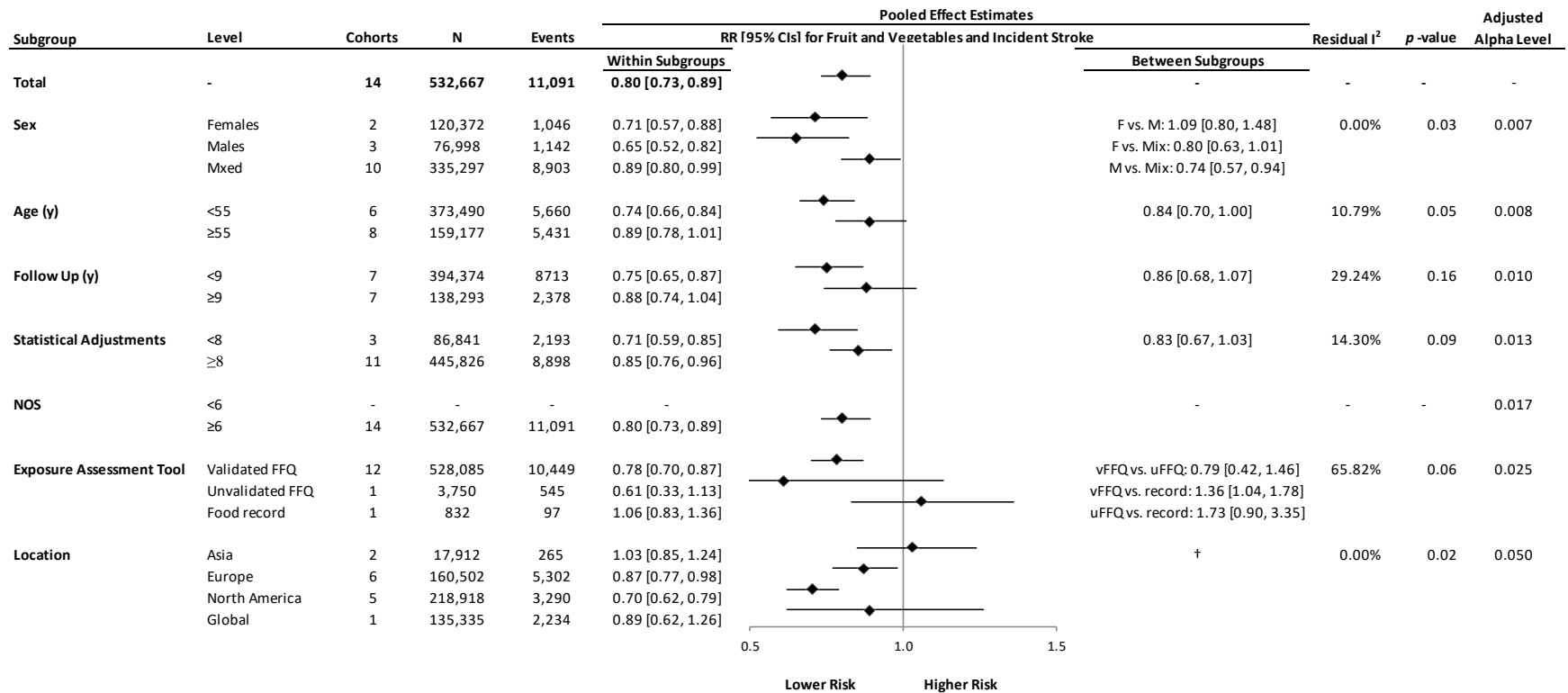


Figure S184. Categorical subgroup analyses of total fruit and vegetable intake and stroke incidence. Point estimates for within subgroup level are the pooled effect estimates and are represented by a black diamond. The residual I² value indicates the inter-study heterogeneity unexplained by the subgroup. CHD – coronary heart disease; FFQ – food frequency questionnaire; NOS – Newcastle-Ottawa Scale; RR – relative risk; 95% CIs – 95% confidence intervals.

† Europe vs Asia 1.17 [0.94, 1.47]; Europe vs Global 1.02 [0.70, 1.48]; Europe vs NA 0.81 [0.68, 0.96]; Asia vs Global 1.16 [0.77, 1.72]; Asia vs NA 1.46 [1.16, 1.84]; Global vs NA 1.27 [0.87, 1.84]

FRUIT AND STROKE INCIDENCE

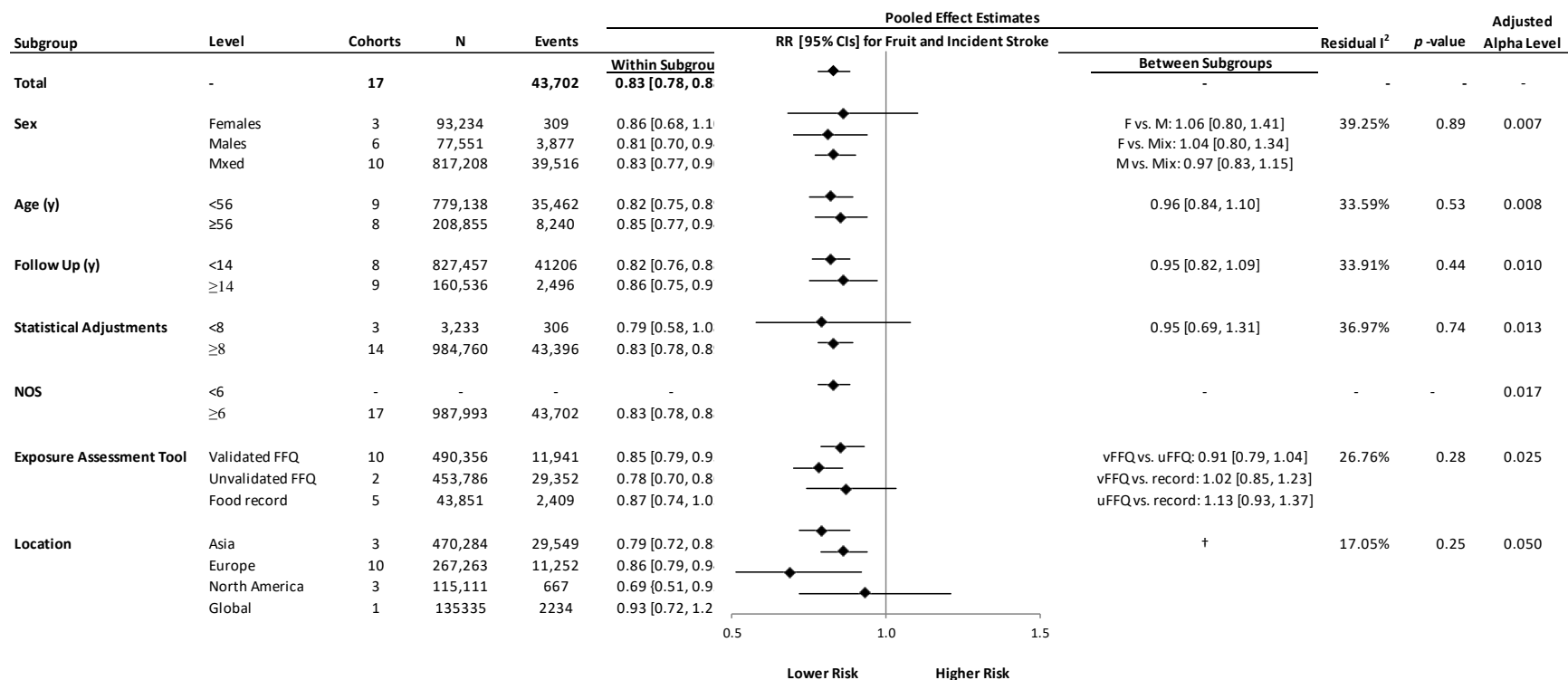


Figure S185. Categorical subgroup analyses of fruit intake and stroke incidence. Point estimates for within subgroup level are the pooled effect estimates and are represented by a black diamond. The residual I² value indicates the inter-study heterogeneity unexplained by the subgroup. CHD – coronary heart disease; FFQ – food frequency questionnaire; NOS – Newcastle-Ottawa Scale; RR – relative risk; 95% CIs – 95% confidence intervals. † Europe vs. Asia 0.92 [0.81, 1.05]; Europe vs. Global 1.09 [0.82, 1.42]; Europe vs. North America 0.80 [0.59, 1.09]; Asia vs. Global 0.85 [0.65, 1.12]; Asia vs. North America 1.15 [0.85, 1.57]; Global vs. North America 1.36 [0.92, 2.01]

