Online Supplemental Material

The following tables and figures are included in the Online Supplemental Material.

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Supplemental Methods. Literature search strategy in Pubmed.

#1 Search "Fatty Acids, Omega-3"[Mesh] OR "n-3 fatty acid*"[tiab] OR "omega-3 fatty acid*"[tiab] OR "essential fatty acid*"[tiab] OR "polyunsaturated fatty acid*"[tiab] OR "ALA"[tiab] OR "alpha-linolenic acid"[tiab] OR "flaxseed oil"[tiab]

#2 Search "Neoplasms"[Mesh] OR "cancer*"[tiab] OR "carcinoma*"[tiab] OR "tumor*"[tiab]

#3 Search "Cerebrovascular Disorders"[Mesh] OR "stroke*"[tiab] OR "cerebrovascular accident*"[tiab]

#4 Search "Cardiovascular diseases"[Mesh] OR "cardiovascular"[tiab] OR "heart"[tiab] OR "myocardial infarction*"[tiab] OR "sudden death*"[tiab]

#5 Search "Diabetes Mellitus"[Mesh] OR "diabet*" [tiab]

#6 Search “Mortality”[Mesh] OR “Death”[Mesh] OR “mortality”[tiab] OR “death”[tiab] OR “fatal”[tiab]

#7 Search "Epidemiology "[MESH] OR "Epidemiologic Studies"[MESH] OR “Intervention Studies” [MESH] OR "cohort*"[tiab] OR "incident*"[tiab] OR "incidence*"[tiab] OR "prospective"[tiab] OR "follow-up"[tiab] OR "predict*”[tiab] OR "prognos*"[tiab] OR "case-control"[tiab] OR "cross-sectional"[tiab] OR "intervention*”[tiab] OR "clinical trial*"[tiab] OR "randomized*"[tiab]

