

Supplementary Online Content

Barbarawi M, Kheiri B, Zayed Y, et al. Vitamin D supplementation and cardiovascular disease risks in more than 83 000 individuals in 21 randomized clinical trials: a meta-analysis. Published online June 19, 2019. *JAMA Cardiol*. doi:10.1001/jamacardio.2019.1870

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This supplementary material has been provided by the authors to give readers additional information about their work.

eTable 1: Major adverse cardiovascular event definition per each study.

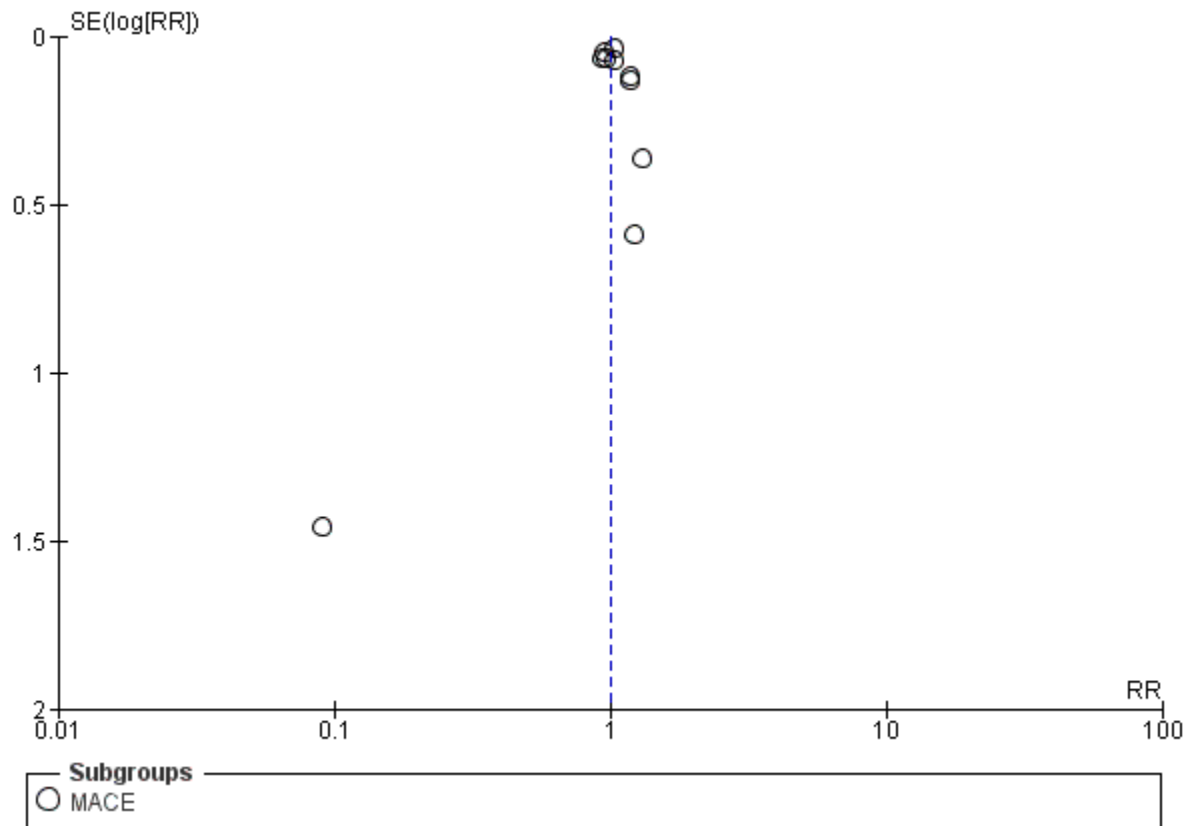
Trial/First author Name, Year of publication	Major adverse cardiovascular event definition
Trivedi et al 2003	The composite of ischemic heart disease, stroke, or other cardiovascular disease
RECORD\Grant et al 2005	The composite of myocardial infarction, stroke, and heart failure.
Brazier et al 2005	The composite of myocardial infarction, stroke, atrial fibrillation, and heart failure.
Vital D\Sanders et al 2010	The composite of myocardial infarction, stroke, and heart failure.
WHI\Jackson et al 2012	The composite of coronary heart disease, revascularization, angina, and congestive heart failure
OPERA\Wang et al 2014	The composite of myocardial infarction, stroke, Syncope, bradycardia and heart failure.
EVITA\Zitterman et al 2017	The composite of myocardial infarction, heart failure and cardiovascular hospitalization.
ViDA\Scragg et al 2017	The composite of ischemic heart disease, pulmonary embolism, inflammatory cardiac conditions, conduction disorders, cardiac arrest, arrhythmias, ill-defined heart disease, diseases of the arteries, and diseases of the veins (including venous thrombosis).
J-DAVID\Shoji et al 2018	The composite of acute myocardial infarction, Congestive heart failure, Stroke, Aortic dissection/Rupture, Amputation of ischemic limb, and Cardiac sudden death.
VITAL\Manson et al 2018	The composite of myocardial infarction, stroke, or death from cardiovascular causes