VEGETABLES AND STROKE INCIDENCE

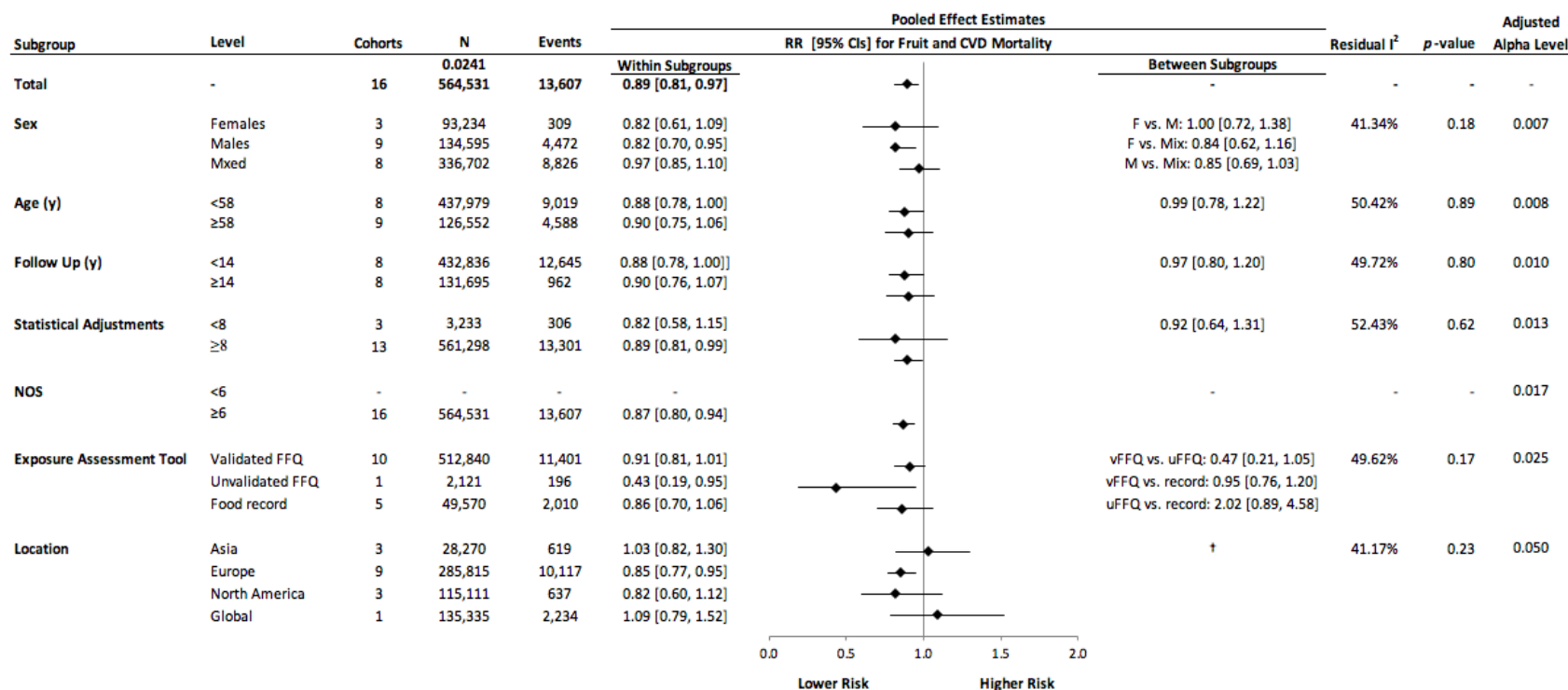


Figure S186. Categorical subgroup analyses of intake of vegetables and stroke incidence. Point estimates for within subgroup level are the pooled effect estimates and are represented by a black diamond. The residual I² value indicates the inter-study heterogeneity unexplained by the subgroup. CHD – coronary heart disease; FFQ – food frequency questionnaire; NOS – Newcastle-Ottawa Scale; RR – relative risk; 95% CIs – 95% confidence intervals.
 † Europe vs. Asia 1.21 [0.94, 1.56]; Europe vs. Global 1.28 [0.91, 1.81]; Europe vs. NA 0.96 [0.69, 1.33]; Asia vs. Global 0.94 [0.63, 1.40]; Asia vs. NA 1.26 [0.86, 1.86]; Global vs. NA 1.34 [0.85, 2.10]

FRUIT AND STROKE MORTALITY

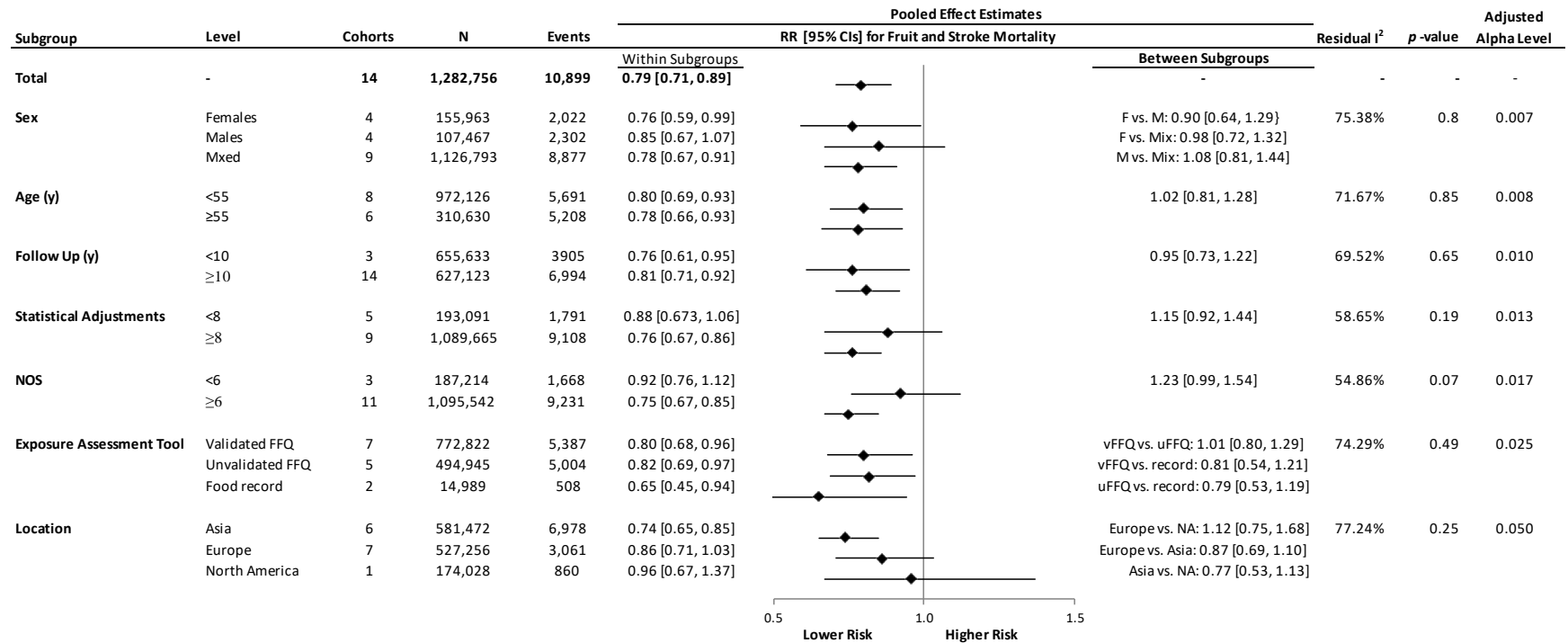


Figure S187. Categorical subgroup analyses of fruit intake and stroke mortality. Point estimates for within subgroup level are the pooled effect estimates and are represented by a black diamond. The residual I² value indicates the inter-study heterogeneity unexplained by the subgroup. FFQ – food frequency questionnaire; NOS – Newcastle-Ottawa Scale; RR – relative risk; 95% CIs – 95% confidence intervals.

VEGETABLES AND STROKE MORTALITY

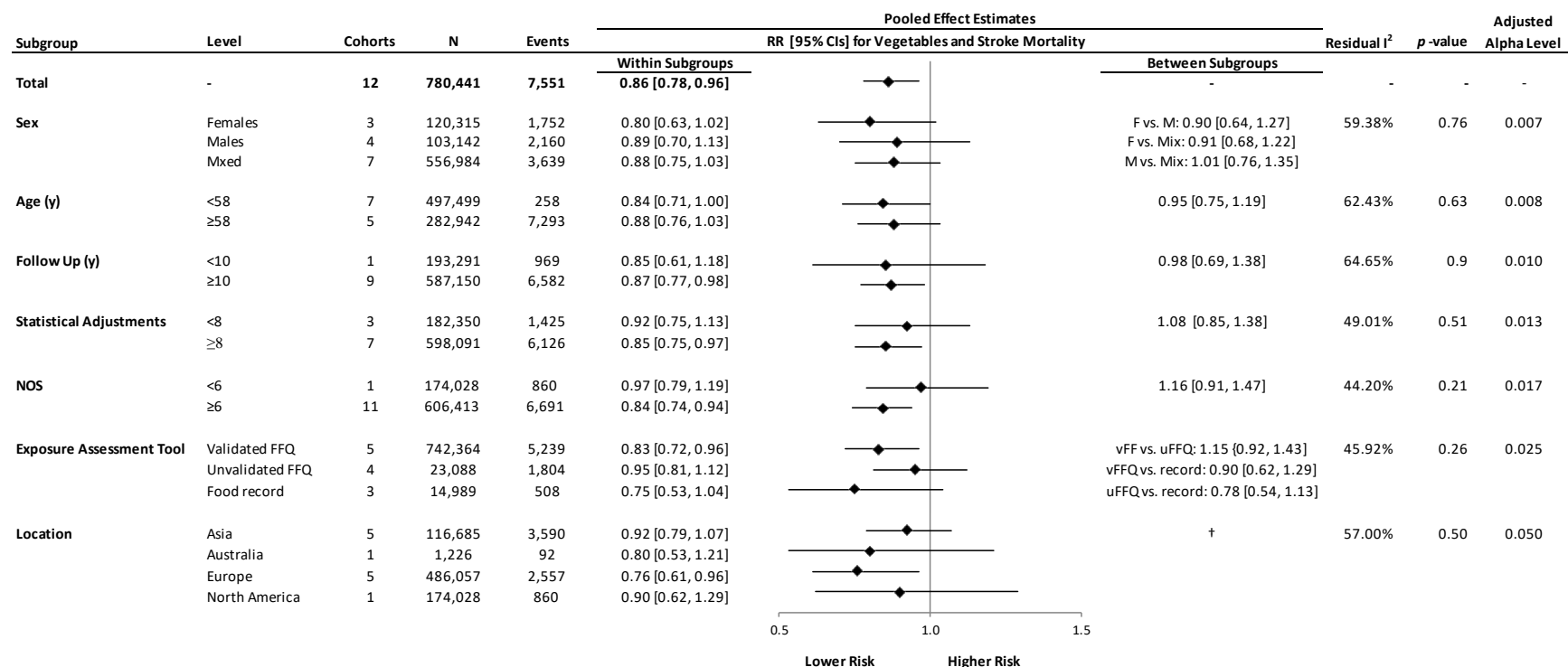


Figure S188. Categorical subgroup analyses of intake of vegetables and stroke mortality. Point estimates for within subgroup level are the pooled effect estimates and are represented by a black diamond. The residual I² value indicates the inter-study heterogeneity unexplained by the subgroup. FFQ – food frequency questionnaire; NOS – Newcastle-Ottawa Scale; RR – relative risk; 95% CIs – 95% confidence intervals.

