

Supplementary data

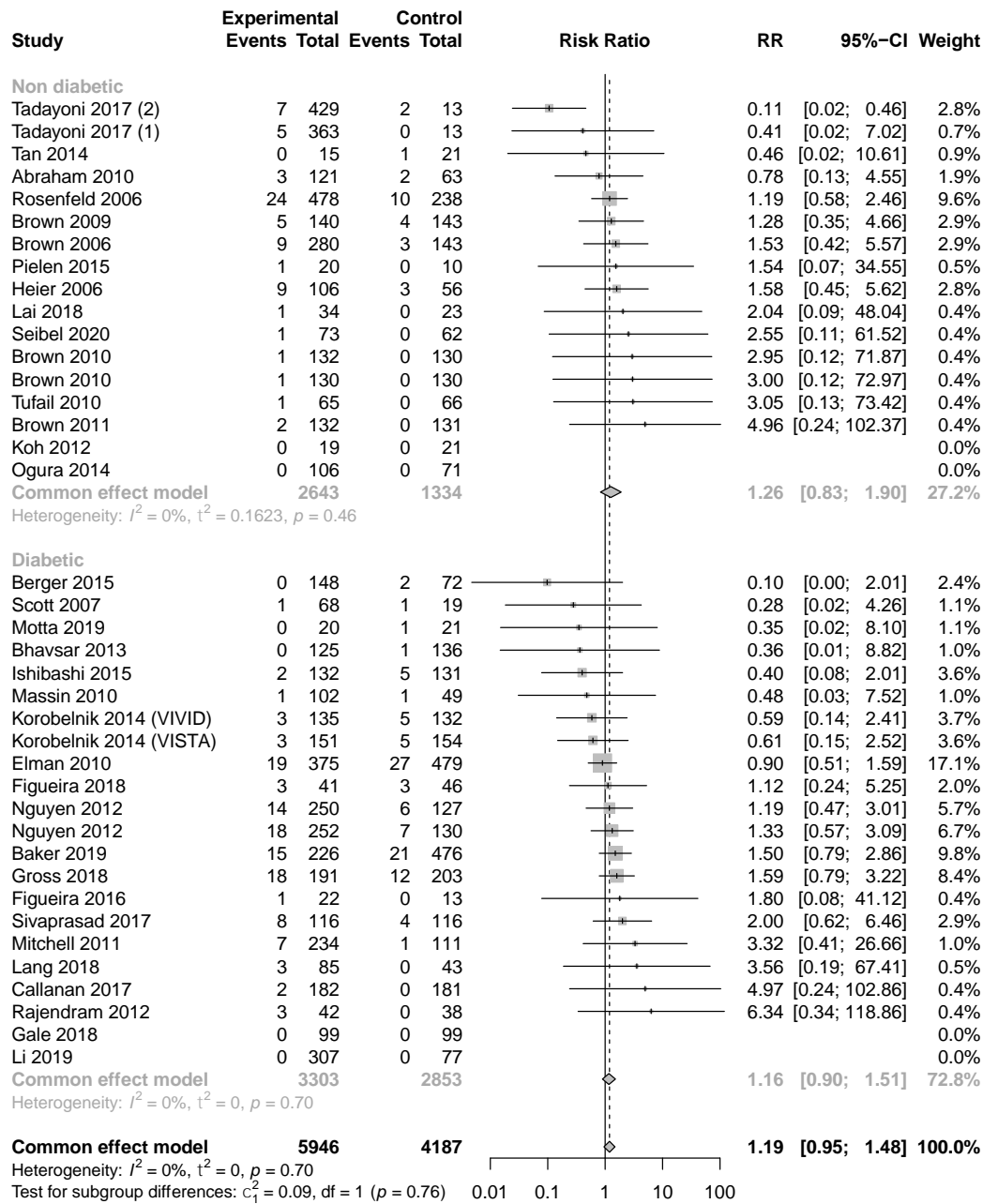
Supplementary Table S1

Outcome and variable	Unadjusted			
HYPERTENSION	Coefficient	95% CI	P	Tau²
No covariate				0.106
Diabetic eye disease	0.122	-0.390; 0.634	0.641	0.115
VEGFi type – Aflibercept	-0.753	-2.692; 1.186	0.447	0.108
VEGFi type – Ranibizumab	-0.254	-1.942; 1.434	0.768	0.108
Number of injections	0.010	-0.030; 0.050	0.640	0.136
Duration of treatment	0.006	-0.011; 0.023	0.488	0.112
HEART FAILURE	Coefficient	95% CI	P	Tau²
No covariate				0.283
Diabetic eye disease	NA	NA	NA	0.283
VEGFi type – Aflibercept	0.284	-2.632; 3.200	0.849	0.502
VEGFi type – Ranibizumab	0.362	-2.232; 2.955	0.785	0.502
Number of injections	0.024	-0.082; 0.131	0.654	0.427
Duration of treatment	0.016	-0.071; 0.103	0.718	0.428
CKD	Coefficient	95% CI	P	Tau²
No covariate				0
Diabetic eye disease	-0.478	-3.724; 2.768	0.773	0
VEGFi type – Aflibercept	-0.734	-2.185; 0.718	0.322	0
VEGFi type – Ranibizumab	NA	NA	NA	0
Number of injections	0.034	-0.059; 0.127	0.475	0

Duration of treatment	0.000	-0.085; 0.086	0.992	0
CARDIOVASCULAR EVENTS	Coefficient	95% CI	P	Tau²
No covariate				0
Diabetic eye disease	0.067	-0.439; 0.572	0.795	0
VEGF_i type – Aflibercept	0.126	-1.052; 1.305	0.833	0
VEGF_i type – Ranibizumab	-0.012	-1.116; 1.092	0.983	0
Number of injections	0.010	-0.022; 0.042	0.536	0
Duration of treatment	0.008	-0.008; 0.024	0.317	0
DEATH	Coefficient	95% CI	P	Tau²
No covariate				0.072
Diabetic eye disease	1.004	0.283; 1.726	0.006	0
VEGF_i type – Aflibercept	-0.363	-1.07; 0.975	0.595	0.081
VEGF_i type – Ranibizumab	-0.799	-1.995; 0.397	0.190	0.081
Number of injections	-0.013	-0.070; 0.044	0.661	0.124
Duration of treatment	-0.021	-0.082; 0.039	0.492	0.126