Abbreviations: EVITA: Effect of vitamin D on all-cause mortality in heart failure patients; J-DAVID: Japan dialysis active vitamin D; OPERA: Oral paricalcitol in retarding cardiac hypertrophy, reducing inflammation and atherosclerosis in stage 3 - 5 chronic kidney disease; RECORD: Randomized evaluation of calcium or vitamin D; ViDA : Vitamin D assessment, VITAL: Vitamin D and omega-3 trial; WHI: Women's health initiative.

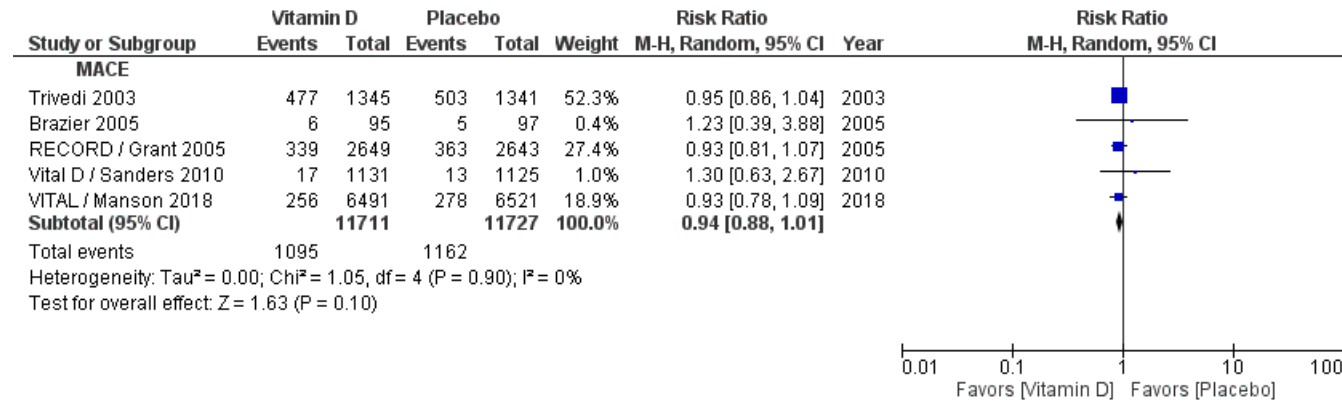
eFigure 1: Risk of bias summary: review authors' judgments about each risk of bias item for each included study.

	Random sequence generation (selection bias)	Allocation concealment (selection bias)	Blinding of participants and personnel (performance bias)	Blinding of outcome assessment (detection bias)	Incomplete outcome data (attrition bias)	Selective reporting (reporting bias)	Other bias
Aloia 1988			+		-	-	
Baron 2015	+	+	+	+	+	+	+
Berggren 2007	-	-			-	-	-
Brazier 2005	+	+	+		+		
EVITA / Zitterman 2017	+	+	+	+	+	+	+
J-DAVID / Shoji 2018	+	+	+	+	+	+	
Komulainen 1999	+		+	+			
Lehouck 2012	+	+	+	+	+	+	
OPERA / Wang 2014	+	+					-
Ott 1889			-	-	-	-	
Prince 2008	+	+	+	+	+	+	
RECORD / Grant 2005	+	+	+	+	+	+	+
Schleithoff 2006	+	+	+				-
STOP IT / Gallagher 2001	+	+	+	+			+
Trivedi 2003	+		+				-
VIDA / Scragg 2017	+	+	+	+	+	+	+
VITAL / Manson 2018	+	+	+	+	+	+	+
Vital D / Sanders 2010	+	+	+	+	+	+	
VitDISH / Witham 2013	+	+	+	+	+	+	
WHI / Jackson 2006	+	+	+	+	+	+	+
Zhu 2008	+	+	+	+	+	+	