† Europe vs. Asia 1.20 [0.92, 1.57]; Europe vs. Australia 1.05 [0.66, 1.67]; Europe vs. North America 1.17 [0.76, 1.80]; Asia vs. Australia 1.44 [0.74, 1.77]; Asia vs. North America 1.03 [0.69, 1.53]; Australia vs. North America 0.90 [0.52, 1.55]

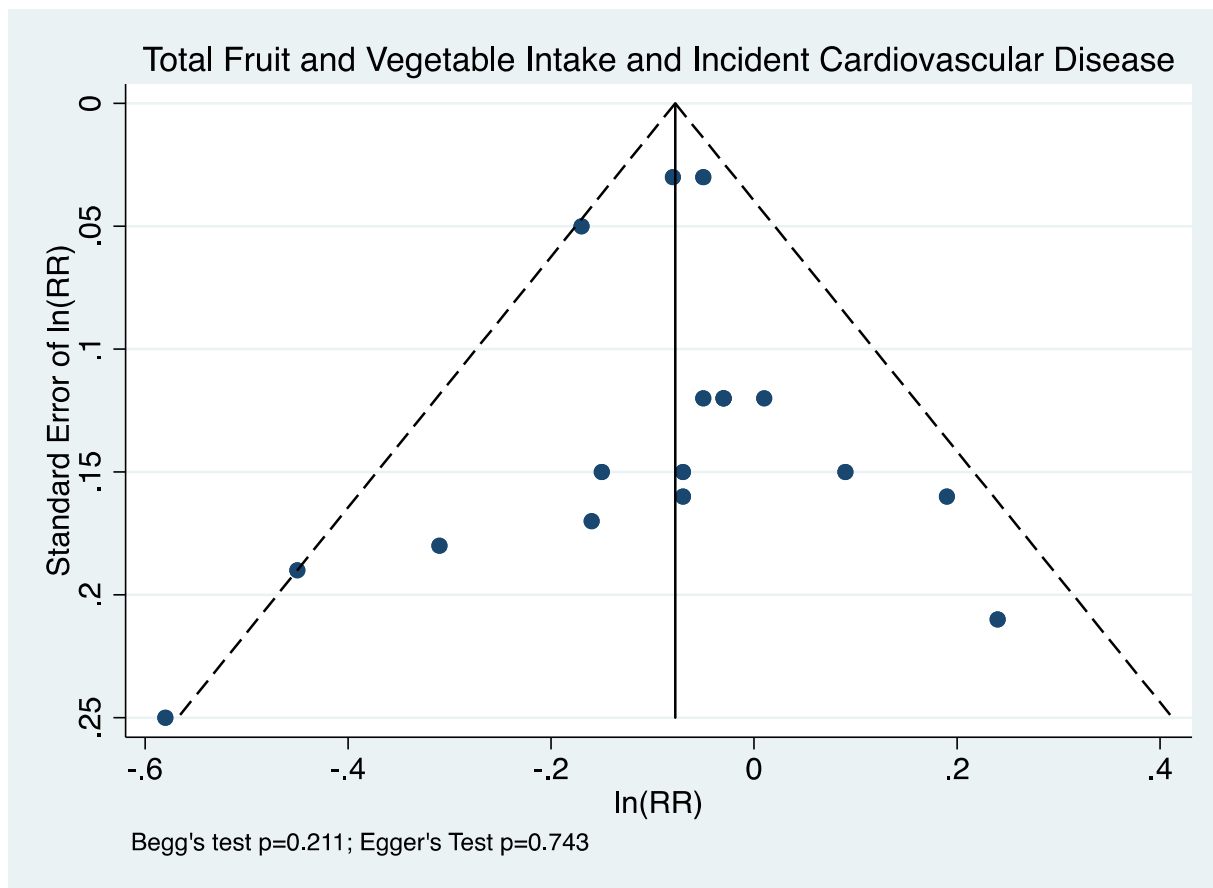
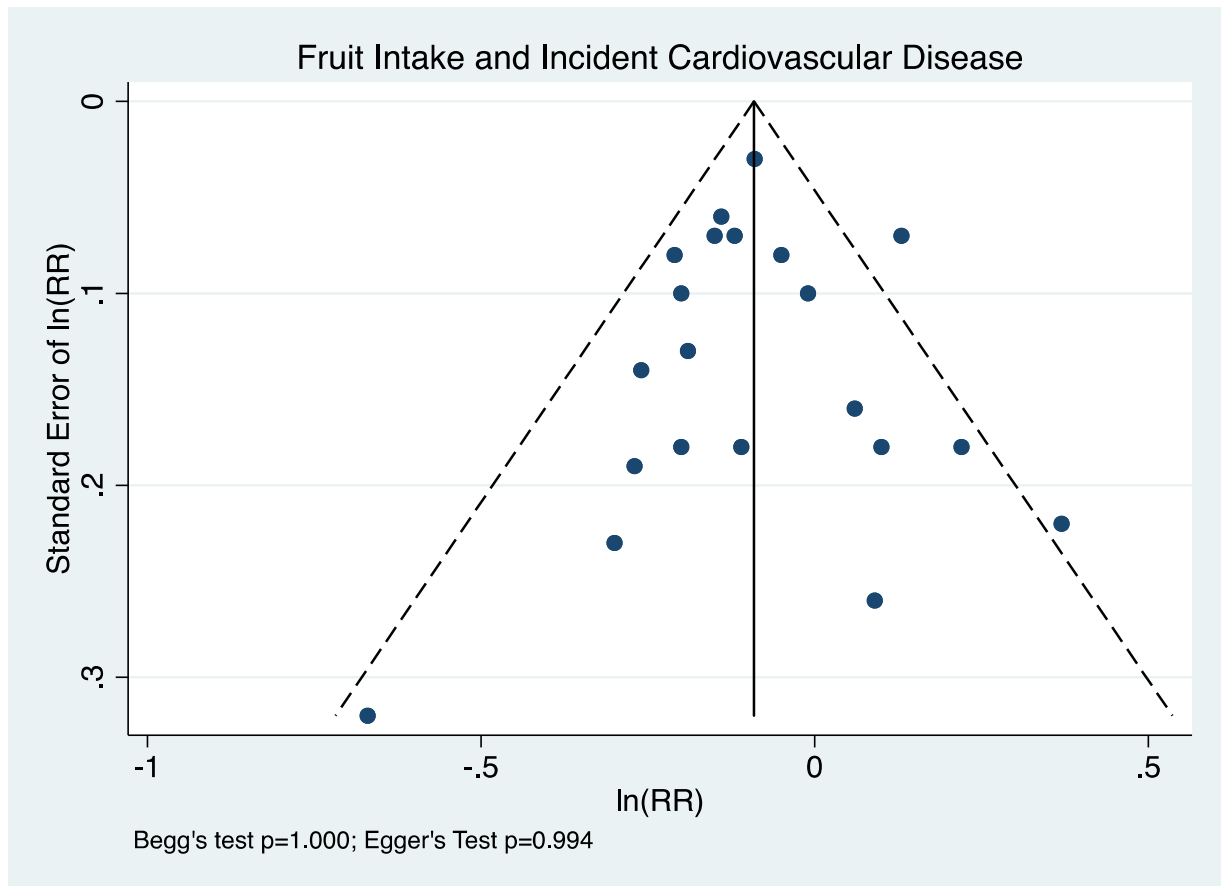


Figure S189. Funnel plot of natural logarithm relative risk [$\ln(RR)$] for cardiovascular disease incidence comparing the highest and lowest quantiles of total fruit and vegetable intake. The vertical line represents the pooled effect estimated expressed as $\ln(RR)$. Dashed lines represent pseudo-95% confidence intervals. The circles represent risk estimates for each comparison, and the horizontal lines represent standard errors of the $\ln(RR)$.



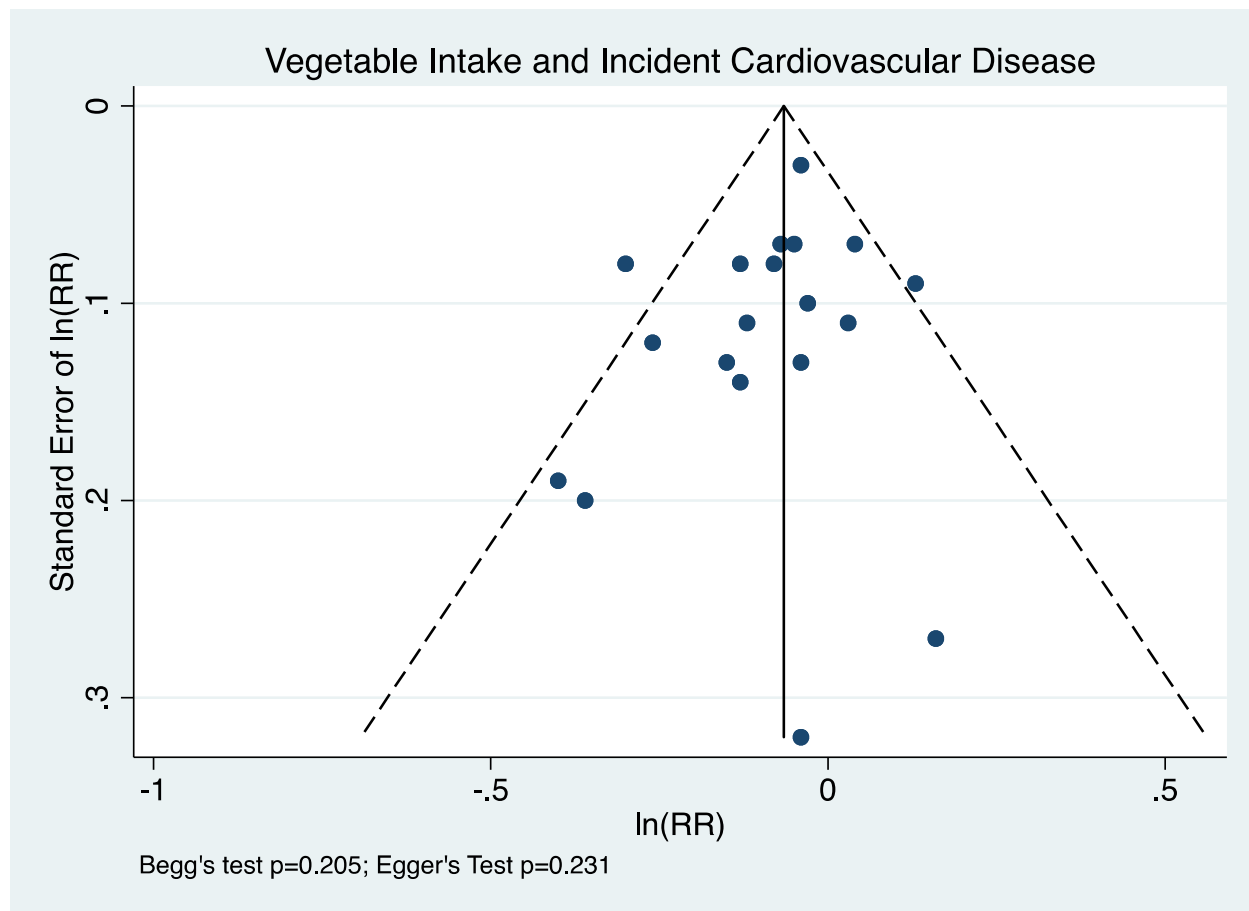


Figure S191. Funnel plot of natural logarithm relative risk [$\ln(RR)$] for cardiovascular disease incidence comparing the highest and lowest quantiles of vegetable intake. The vertical line represents the pooled effect estimated expressed as $\ln(RR)$. Dashed lines represent pseudo-95% confidence intervals. The circles represent risk estimates for each comparison, and the horizontal lines represent standard errors of the $\ln(RR)$.