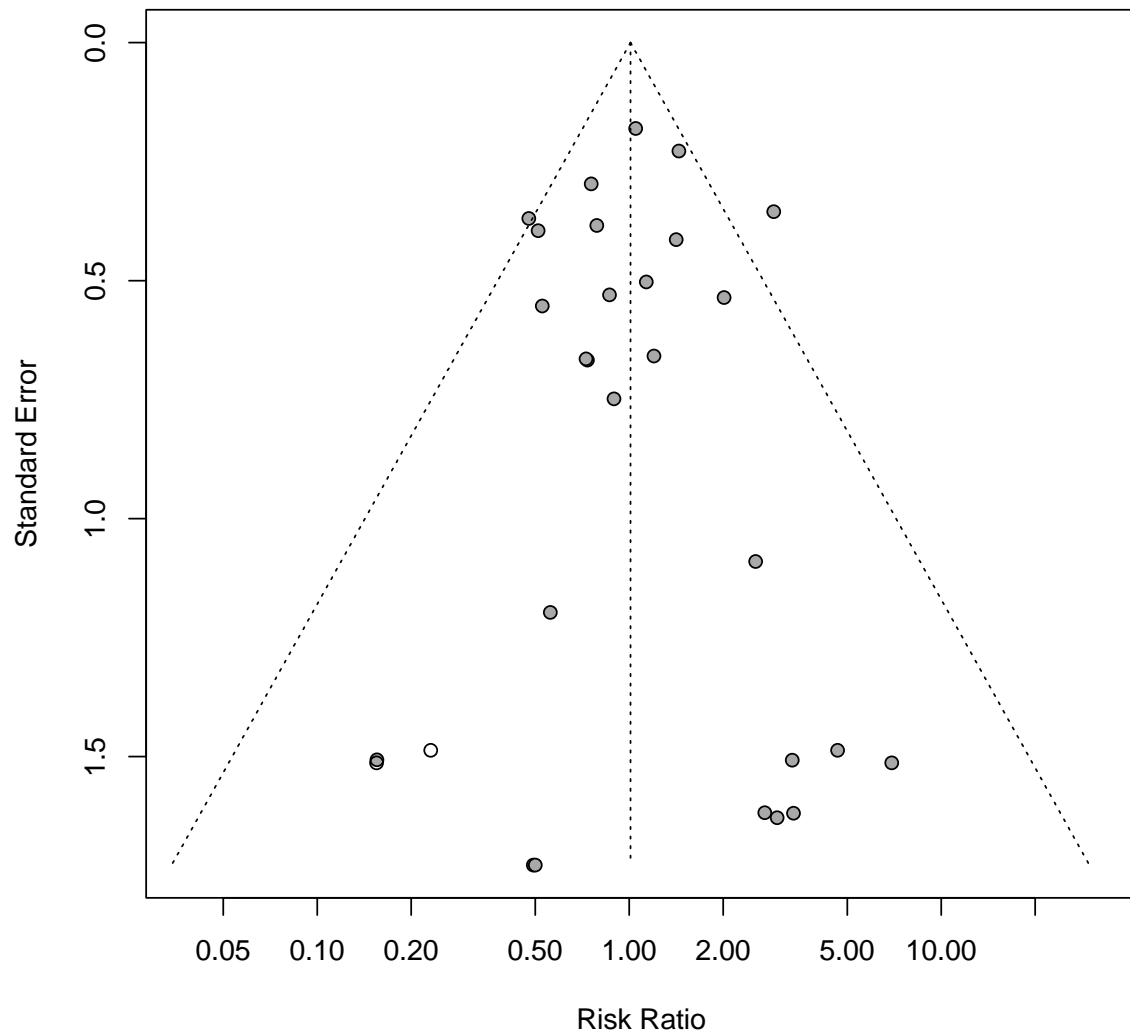
Meta-regression models to assess potential sources of heterogeneity for rate of each outcome. Tau² estimated between-study heterogeneity (lower value suggests lower between-study heterogeneity). Proteinuria was not included as an outcome of interest as data were insufficient to perform meta-regression.

