SUPPLEMENTAL MATERIAL

Table S1. Search terms used to identify relevant articles
PubMed
("OPG" [All Fields] OR "Osteoprotegerin" [All Fields] OR "OCIF Protein" [All Fields] OR "Osteoclastogenesis Inhibitory Factor" [All Fields] OR "Tumor Necrosis Factor Receptor 11b" [All Fields] OR "Osteoprotegerin"[MeSH]) AND ("Cardiovascular Diseases" [MeSH] OR "Coronary Artery Disease" [MeSH] OR "Atherosclerosis" [MeSH] OR "Coronary Disease" [MeSH] OR "Myocardial Infarction" [MeSH] OR "Myocardial Ischemia" [MeSH] OR "Stroke" [MeSH] OR "Cerebrovascular" [All fields]) NOT ("Animals"[MeSH] NOT "Humans"[MeSH])
Web of Science
TS=("OPG" OR "Osteoprotegerin" OR "OCIF Protein" OR "Osteoclastogenesis Inhibitory Factor" OR "Tumor Necrosis Factor Receptor 11b") AND TS=("Cardiovascular Diseases" OR "Coronary Artery Disease" OR "Atherosclerosis" OR "Coronary Disease" OR "Myocardial Infarction" OR "Myocardial Ischemia" OR "Stroke" OR "Cerebrovascular")
EMBASE
("OPG" OR "Osteoprotegerin" OR "OCIF Protein" OR "Osteoclastogenesis Inhibitory Factor" OR "Tumor Necrosis Factor Receptor 11b").af AND ("Cardiovascular Diseases" OR "Coronary Artery Disease" OR "Atherosclerosis" OR "Coronary Disease" OR "Myocardial Infarction" OR "Myocardial Ischemia" OR "Stroke" OR "Cerebrovascular").af

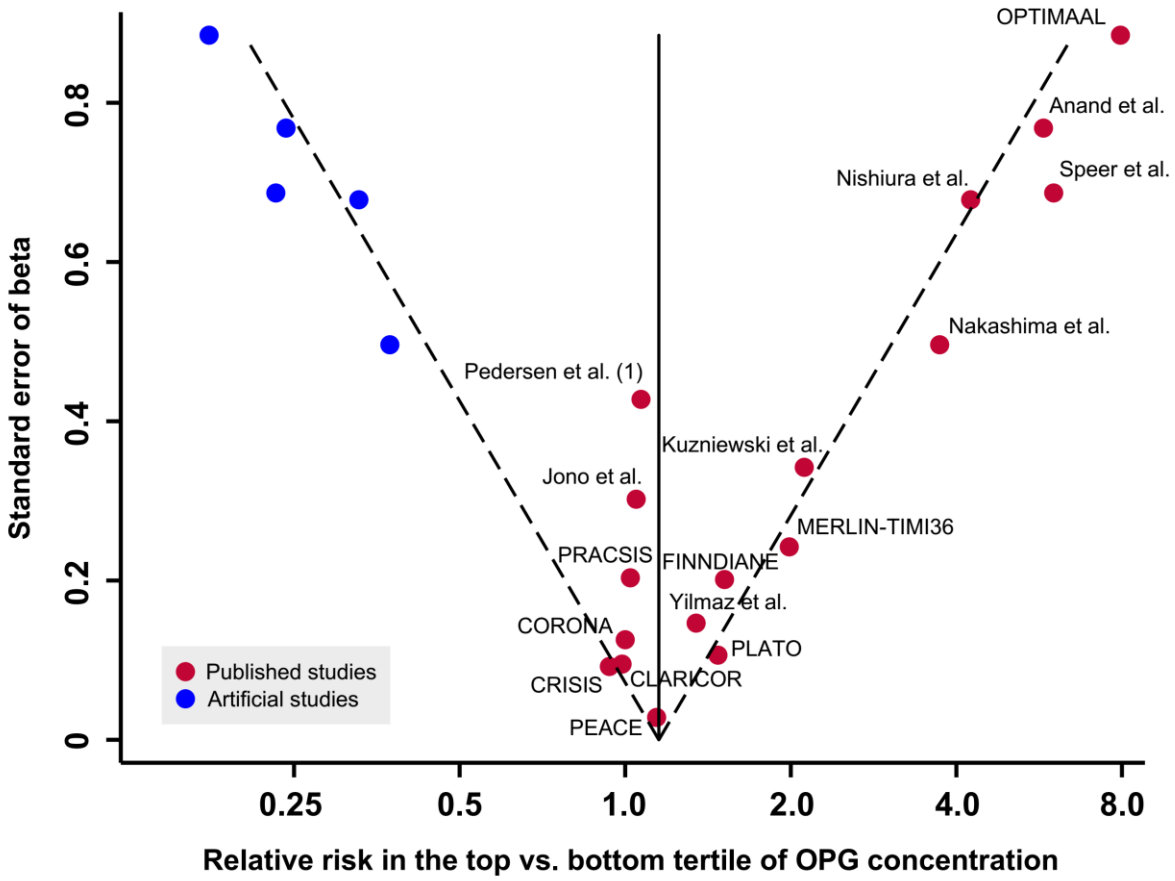
No language restrictions were applied.