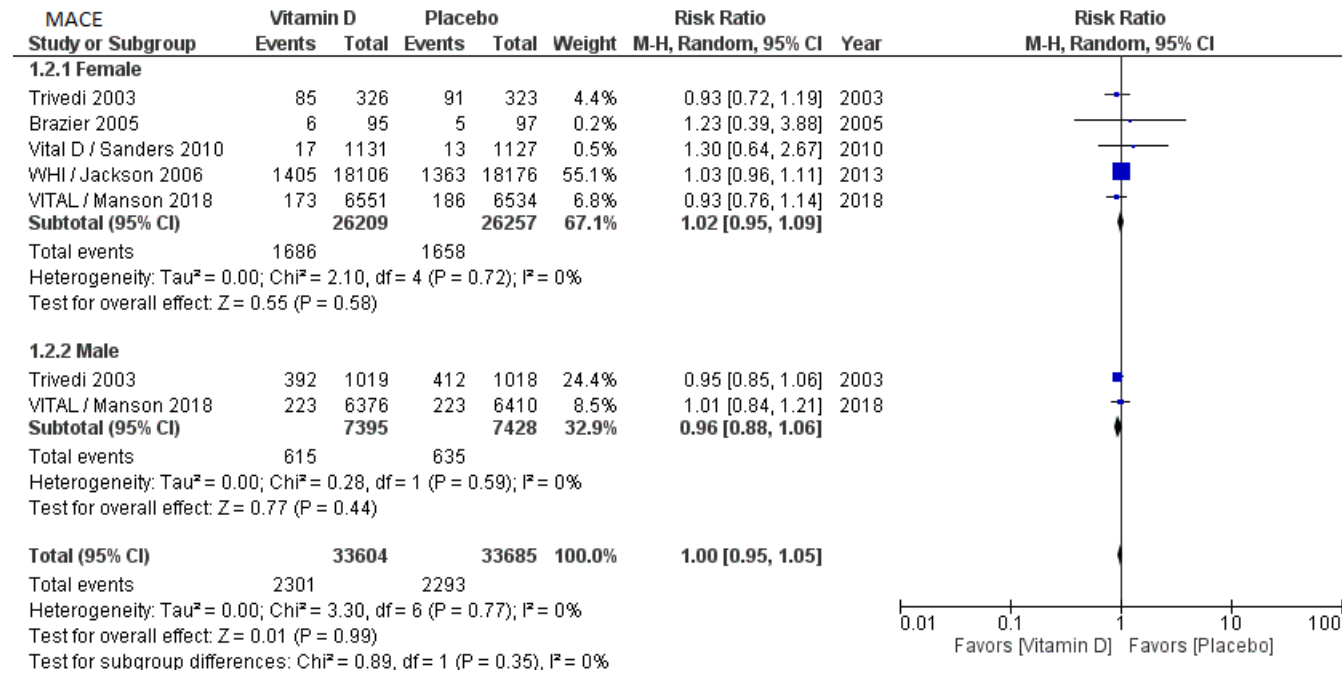
eFigure 2: Funnel plot of primary endpoints (major adverse cardiovascular events).



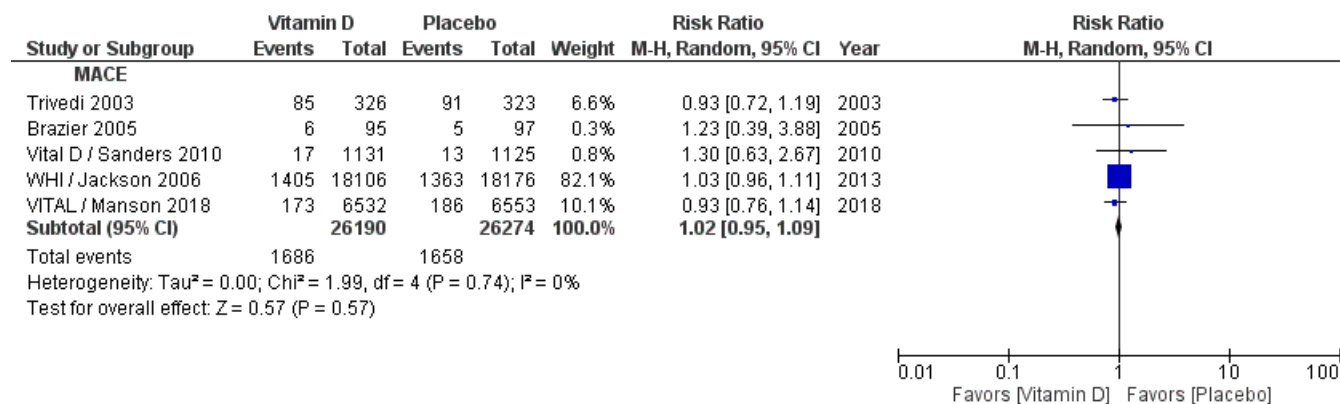
eFigure 3: Forest plot of the sensitivity analysis for elderly patients.