Supplementary Figure S1



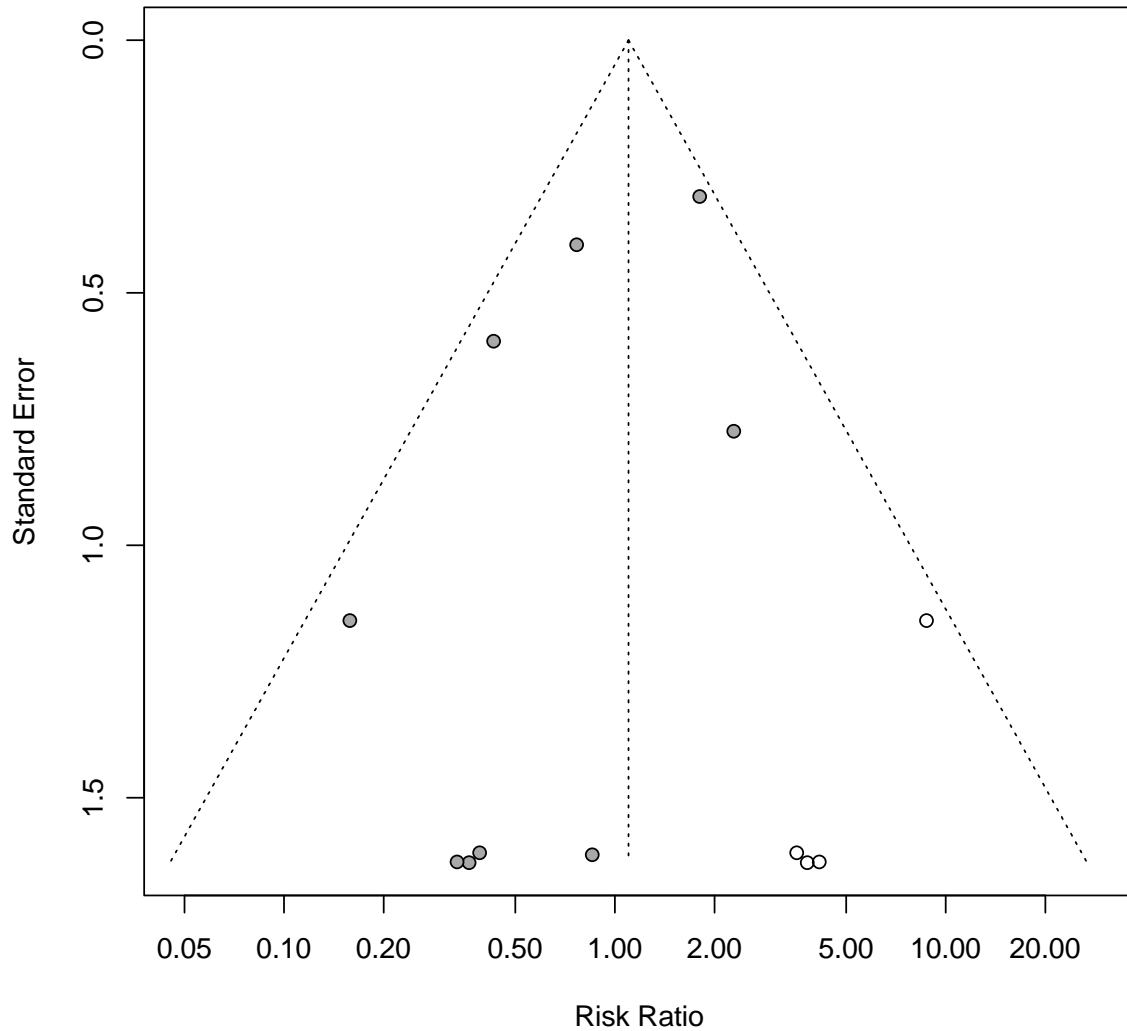
Forest plot of risk ratios for arterial thrombotic cardiovascular events: frequentist meta-analysis using fixed and random effects models, stratified by diabetic versus non-diabetic eye disease.