Table S2. Detailed baseline conditions of contributing studies	
Study acronym or first author	**Baseline diseases**
Populations with diabetes at baseline	
Anand[1]	Type 2 diabetes
FINNDIANE[2]	Type 1 diabetes
Populations with kidney disease at baseline	
ALERT[3]	Renal transplant recipients (did not report on cause of kidney disease)
CRISIS[4]	All cause chronic kidney disease
Kuzniewski[5]	Chronic glomerulonephritis, pyelonephritis, polycystic kidney disease, diabetic nephropathy, unknown cause
Nakashima[6]	Long term hemodialysis patients (did not report on cause of kidney disease)
Nishiura[7]	Consecutive hemodialysis patients (diabetic nephropathy, chronic glomerulonephritis, nephrosclerosis, other cause)
Speer[8]	Chronic hemodialysis patients (vascular-tubulointerstitial [including hypertension], diabetes mellitus, glomerulonephritis, other cause)
Yilmaz[9]	Chronic kidney disease (did not report on cause of kidney disease)
Populations with pre-existing heart disease at baseline	
CLARICOR[10]	Stable coronary artery disease
CORONA[11]	Chronic heart failure of ischemic cause (NYHA class II to IV, LV ejection fraction ≤40% [≤35% if NYHA II])
Jono[12]	Stable coronary artery disease
PEACE[13]	Stable coronary artery disease

Pedersen (1)[14]	Stable angina pectoris
Populations with recent acute coronary syndromes at baseline	
MERLIN-TIMI36[15]	Non-ST elevation acute coronary syndromes
OPTIMAAL[16]	Acute myocardial infarction complicated with heart failure during the acute phase
PLATO[17]	Acute coronary syndromes
PRACSIS[18]	Acute coronary syndromes (unstable angina, non-ST-segment elevation myocardial infarction, or ST-segment elevation myocardial infarction)
Pedersen (2)[19]	ST-segment elevation myocardial infarction treated with primary percutaneous coronary intervention

