

Table S1: Meta-regression for CVD events by age in Randomized controlled trial

LnRR	Coefficient	SE	t	P-value	95% CI	
					Lower limit	Upper limit
age	-0.008	0.003	-2.28	0.036	-0.015	-0.0006
constant	0.522	0.233	2.24	0.039	0.028	1.015
Number of observations=18; Adjusted R ² =100%						

Table S2: Meta-regression for CVD deaths by age in Randomized controlled trial

LnRR	Coefficient	SE	t	P-value	95% CI	
					Lower limit	Upper limit
age	-0.014	0.006	-2.30	0.036	-0.027	-0.001
constant	0.921	0.414	2.22	0.042	0.038	1.804
Number of observations=17; Adjusted R ² =100%						

	Risk of bias domains					
	D1	D2	D3	D4	D5	Overall
Virtanen 2022	+	+	+	+	+	+
Naele 2022	+	+	+	+	+	+
Chatterjee 2021	+	+	+	+	+	+
Manson 2019	+	+	+	+	+	+
Shoji 2018	+	+	+	+	+	+
Scragg 2017	+	+	+	+	+	+
Zittermann 2017	+	+	+	+	+	+
Jorde 2016	-	+	+	+	-	-
Baron 2015	+	+	+	+	+	+
Martineau 2014	+	+	+	+	+	+
Ford 2014	+	+	+	+	+	+
Wang 2014	+	+	+	+	-	-
Witham 2013	+	+	+	+	+	+
Gallagher 2012	+	+	+	+	+	+
Lehouck 2012	+	+	+	+	+	+
Sanders 2010	+	+	+	+	+	+
Prince 2008	+	+	+	+	+	+
Zhu 2008	+	+	+	+	-	-
Berggren 2007	+	×	+	+	-	×
Hsia 2007	-	+	+	×	-	×
Jackson 2006	+	+	+	+	+	+
Brazier 2005	-	+	+	×	-	×
Grant 2005	+	+	+	+	+	+
Trivedi 2003	+	+	+	+	-	-
Komulainen 1999	-	+	+	-	-	×
Ott 1989	-	-	+	×	-	×
Aloia 1988	-	-	+	×	-	×
Inkovaara 1983	-	-	+	×	-	×
Brohult 1973	-	-	+	×	+	×

Domains:
 D1: Bias arising from the randomization process.
 D2: Bias due to deviations from intended intervention.
 D3: Bias due to missing outcome data.
 D4: Bias in measurement of the outcome.
 D5: Bias in selection of the reported result.