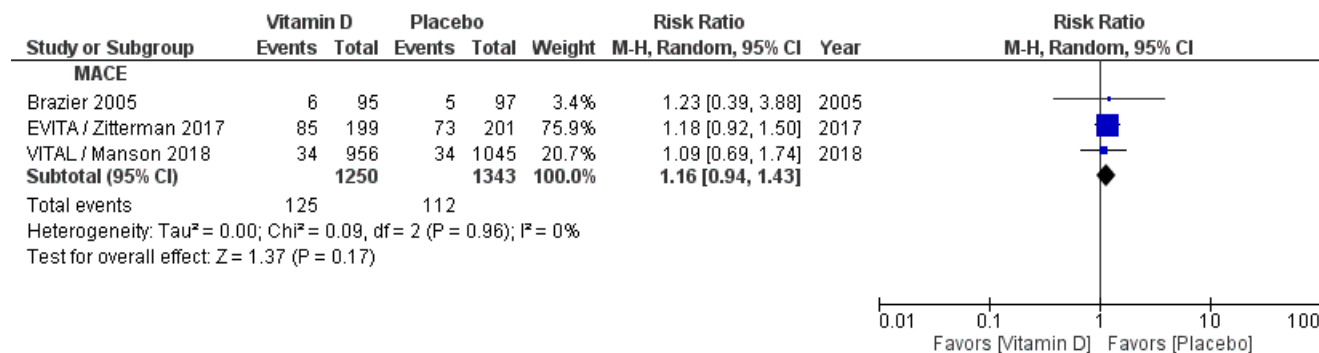
eFigure 4: Forest plot of the sensitivity analysis for female and male patients.



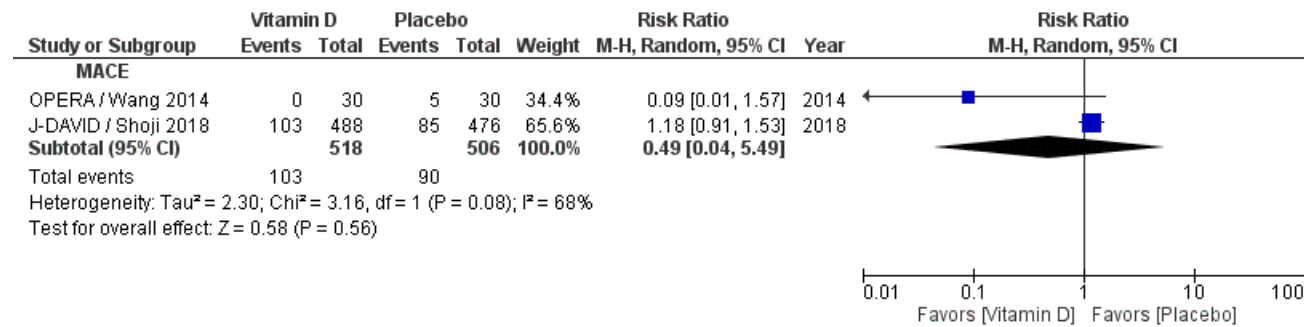
eFigure 5: Forest plot of the sensitivity analysis for postmenopausal women.