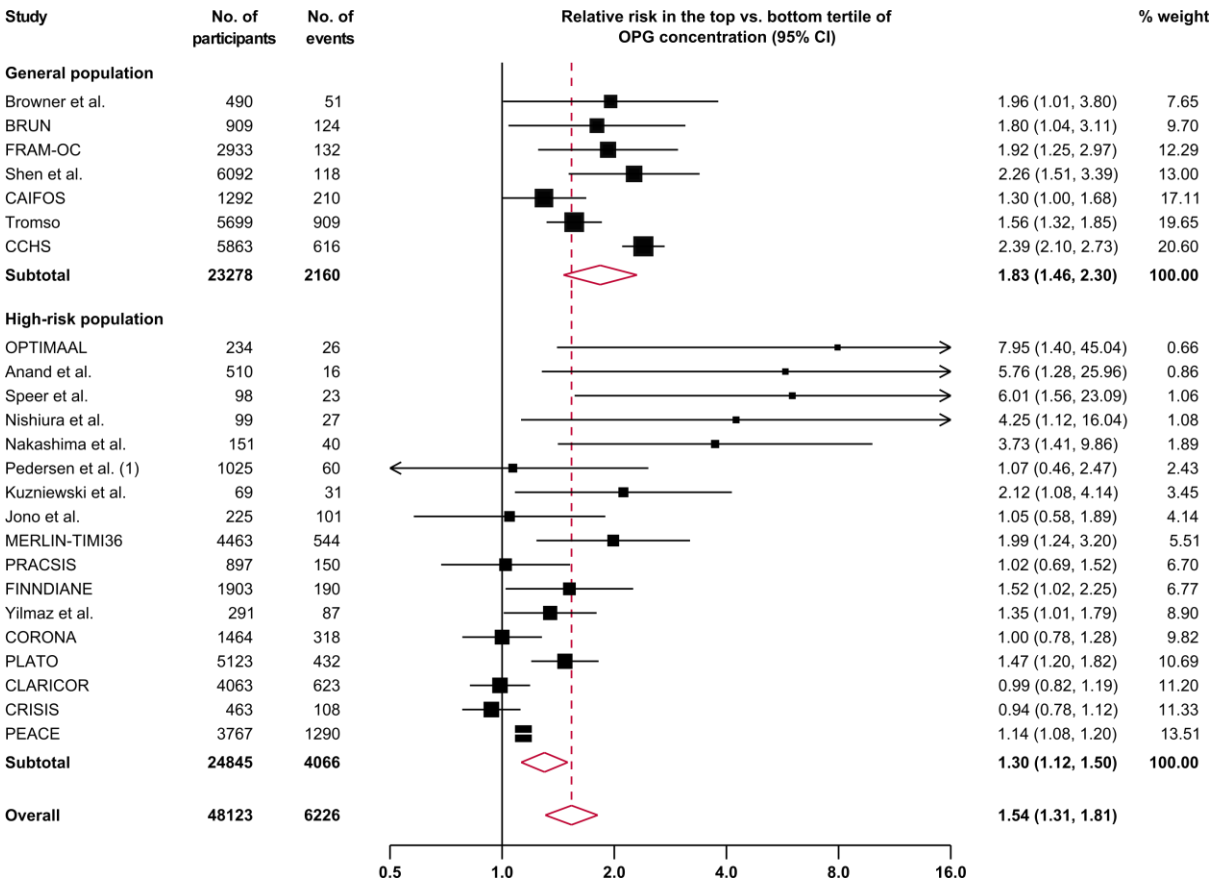
ALERT, Assessment of Lescol in Renal Transplantation Study; CLARICOR, Effect of Clarithromycin on Mortality and Morbidity in Patients With Ischemic Heart Disease; CORONA, Controlled Rosuvastatin Multinational Trial; CRISIS, Chronic Renal Insufficiency Standards Implementation Study; FINNDIANE, Finnish Diabetic Nephropathy Study; MERLIN-TIMI36, Metabolic Efficiency with Ranolazine for Less Ischemia in Non–ST-elevation acute coronary syndromes trial; NYHA, New York Heart Association; OPTIMAAL, Optimal Trial in Myocardial Infarction with Angiotensin II Antagonist Losartan; PEACE, Prevention of Events with Angiotensin Converting Enzyme Inhibition Trial; PLATO, PLATelet inhibition and patient Outcomes trial; PRACSIS, Prognosis and Risk in Acute Coronary Syndrome in Sweden.

Figure S1. Funnel plot including artificial studies generated with the 'trim and fill' method.



Full study names are listed in the footnote of **Table S2**. The dotted lines show pseudo 95% confidence intervals around the overall pooled estimate. The P value from Egger's asymmetry test of associations was 0.013. Blue dots indicate artificial studies included by the 'trim and fill' method. OPG, osteoprotegerin.

Figure S2. Comparison of combined relative risk for cardiovascular events in the top vs. the bottom tertile of osteoprotegerin concentration of high-risk populations and general population results[20].



Sizes of data markers indicate the weight of each study in the analysis. Study-specific relative risks were pooled using random-effects meta-analysis. Full names of studies in high-risk populations are listed in the footnote of **Table S2**. The overall I^2 value was 87.0% (P<0.001). BRUN, Bruneck Study; CAIFOS, Calcium Intake Fracture Outcome study; CCHS, Copenhagen City Heart Study; CI, confidence interval; FRAM-OC, Framingham Study-Offspring Cohort; OPG, osteoprotegerin; Tromso, The Tromso Study.

Supplemental References:

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