Judgement
 × High
 - Some concerns
 + Low

Figure S1: Risk of bias in Randomized Controlled Trial

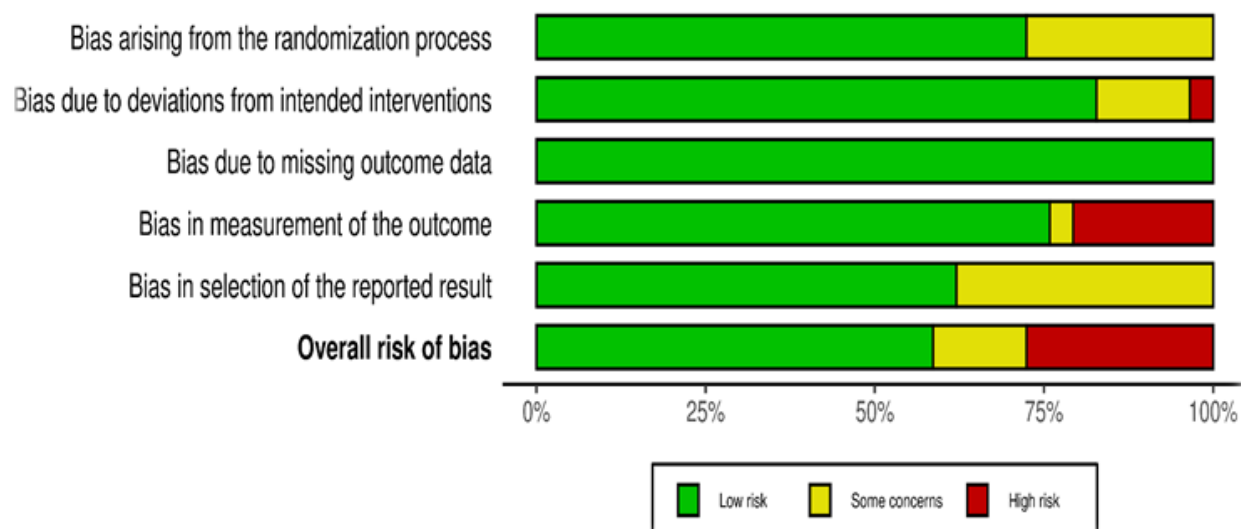


Figure S2: Risk of Bias in Randomized Controlled Trials

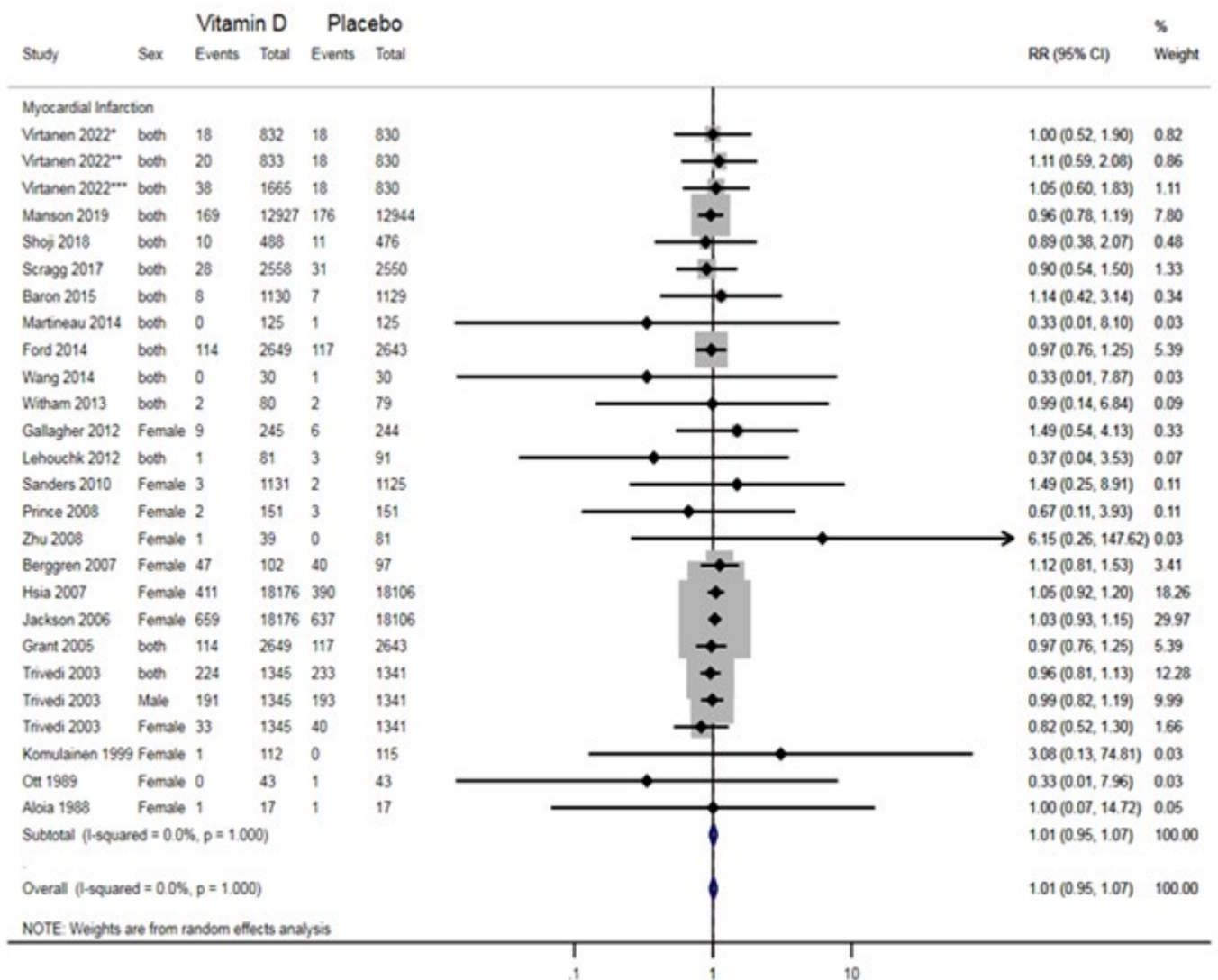


Figure S3: Forrest plot for Myocardial Infarction in Randomized Controlled Trials