Supplementary Figure S2



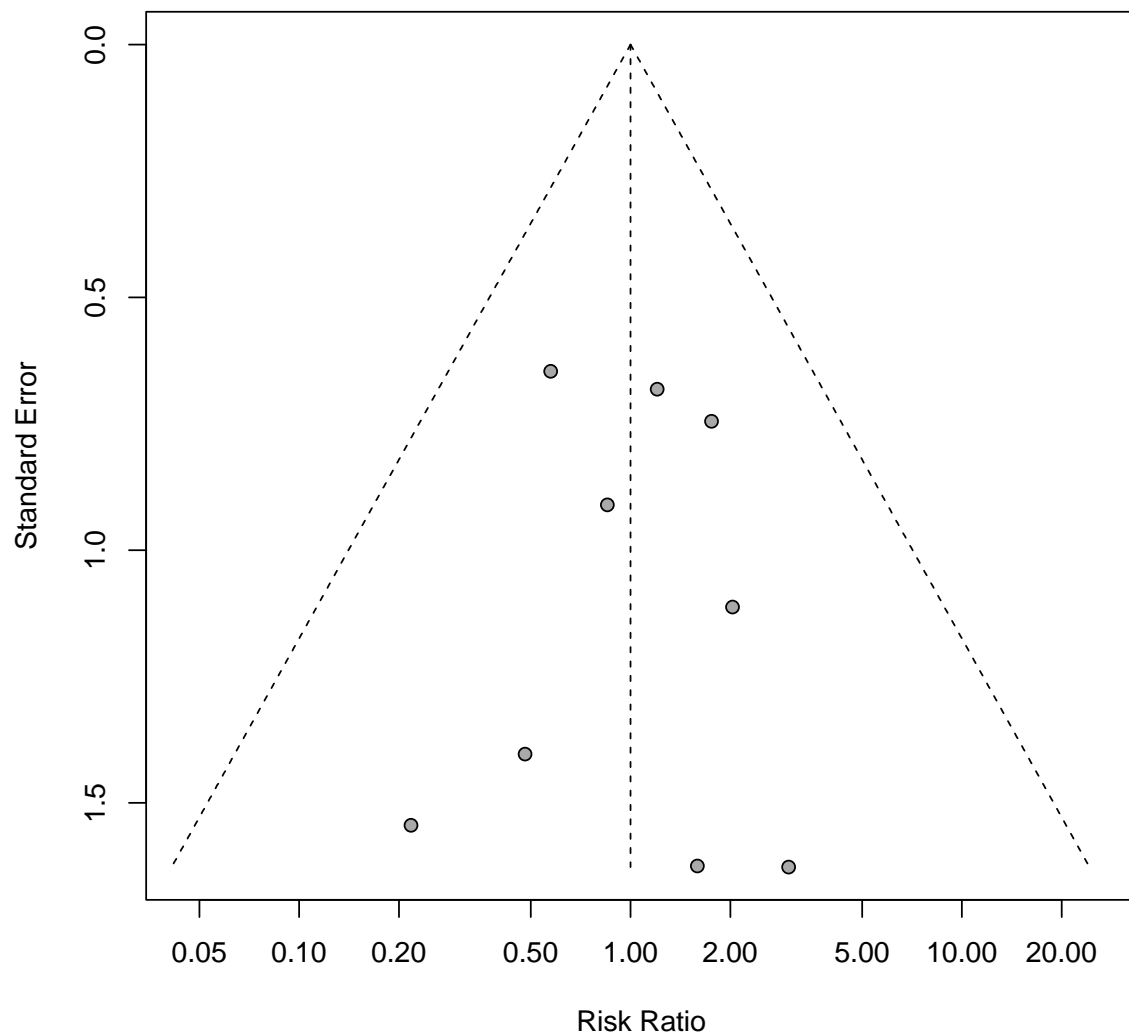
Funnel plot including Trim and Fill analysis for assessment of publication bias for intravitreal vascular endothelial growth factor inhibitor (VEGFi) studies measuring effect on hypertension. Filled circles represent risk ratio ratio plotted against standard error for published results. Unfilled circles represent studies that would be expected to balance the results. There are unfilled circles to the left suggesting publication bias in favour of positive results (non-significant difference in overall risk ratio on trim and fill analysis: $p=0.941$).