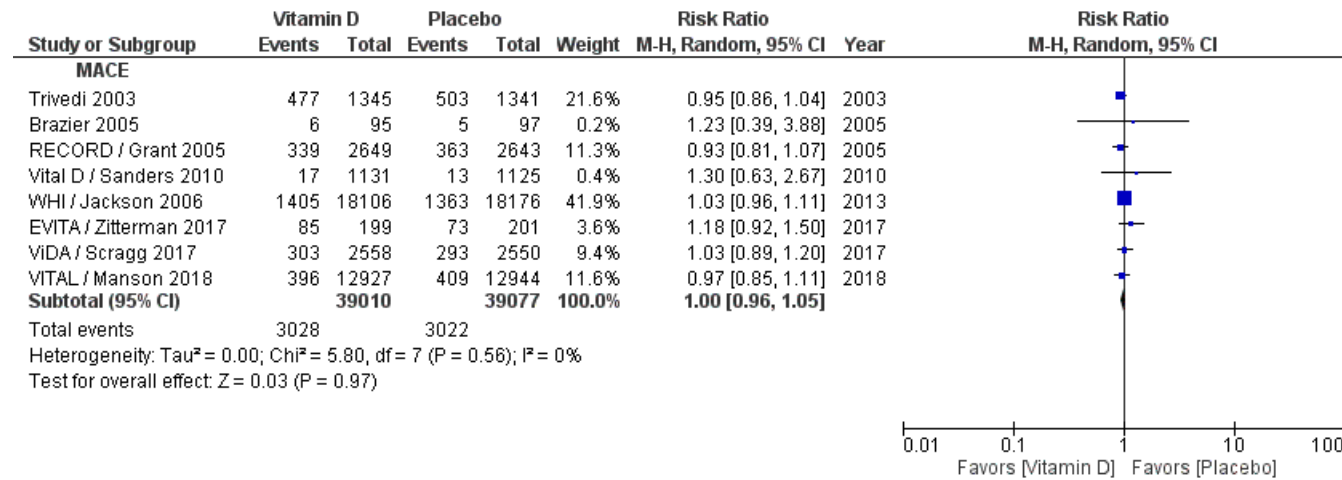
eFigure 6: Forest plot of the sensitivity analysis for studies with pretreatment 25-hydroxyvitamin D level less than 25 ng/ml.



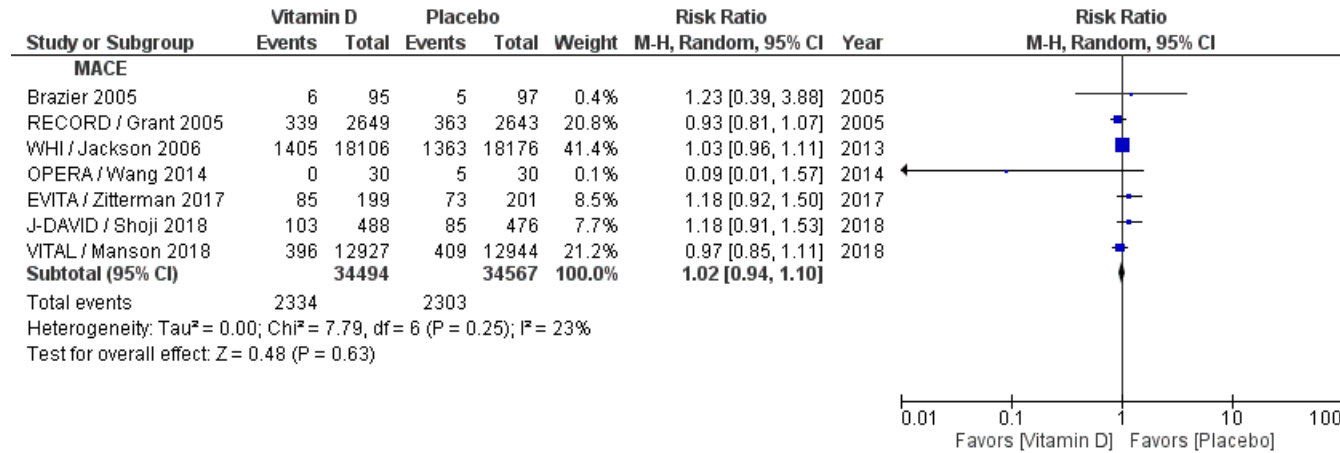
eFigure 7: Forest plot of the sensitivity analysis for chronic kidney disease.