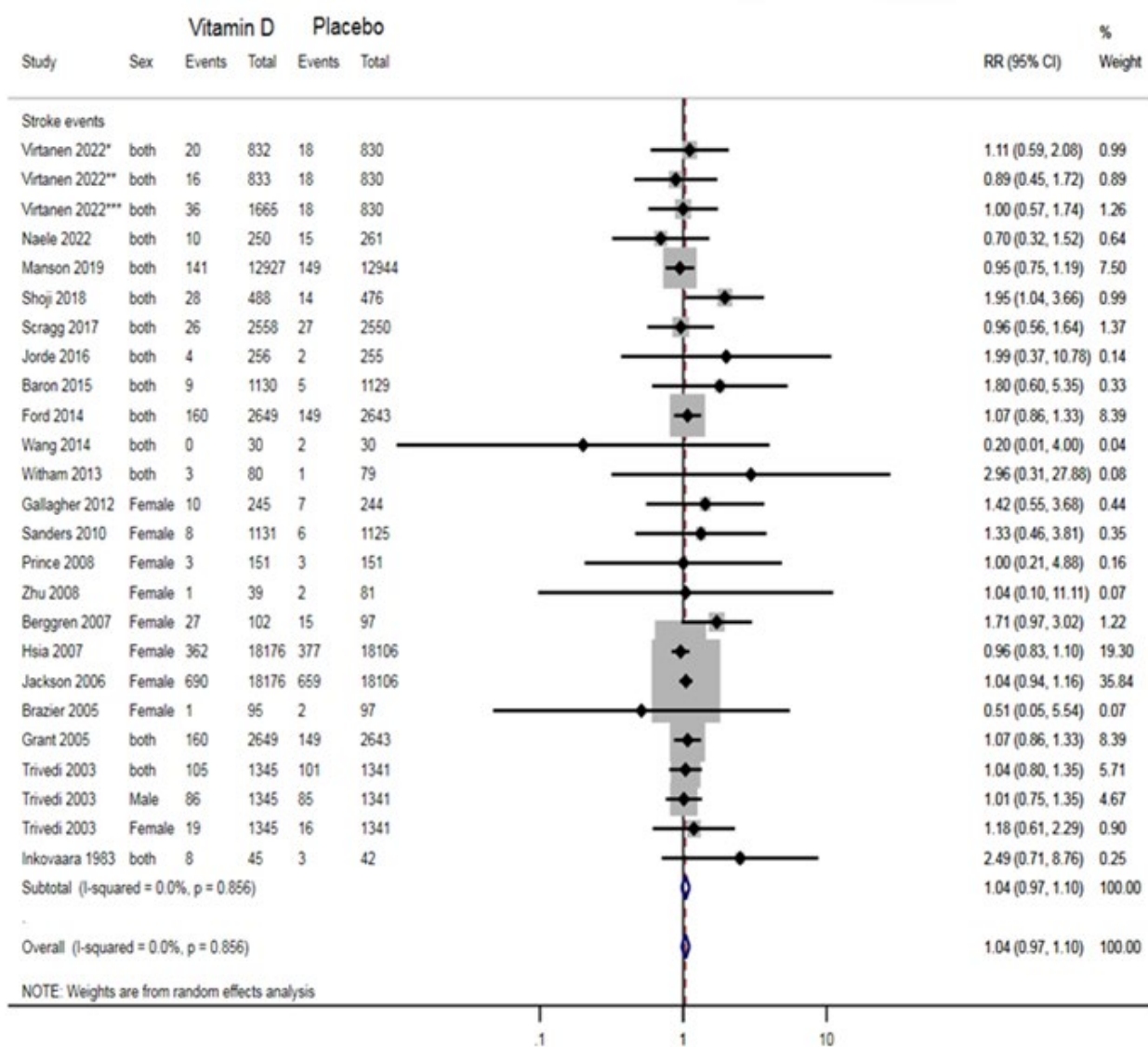


Figure S4: Forrest plot for Stroke in Randomized Controlled Trials