#8 Search #2 OR #3 OR #4 OR #5 OR #6

#9 Search #1 AND #8

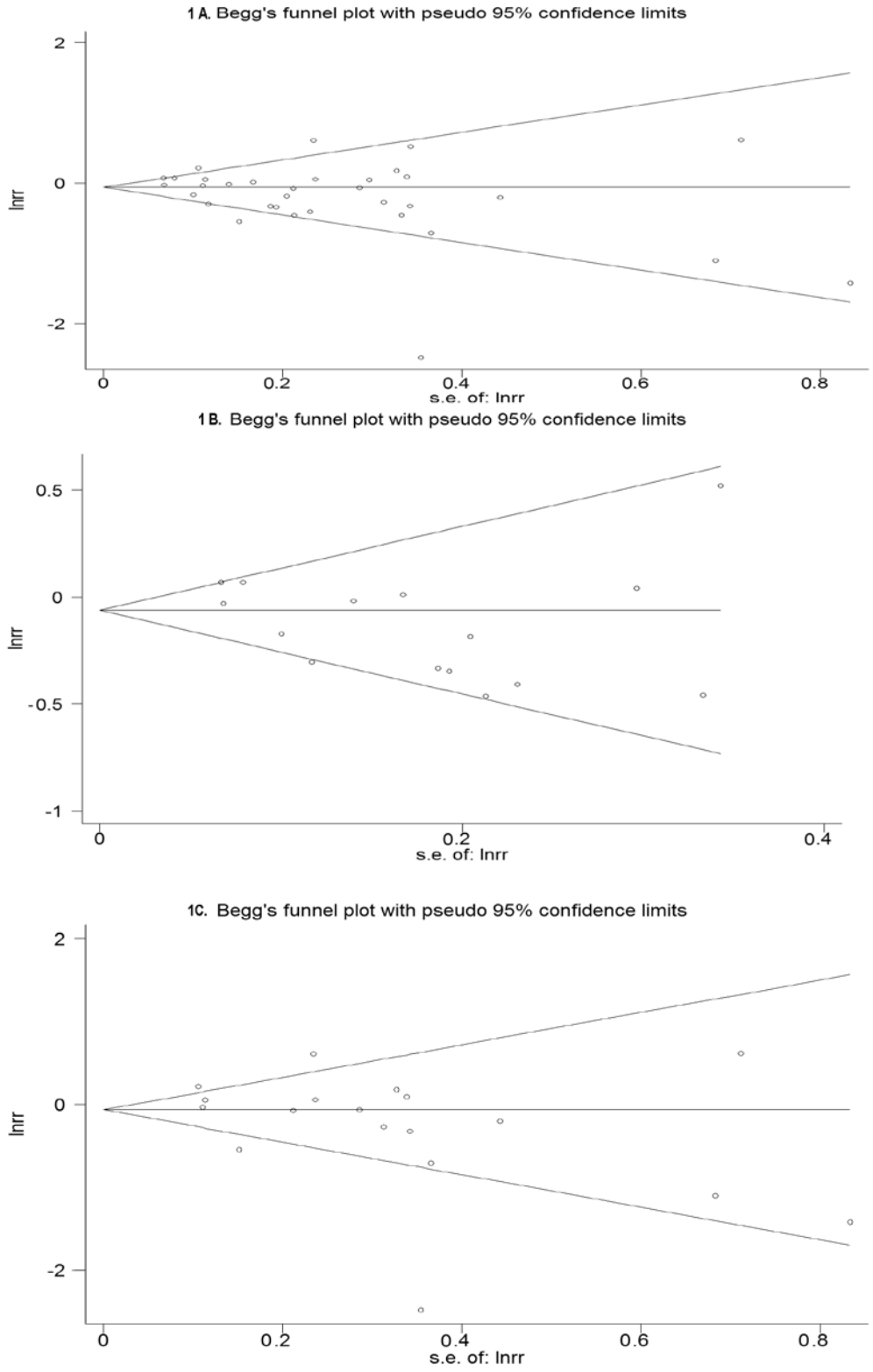
#10 Search #7 AND #9

Supplemental Table 1. Stratified analyses of pooled relative risk (RR) of total cardiovascular disease (CVD) according to alpha-linolenic acid status.