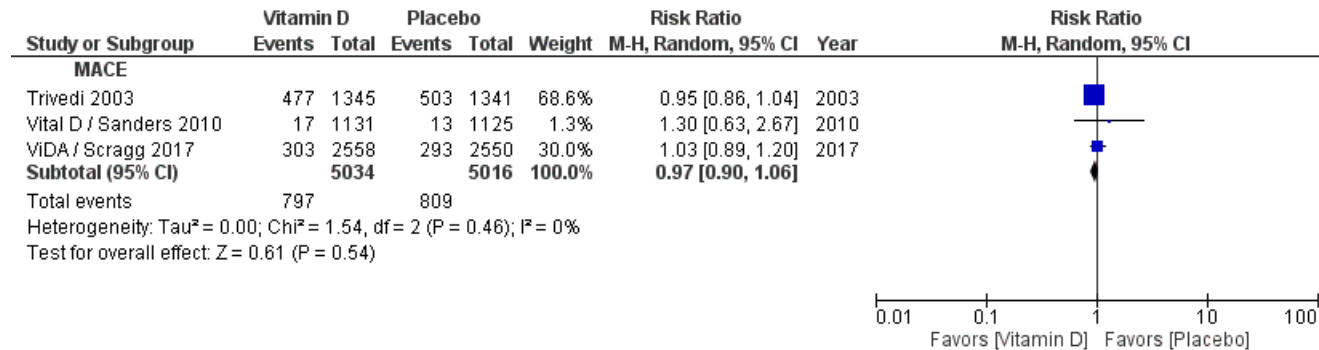
eFigure 8: Forest plot of the sensitivity analysis by excluding studies that used vitamin D analogues.



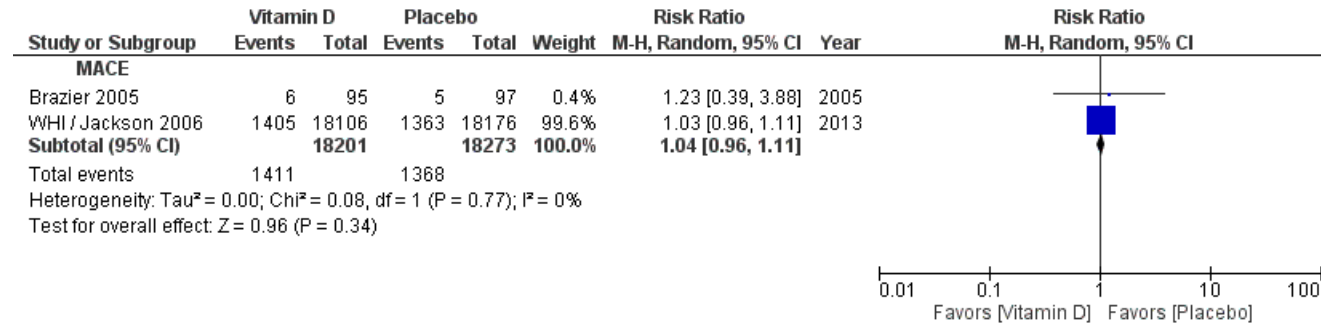
eFigure 9: Forest plot of the sensitivity analysis by including only the studies that used daily vitamin D supplementation.



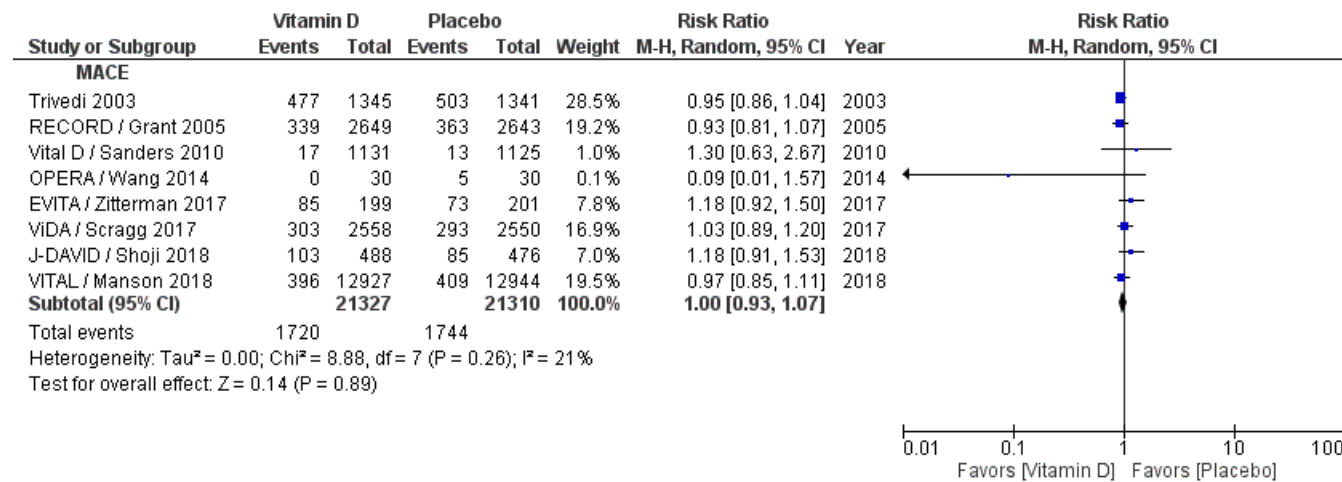
eFigure 10: Forest plot of the sensitivity analysis by including only the studies that used bolus vitamin D supplementation.