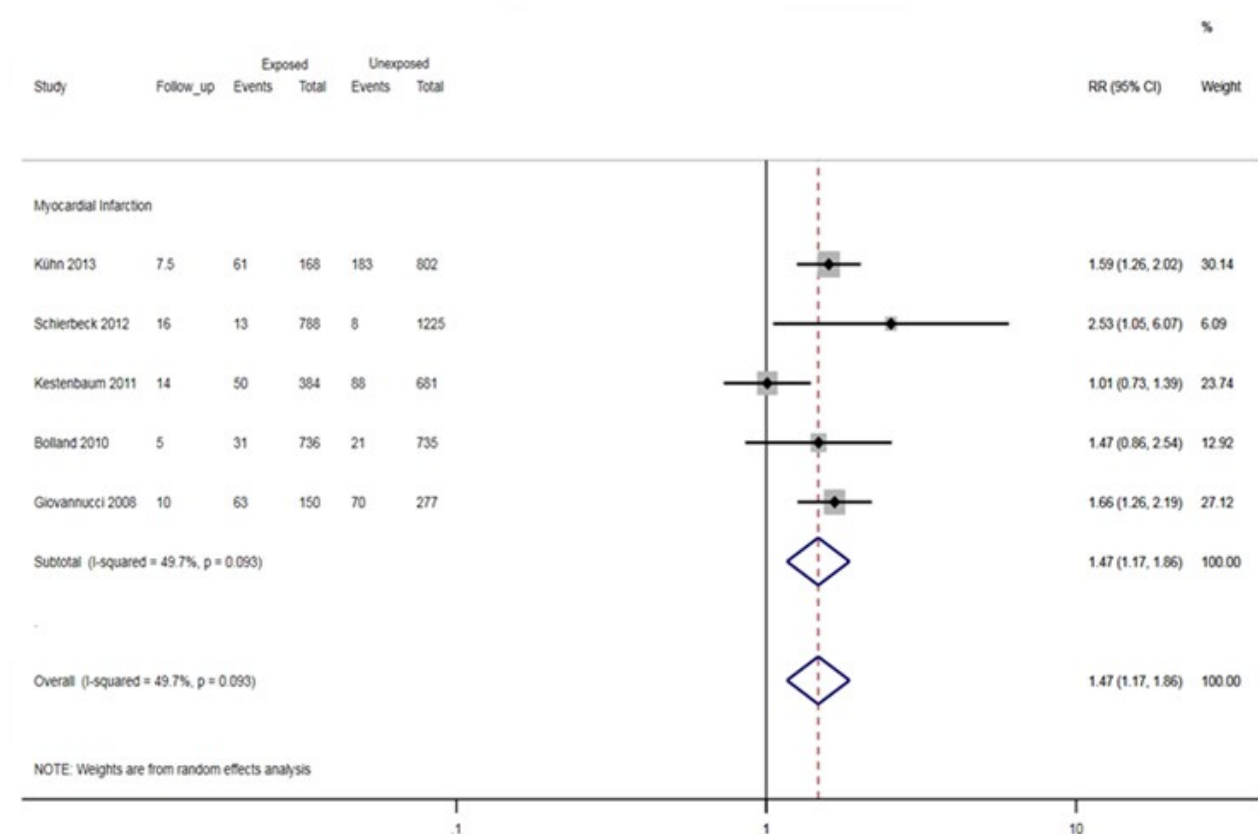


Figure S5: Forest plot for Myocardial Infarction in Prospective Cohort Studies