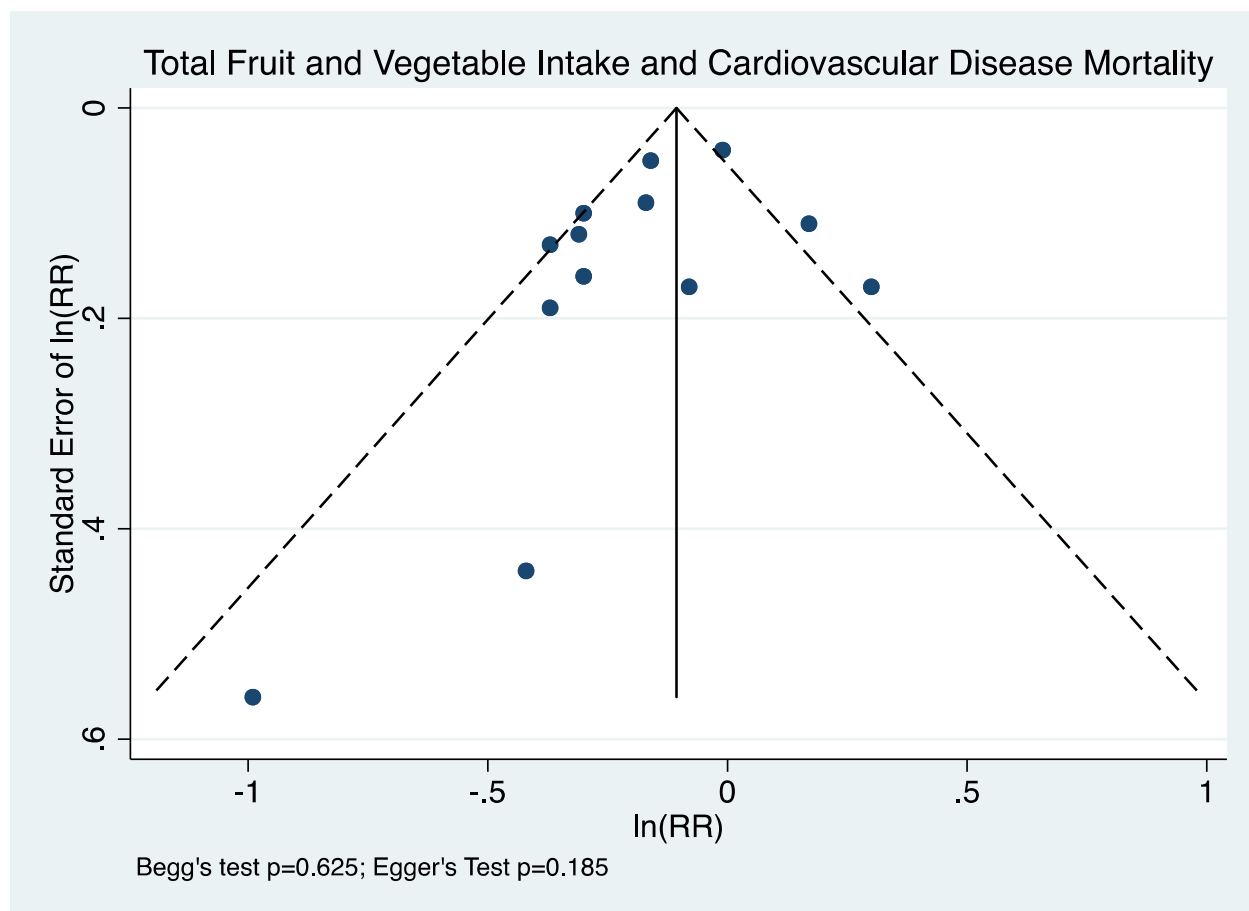


Figure S192. Funnel plot of natural logarithm relative risk [$\ln(RR)$] for cardiovascular disease mortality comparing the highest and lowest quantiles of total fruit and vegetable intake. The vertical line represents the pooled effect estimated expressed as $\ln(RR)$. Dashed lines represent pseudo-95% confidence intervals. The circles represent risk estimates for each comparison, and the horizontal lines represent standard errors of the $\ln(RR)$.

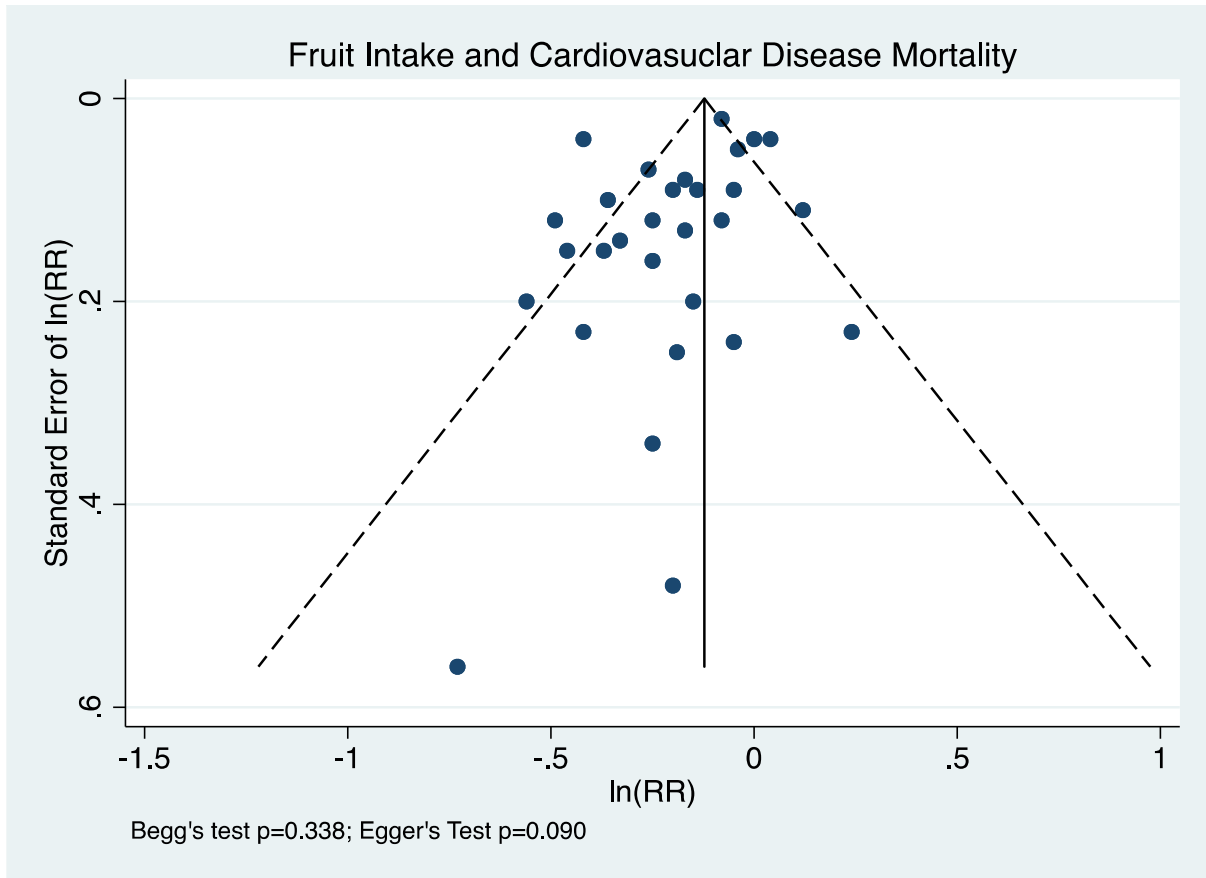
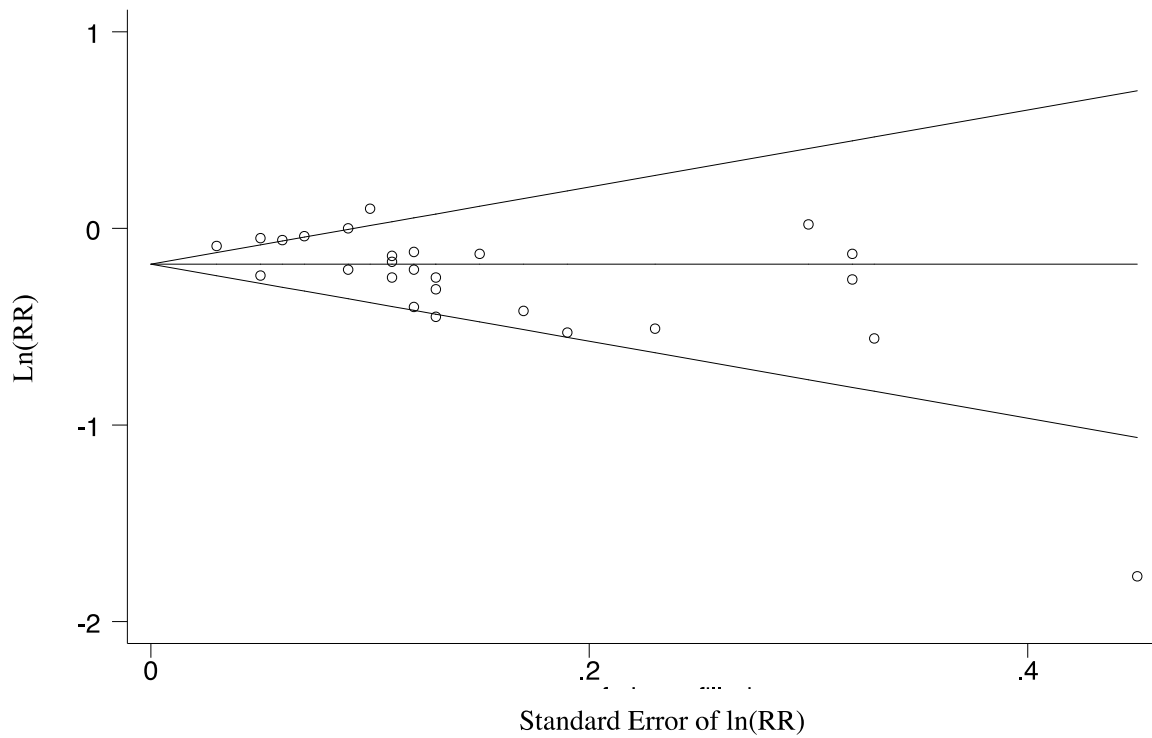


Figure S193. Funnel plot of natural logarithm relative risk [$\ln(RR)$] for cardiovascular disease mortality comparing the highest and lowest quantiles of fruit intake. The vertical line represents the pooled effect estimated expressed as $\ln(RR)$. Dashed lines represent pseudo-95% confidence intervals. The circles represent risk estimates for each comparison, and the horizontal lines represent standard errors of the $\ln(RR)$.