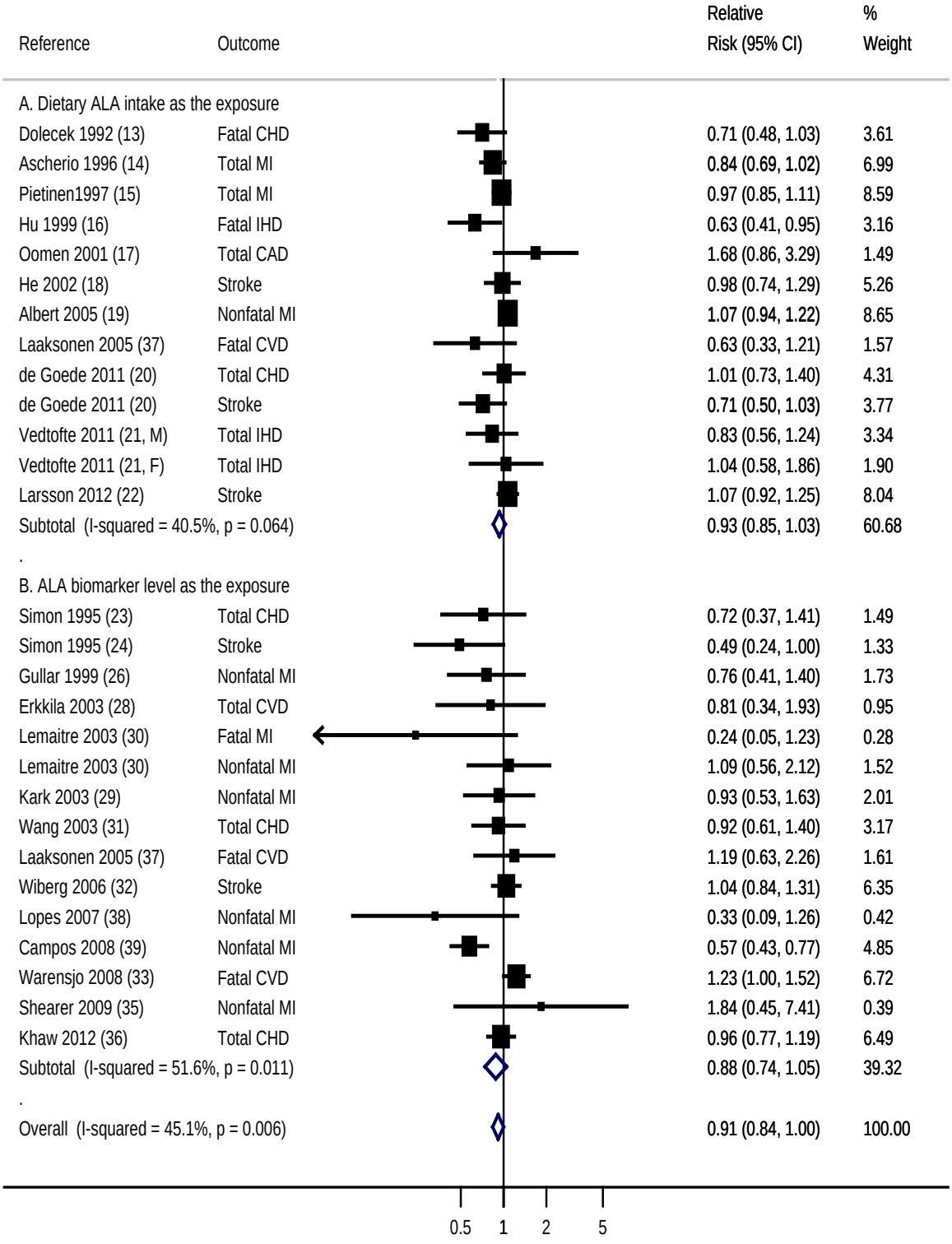
	No. of comparisons	**RR (95% CI)**	**Q-Statistic**	***P* value for heterogeneity**	***I*^{2} value**	***P* value of meta-regression**
Sex						
Male	16	0.92 (0.82-1.03)	25.3	0.05	40.7	
Female	4	1.00 (0.85-1.18)	5.9	0.12	49.3	0.45
Both	13	0.76 (0.57-1.02)	68.4	<0.001	82.5	
Baseline mean age						
<60	27	0.83 (0.73-0.95)	102.2	<0.001	74.6	0.29
≥60	6	1.03 (0.88-1.21)	6.0	0.30	17.1	
Exposure measurement						
Dietary intake	15	0.90 (0.81-0.99)	27.5	0.02	49.0	0.65
Biomarker level	18	0.83 (0.63-1.03)	84.0	<0.001	79.8	
Outcomes						
Fatal CHD	6	0.81 (0.57-1.15)	16.8	0.005	70.2	
Nonfatal CHD	10	0.82 (0.67-1.02)	24.3	0.004	63.0	0.98
Total CHD	12	0.87 (0.68-1.10)	60.5	<0.001	81.8	
Stroke	5	0.94 (0.79-1.12)	8.0	0.09	49.7	
Study quality						
High	22	0.88 (0.79-0.99)	42.7	0.003	50.8	0.49
Low	11	0.79 (0.61-1.02)	66.4	<0.001	84.9	
Study design						
Prospective	23	0.95 (0.88-1.03)	33.3	0.06	34.0	0.10
Retrospective	10	0.68 (0.46-1.02)	61.6	<0.001	85.4	
Study location						
US and Costa Rica	14	0.73 (0.57-0.92)	83.0	<0.001	84.3	0.07
European countries	19	0.99 (0.91-1.08)	21.3	0.27	15.4	
Adjustment for lifestyle factors						
Yes	28	0.88 (0.78-0.99)	104.7	<0.001	74.2	0.38
No	5	0.71 (0.49-1.03)	4.4	0.35	9.6	
Adjustment for other fatty acids						
Yes	15	0.92 (0.80-1.06)	39.9	<0.001	64.9	0.20
No	18	0.78 (0.65-0.94)	71.1	<0.001	76.1	

Meta-regression analysis was conducted by adding the individual variable in the model.

Supplemental Figure 1. Funnel Plots for Detection of Publication Bias for (A) overall results; (B) dietary ALA intake as the exposure; (C) ALA biomarker level as the exposure.



Supplemental Figure 2. Sensitivity analysis of excluding retrospective case-control studies using dietary ALA intake or blood ALA biomarker level as the exposure.



Supplemental Figure 3. Two-stage dose-response meta-analysis of (A) each 1 g/d increment of dietary alpha-linolenic acid (ALA) intake and risk of coronary heart disease (CHD) death; (B) each 0.5% increment of ALA concentration in adipose tissue and risk of nonfatal CHD.