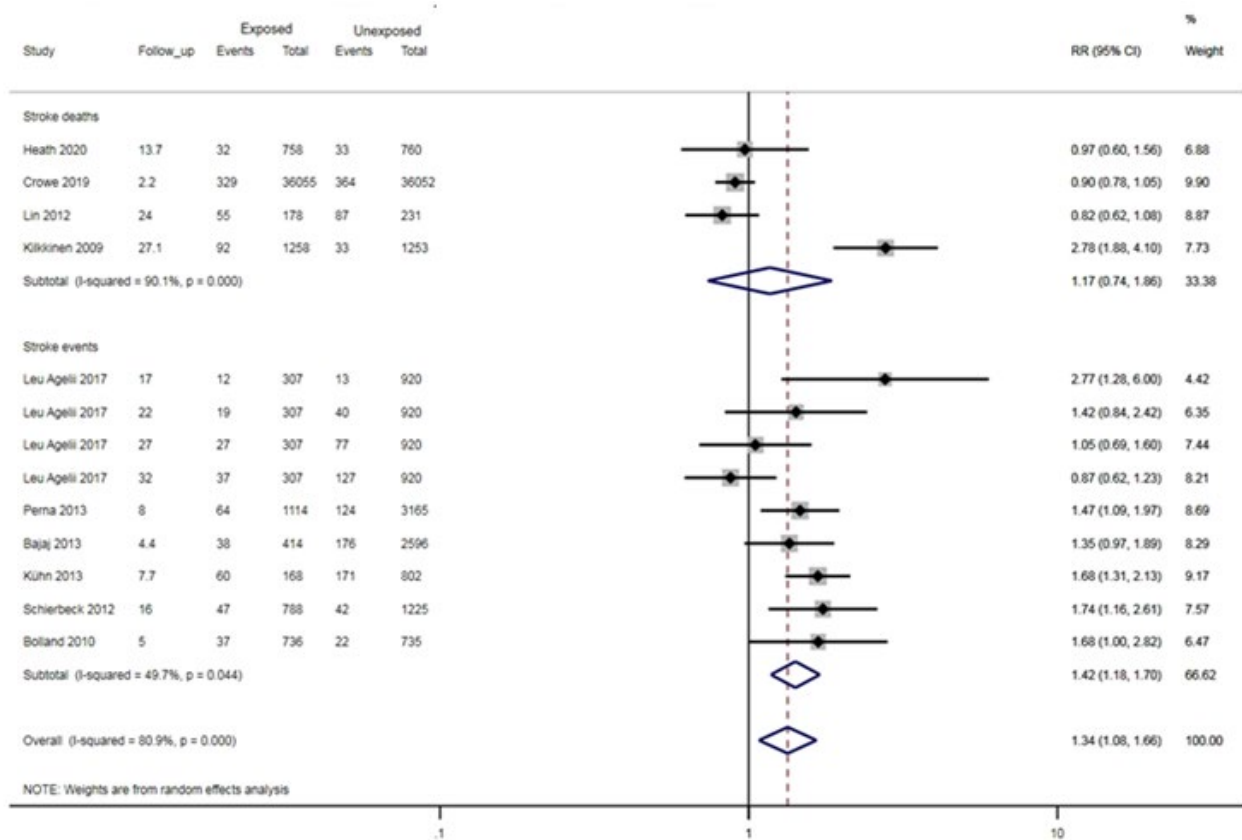


Figure S6: Forest plot for Stroke in Prospective Cohort Studies