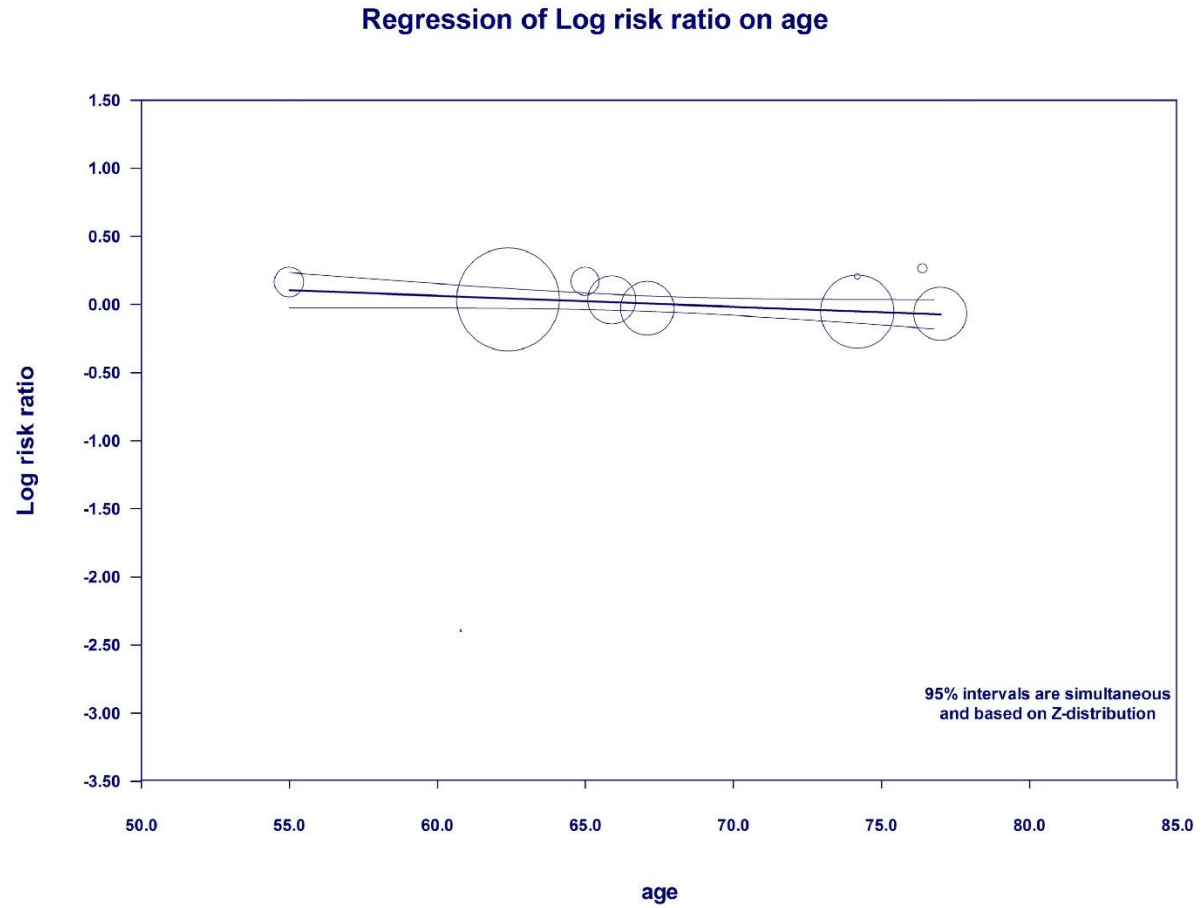
eFigure 11: Forest plot of the sensitivity analysis by including studies that used vitamin D supplementation with calcium.