Vegetable Intake and Cardiovascular Disease Mortality



Imputed RR accounting for publication bias: N/A

P-value: N/A

Figure S194. Funnel plot for trim-and-fill analysis for coronary heart disease mortality comparing the highest and lowest quantiles of vegetable intake. The horizontal line represents the pooled effect estimate expressed as the natural logarithm of relative risk [ln(RR)]. The diagonal lines represent the pseudo-95% confidence intervals of the RR. The clear circles represent the effect estimates for each included study.

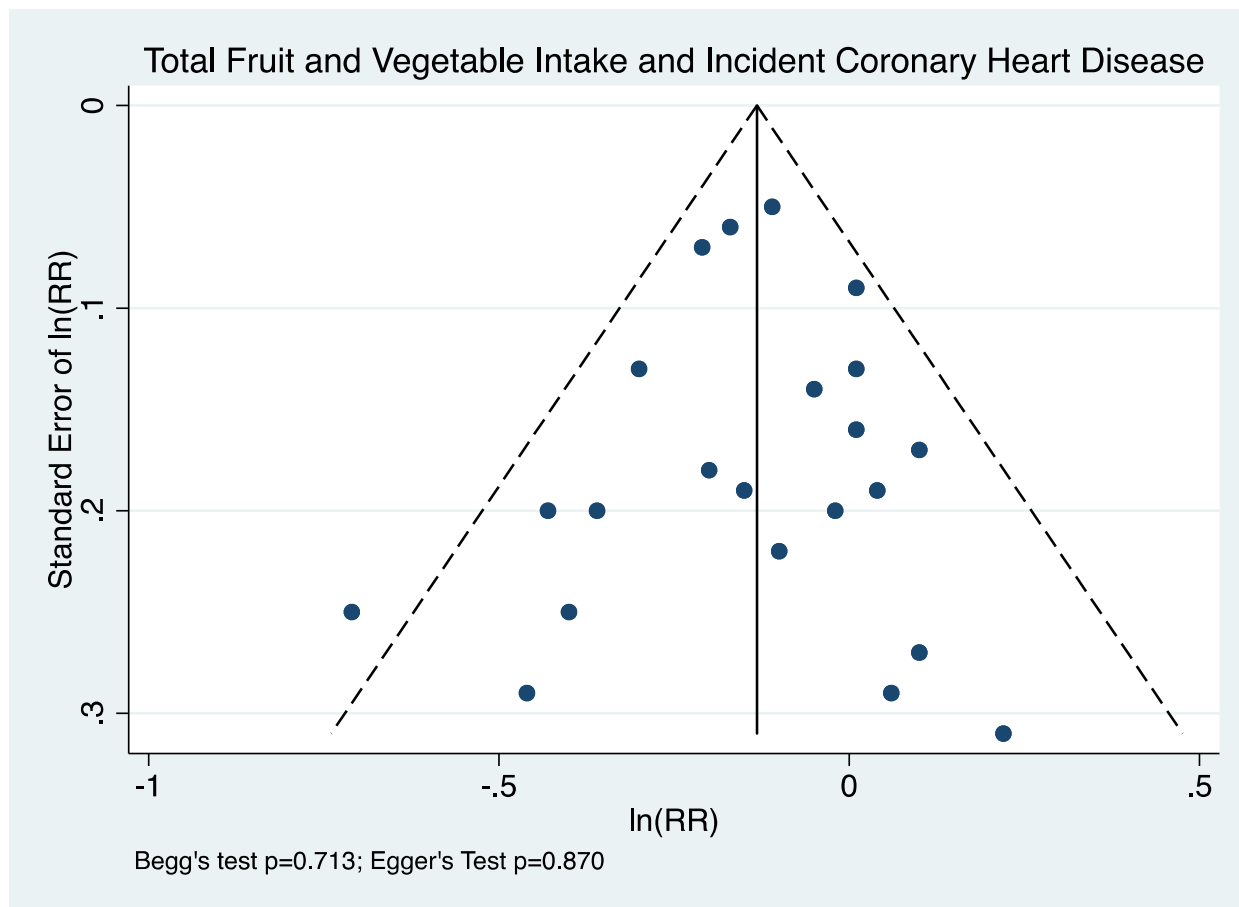


Figure S195. Funnel plot of natural logarithm relative risk [$\ln(RR)$] for coronary heart disease incidence comparing the highest and lowest quantiles of total fruit and vegetable intake. The vertical line represents the pooled effect estimated expressed as $\ln(RR)$. Dashed lines represent pseudo-95% confidence intervals. The circles represent risk estimates for each comparison, and the horizontal lines represent standard errors of the $\ln(RR)$.

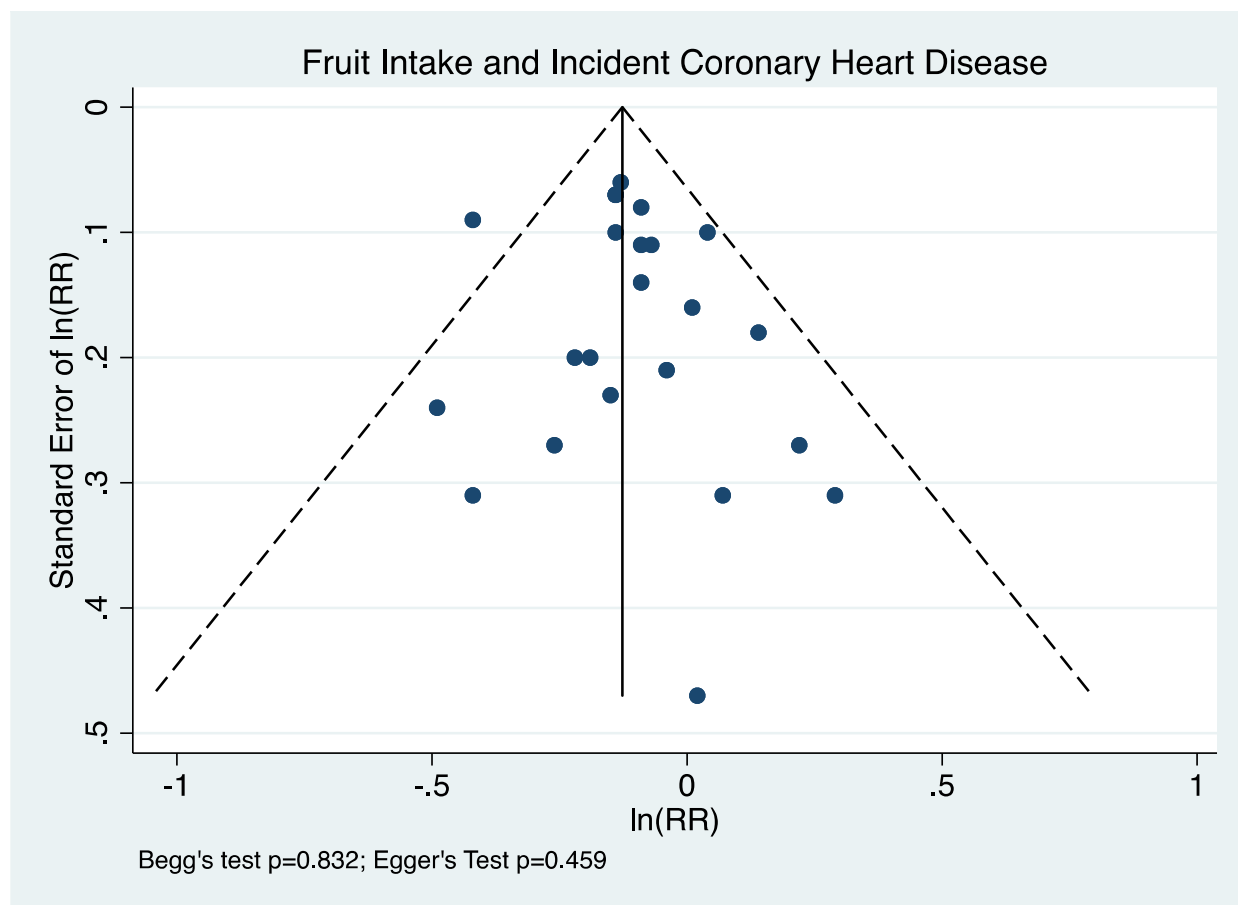


Figure S196. Funnel plot of natural logarithm relative risk [$\ln(RR)$] for coronary heart disease comparing the highest and lowest quantiles of fruit intake. The vertical line represents the pooled effect estimated expressed as $\ln(RR)$. Dashed lines represent pseudo-95% confidence intervals. The circles represent risk estimates for each comparison, and the horizontal lines represent standard errors of the $\ln(RR)$.