Supplementary Figure S3



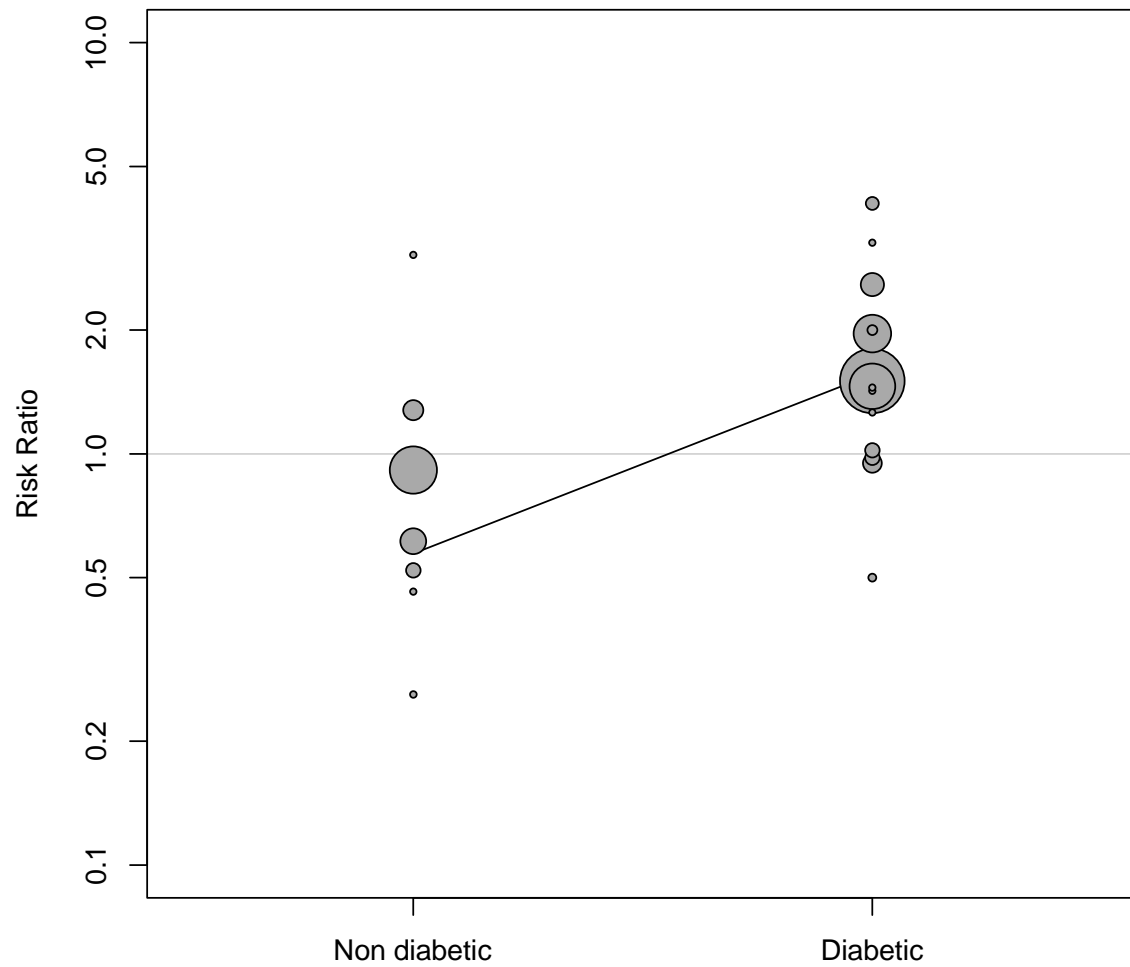
Funnel plot including Trim and Fill analysis for assessment of publication bias for intravitreal vascular endothelial growth factor inhibitor (VEGFi) studies measuring effect on heart failure. Filled circles represent risk ratio ratio plotted against standard error for published results. Unfilled circles represent studies that would be expected to balance the results. There are unfilled circles to the right suggesting publication bias in favour of negative results (non-significant difference in overall risk ratio on trim and fill analysis: $p=0.745$).