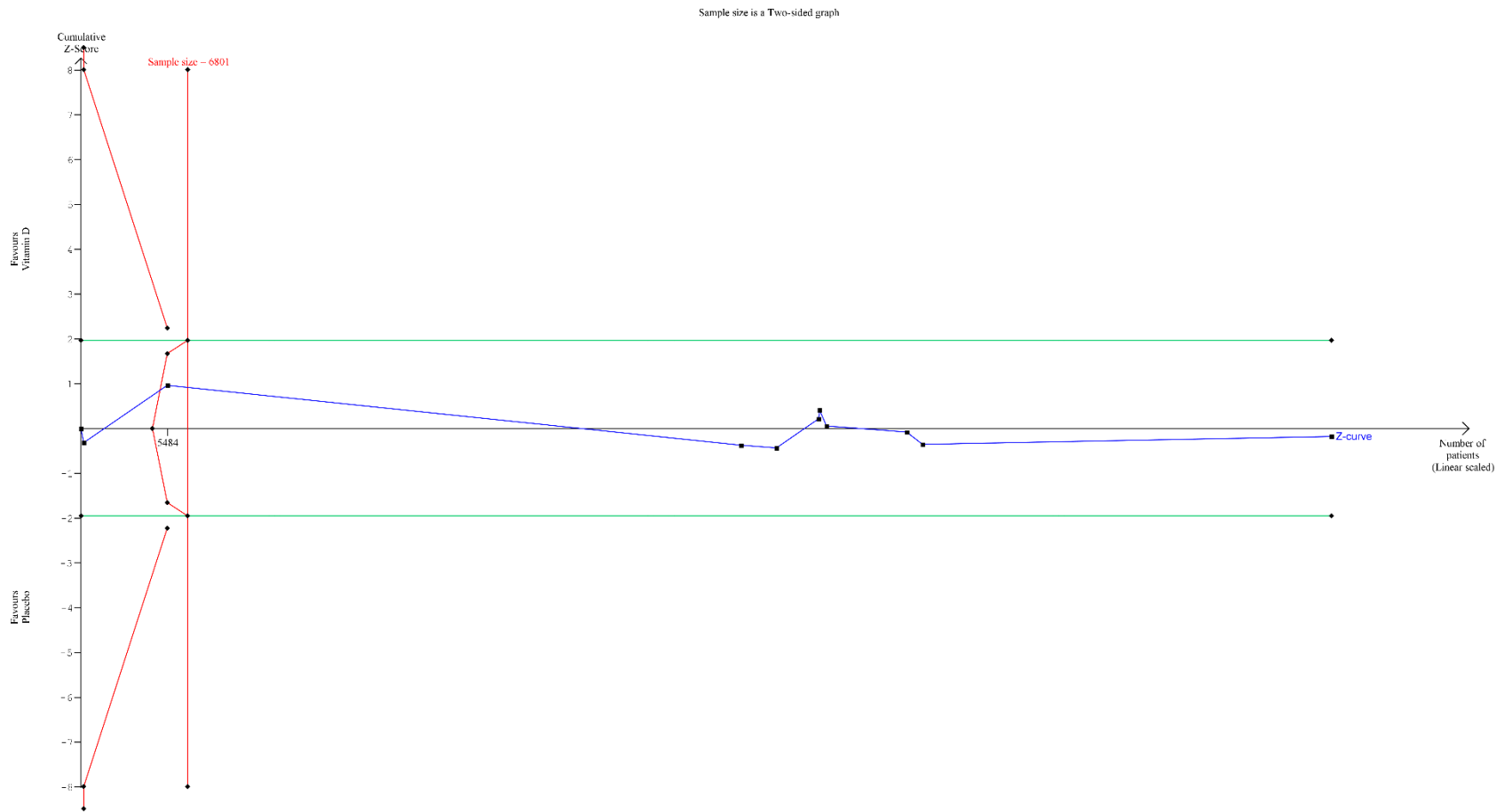
eFigure 12: Forest plot of the sensitivity analysis by including studies that used vitamin D supplementation without calcium.



eFigure 13: Meta-regression analysis on major adverse cardiovascular events according to age.



eFigure 14: Trial sequential analysis for major adverse cardiovascular events.



The diversity-adjusted information size = 6,801. The cumulative Z-curve (blue line with small black squares representing each trial) crosses the futility boundaries (convex red lines), indicating firm evidence for the lack of effects.