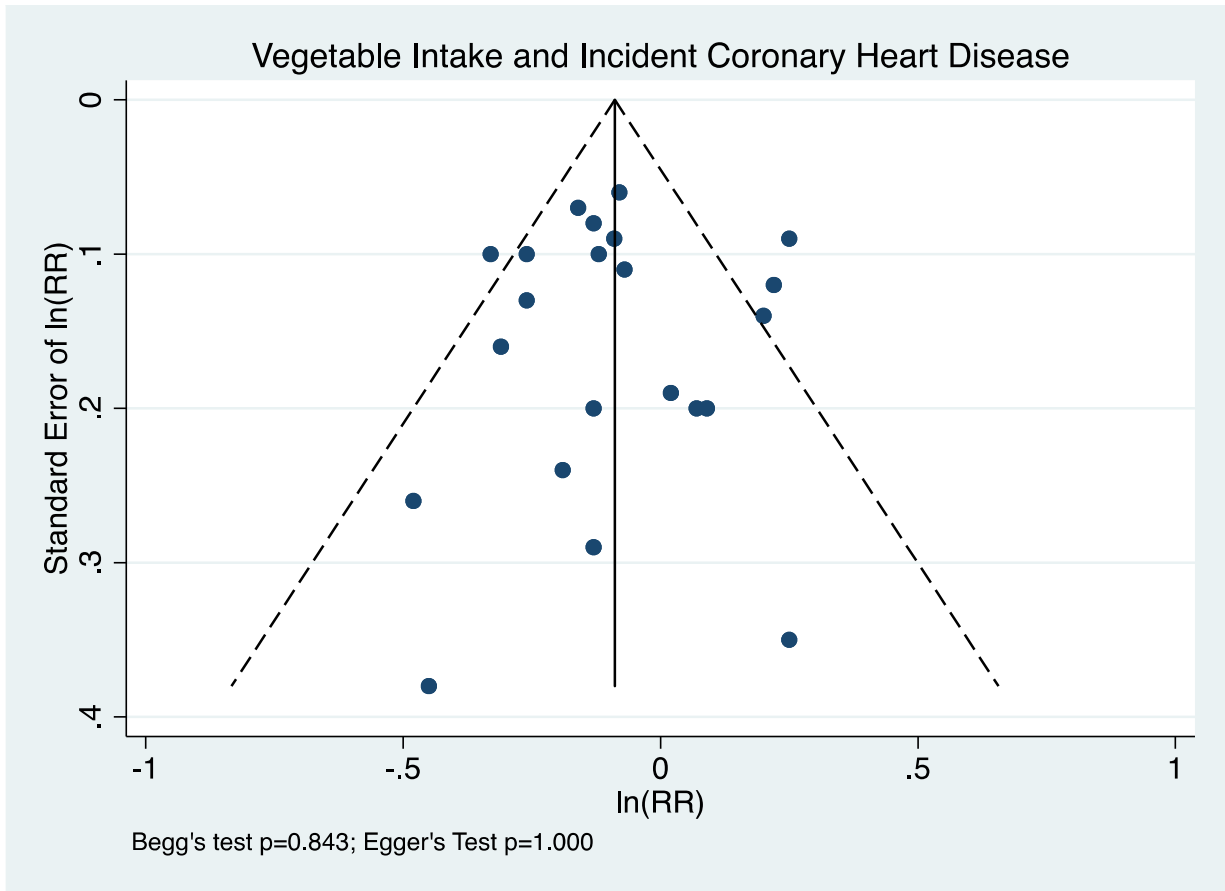


Figure S197. Funnel plot of natural logarithm relative risk [Ln(RR)] for coronary heart disease incidence comparing the highest and lowest quantiles of vegetable intake. The vertical line represents the pooled effect estimated expressed as ln(RR). Dashed lines represent pseudo-95% confidence intervals. The circles represent risk estimates for each comparison, and the horizontal lines represent standard errors of the ln(RR).

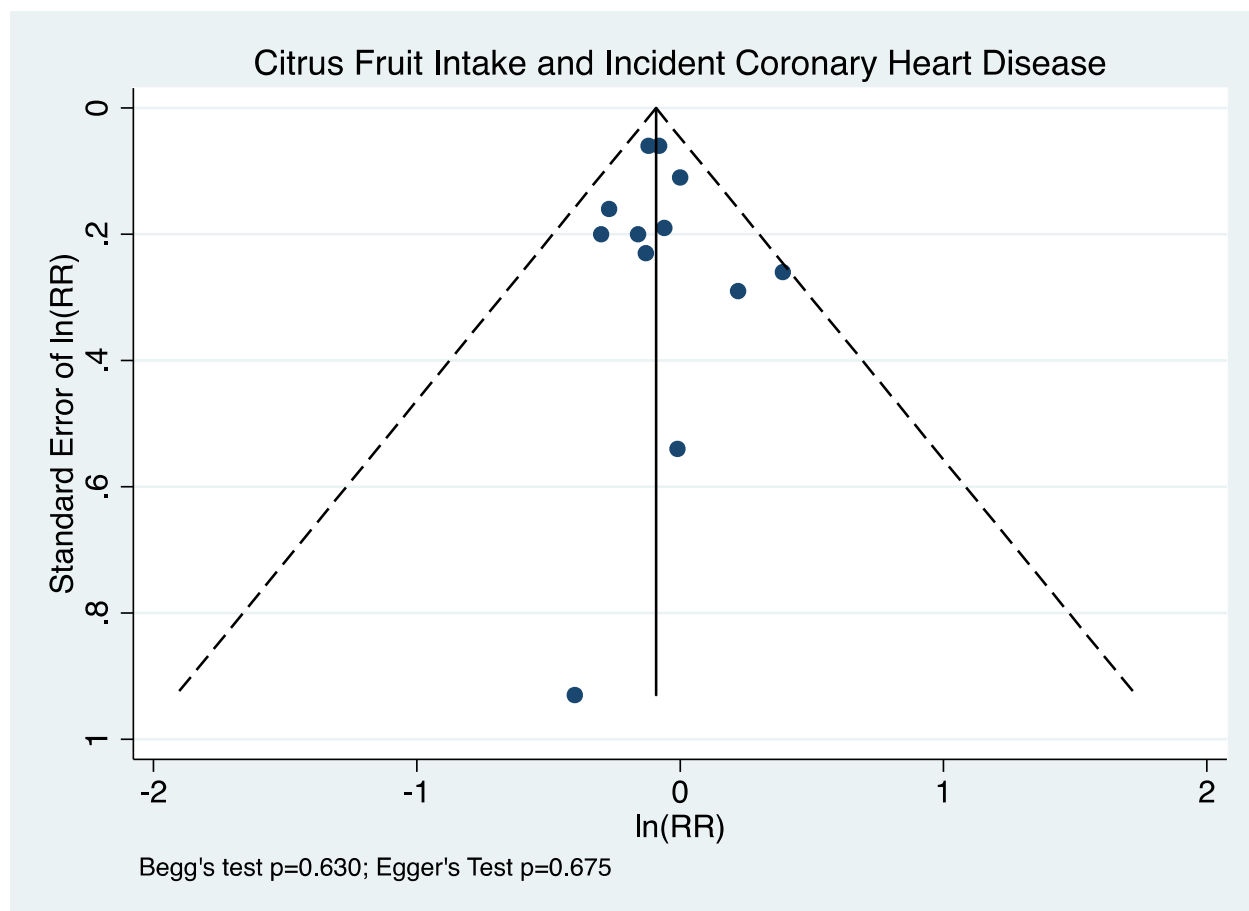


Figure S198. Funnel plot of natural logarithm relative risk [$\ln(RR)$] for coronary heart disease incidence comparing the highest and lowest quantiles of citrus fruit intake. The vertical line represents the pooled effect estimated expressed as $\ln(RR)$. Dashed lines represent pseudo-95% confidence intervals. The circles represent risk estimates for each comparison, and the horizontal lines represent standard errors of the $\ln(RR)$.

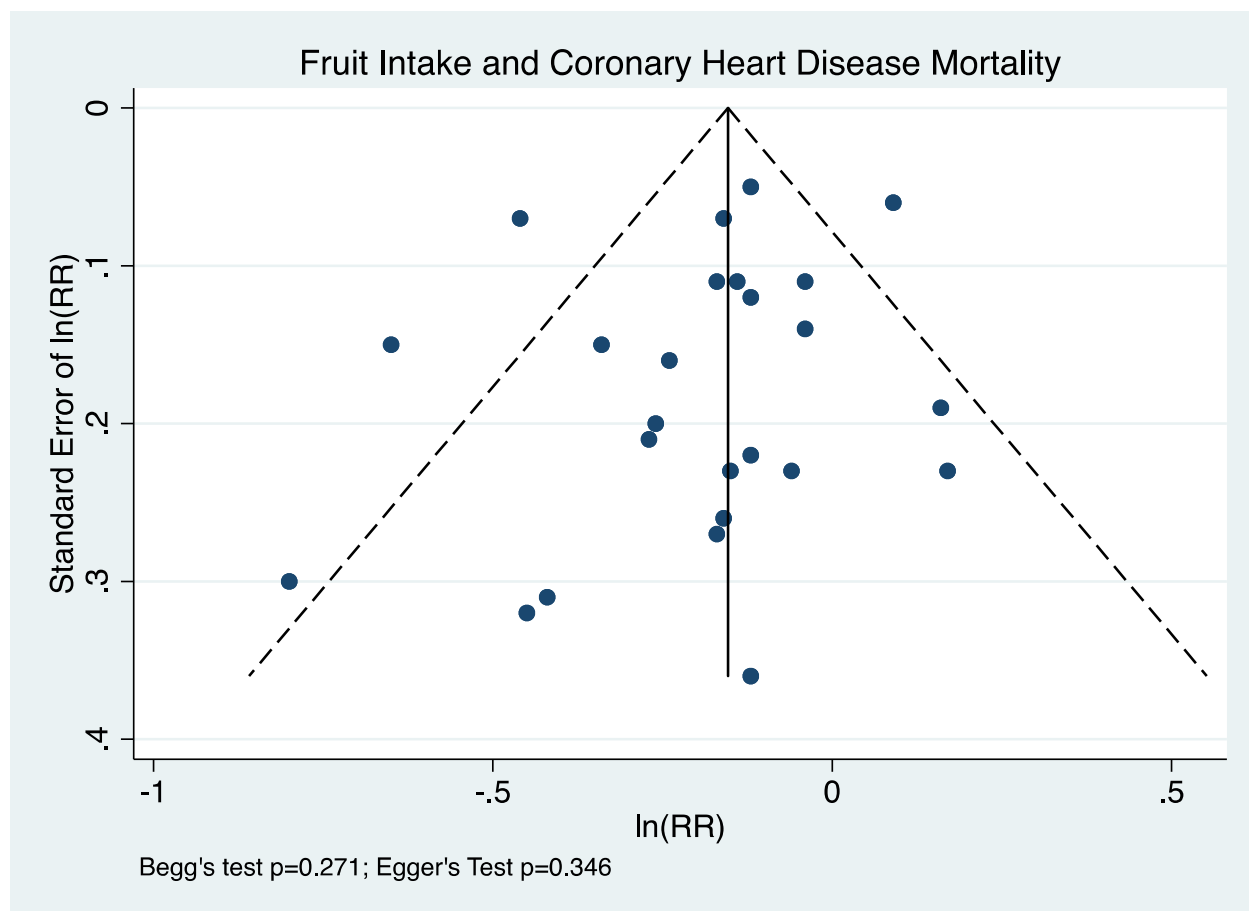
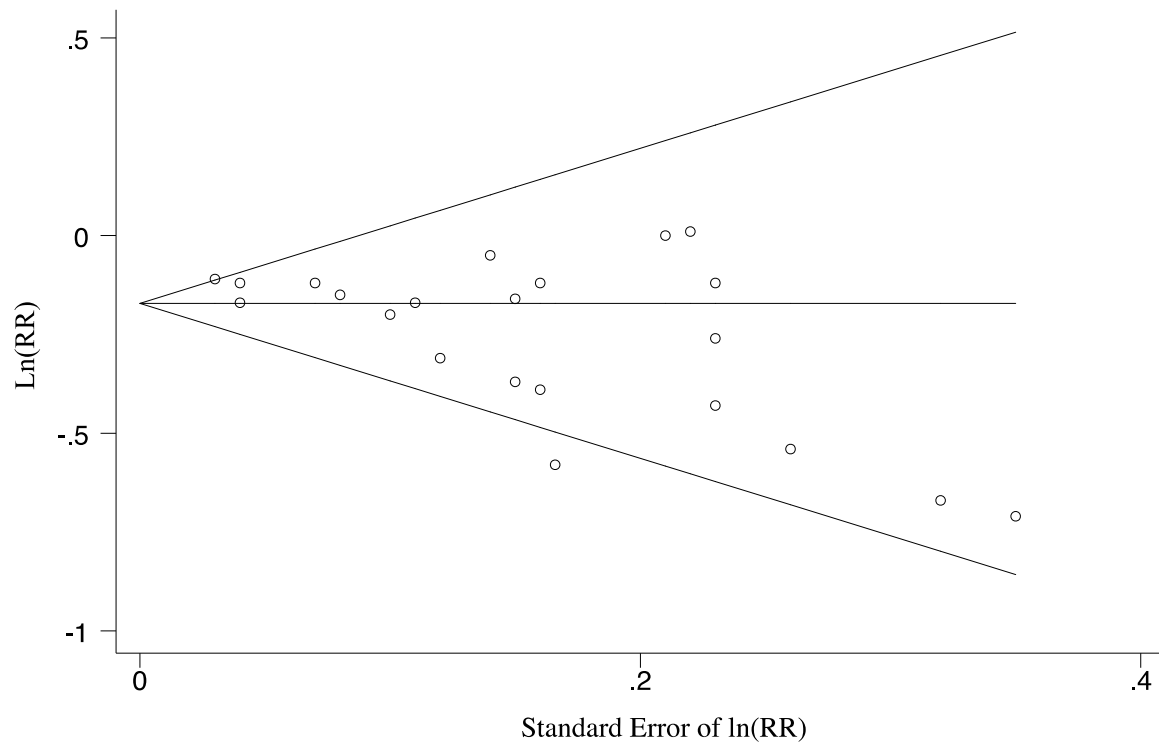