Supplementary Figure S4



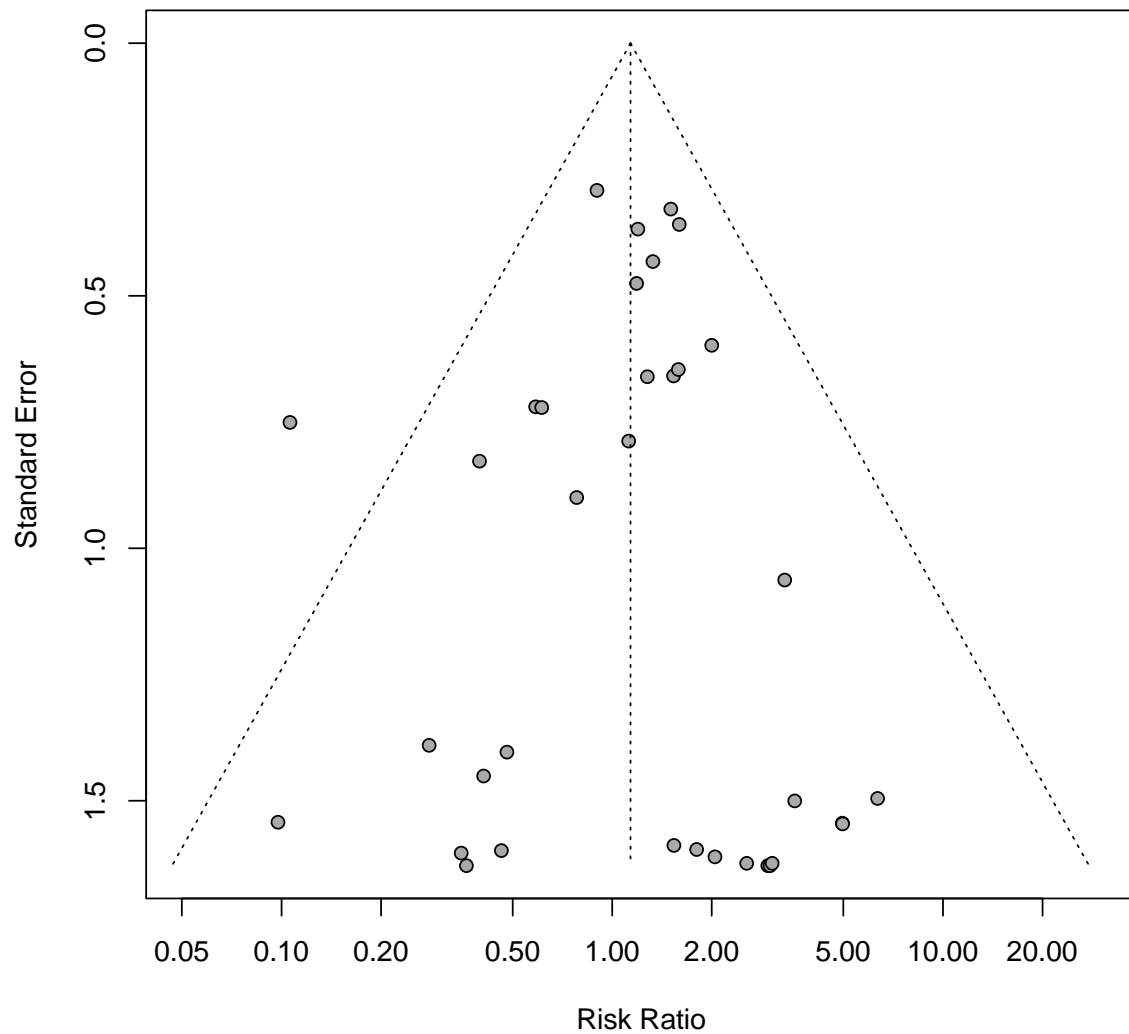
Funnel plot including Trim and Fill analysis for assessment of publication bias for intravitreal vascular endothelial growth factor inhibitor (VEGF_i) studies measuring effect on kidney function decline. Filled circles represent risk ratio ratio plotted against standard error for published results. Unfilled circles represent studies that would be expected to balance the results. There are no unfilled circles suggesting no evidence of publication bias (no difference in overall risk ratio on trim and fill analysis: $p=0.989$).