Figure S199. Funnel plot of natural logarithm relative risk [Ln(RR)] for coronary heart disease mortality comparing the highest and lowest quantiles of fruit intake. The vertical line represents the pooled effect estimated expressed as ln(RR). Dashed lines represent pseudo-95% confidence intervals. The circles represent risk estimates for each comparison, and the horizontal lines represent standard errors of the ln(RR).

Vegetable Intake and Coronary Heart Disease Mortality



Imputed RR accounting for publication bias: N/A
P-value: N/A

Figure S200. Funnel plot for trim-and-fill analysis for coronary heart disease mortality comparing the highest and lowest quantiles of vegetable intake. The horizontal line represents the pooled effect estimate expressed as the natural logarithm of relative risk [ln(RR)]. The diagonal lines represent the pseudo-95% confidence intervals of the RR. The clear circles represent the effect estimates for each included study.

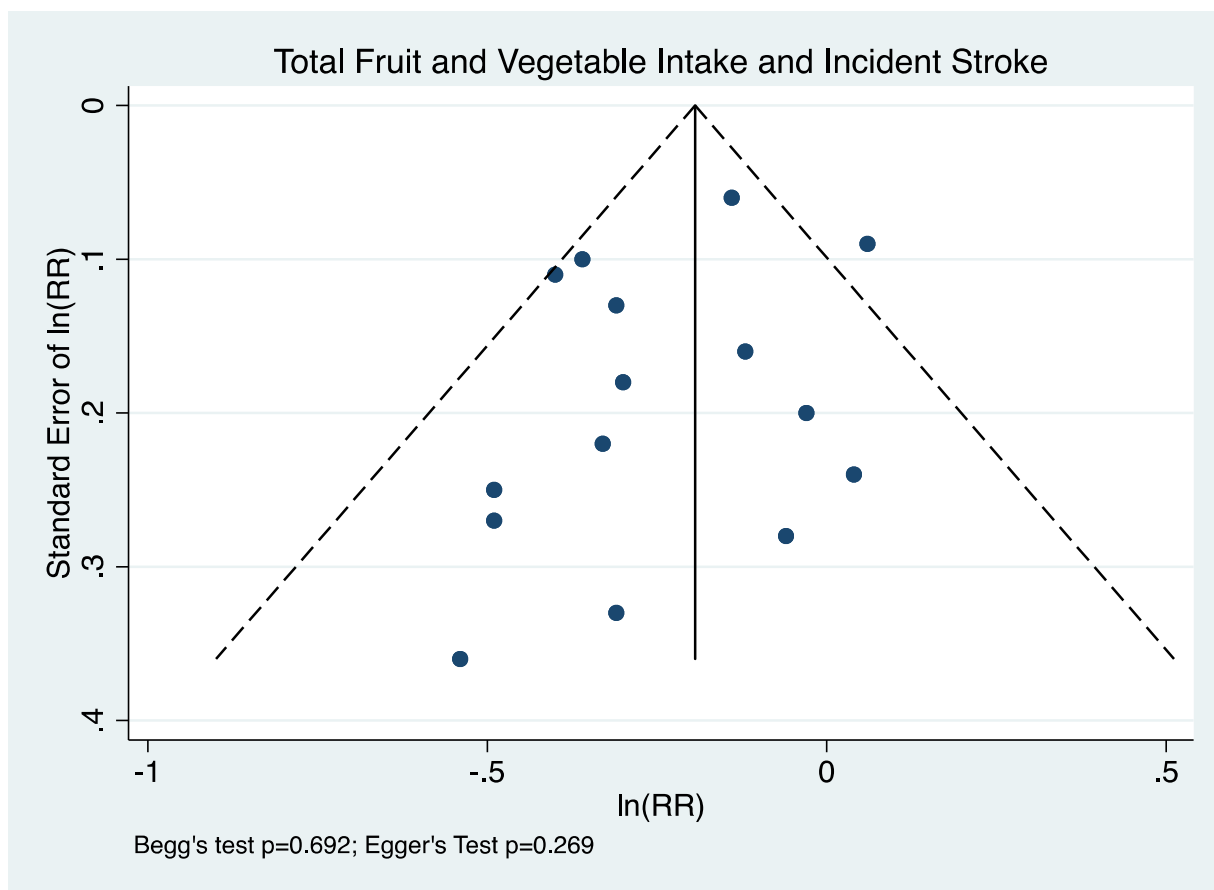


Figure S201. Funnel plot of natural logarithm relative risk [$\ln(RR)$] for stroke incidence comparing the highest and lowest quantiles of total fruit and vegetable intake. The vertical line represents the pooled effect estimated expressed as $\ln(RR)$. Dashed lines represent pseudo-95% confidence intervals. The circles represent risk estimates for each comparison, and the horizontal lines represent standard errors of the $\ln(RR)$.

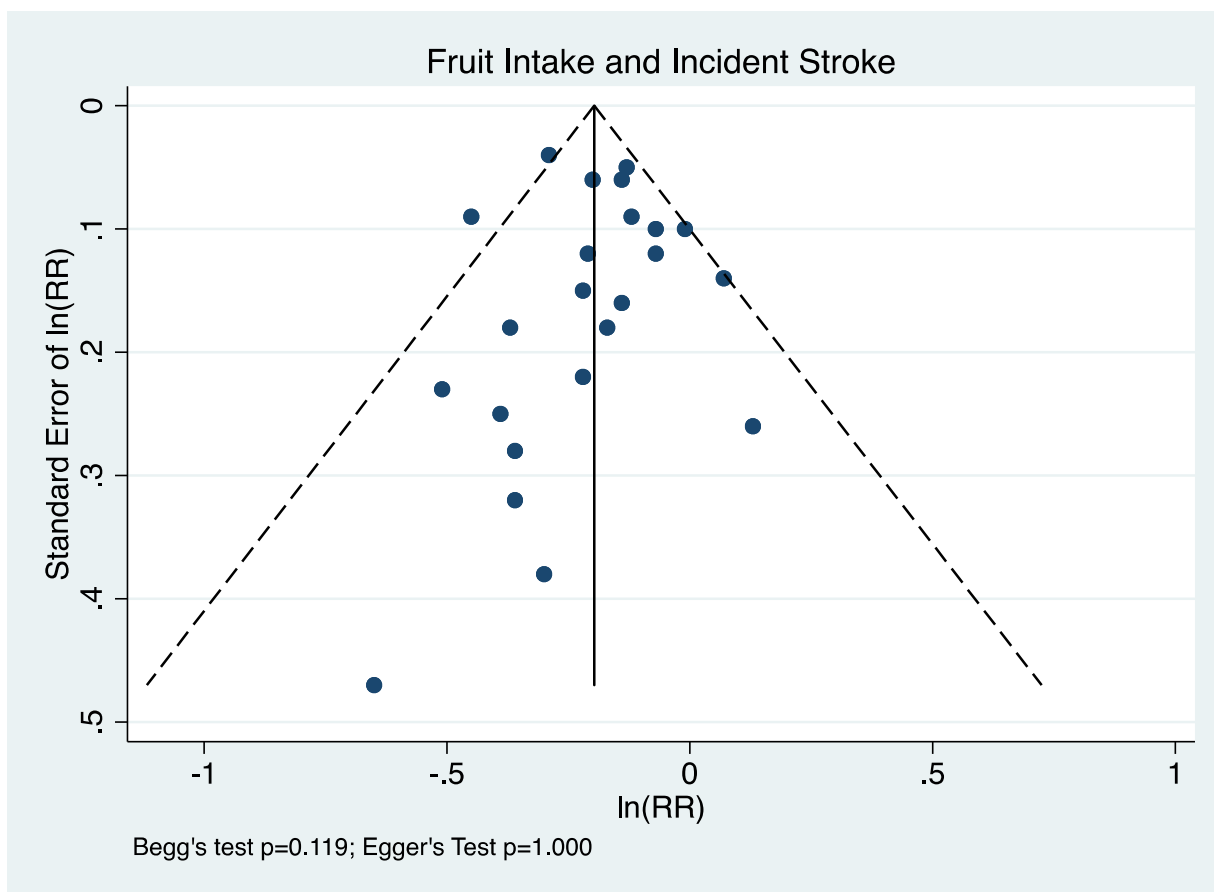


Figure S202. Funnel plot of natural logarithm relative risk [$\ln(RR)$] for stroke incidence comparing the highest and lowest quantiles of fruit intake. The vertical line represents the pooled effect estimated expressed as $\ln(RR)$. Dashed lines represent pseudo-95% confidence intervals. The circles represent risk estimates for each comparison, and the horizontal lines represent standard errors of the $\ln(RR)$.