Supplementary Figure S5



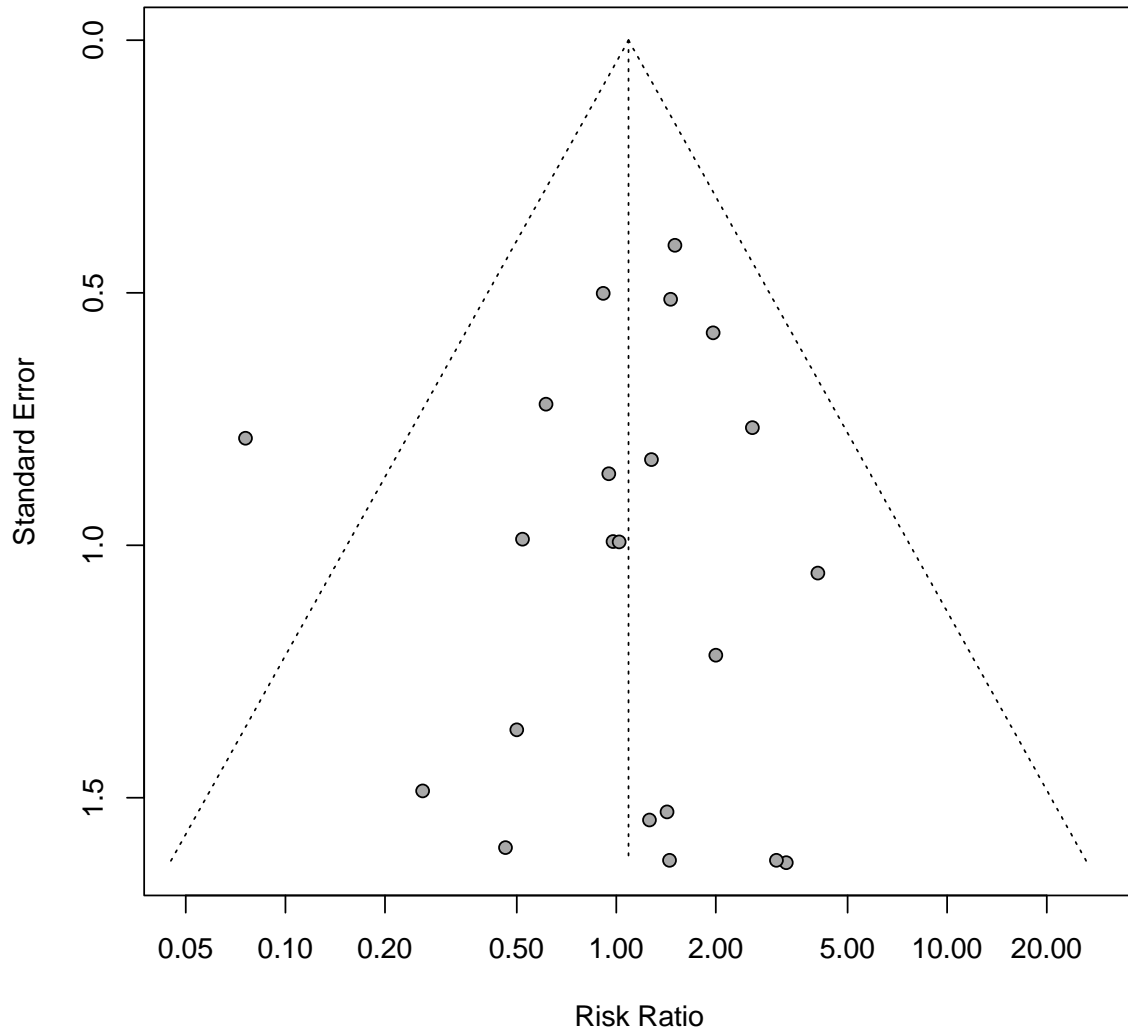
Meta-regression (“bubble”) plot of risk ratio and type of treated eye disease (diabetic versus non-diabetic eye disease $\beta = 1.004$, [0.283; 1.726], $p=0.006$). Circles represent trials included in the meta-analysis. The size of the circle is inversely proportional to the variance of the estimated effect size. The solid line indicates a perfect fit.

Supplementary Figure S6



Funnel plot including Trim and Fill analysis for assessment of publication bias for intravitreal vascular endothelial growth factor inhibitor (VEGFi) studies measuring effect on arterial thrombotic cardiovascular events. Filled circles represent risk ratio ratio plotted against standard error for published results. Unfilled circles represent studies that would be expected to balance the results. There are no unfilled circles suggesting no evidence of publication bias (no difference in overall risk ratio on trim and fill analysis: $p=0.273$).

Supplementary Figure S7



Funnel plot including Trim and Fill analysis for assessment of publication bias for intravitreal vascular endothelial growth factor inhibitor (VEGFi) studies measuring effect on death. Filled circles represent risk ratio ratio plotted against standard error for published results. Unfilled circles represent studies that would be expected to balance the results. There are no unfilled circles suggesting no evidence of publication bias (no difference in overall risk ratio on trim and fill analysis: $p=0.655$).