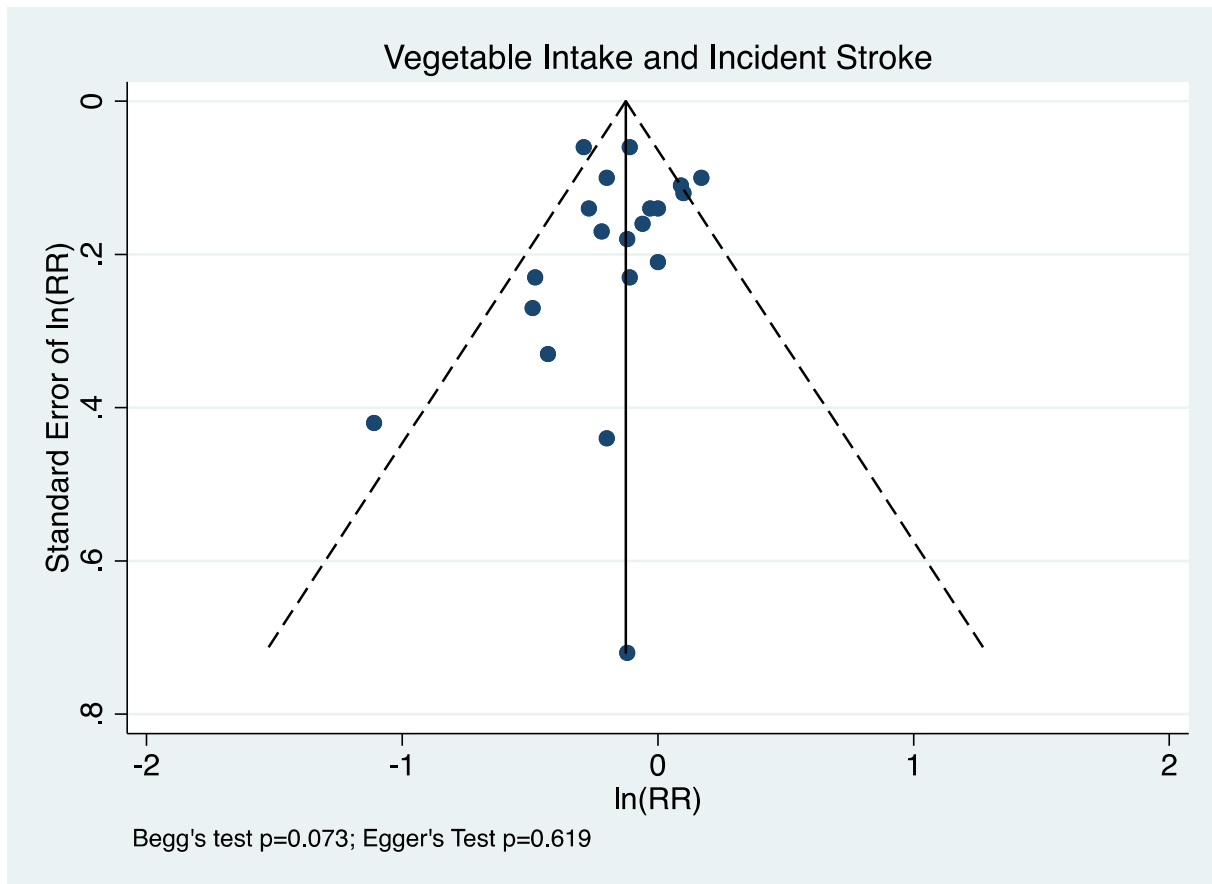


Figure S203. Funnel plot of natural logarithm relative risk [Ln(RR)] for stroke incidence comparing the highest and lowest quantiles of vegetable intake. The vertical line represents the pooled effect estimated expressed as ln(RR). Dashed lines represent pseudo-95% confidence intervals. The circles represent risk estimates for each comparison, and the horizontal lines represent standard errors of the ln(RR).

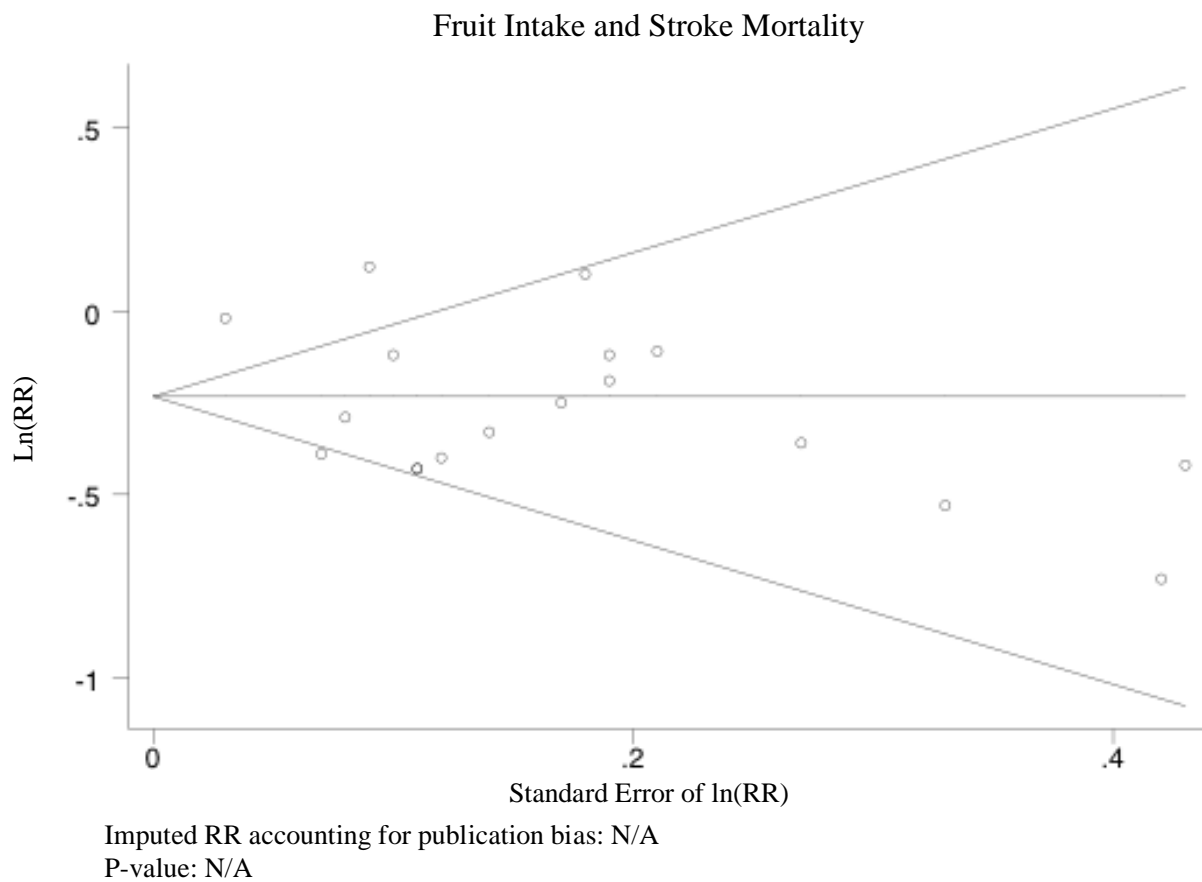
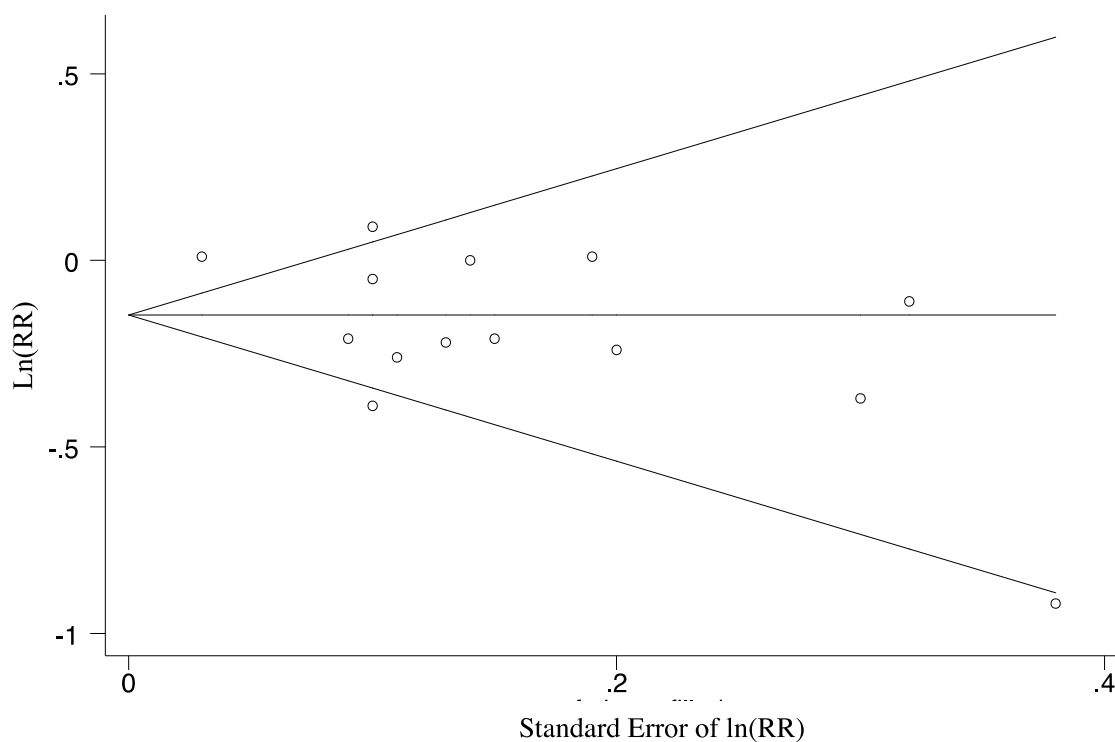


Figure S204. Funnel plot of natural logarithm relative risk [Ln(RR)] for stroke mortality comparing the highest and lowest quantiles of fruit intake. The vertical line represents the pooled effect estimated expressed as ln(RR). Dashed lines represent pseudo-95% confidence intervals. The circles represent risk estimates for each comparison, and the horizontal lines represent standard errors of the ln(RR).

Vegetable Intake and Stroke Mortality



Imputed RR accounting for publication bias: N/A

P-value: N/A

Figure S205. Funnel plot for trim-and-fill analysis for stroke mortality comparing the highest and lowest quantiles of vegetable intake. The horizontal line represents the pooled effect estimate expressed as the natural logarithm of relative risk [ln(RR)]. The diagonal lines represent the pseudo-95% confidence intervals of the RR. The clear circles represent the effect estimates for each included study.