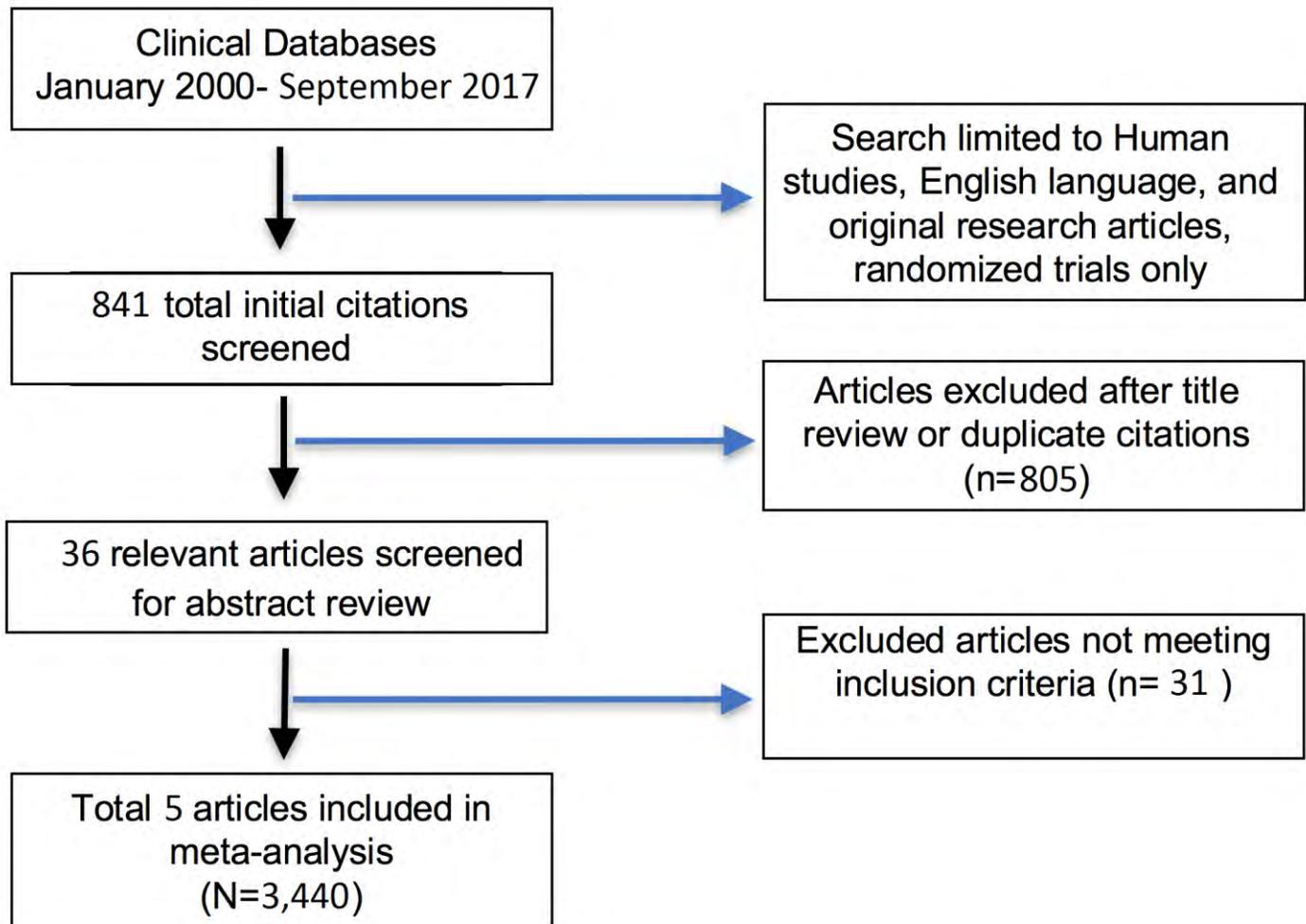
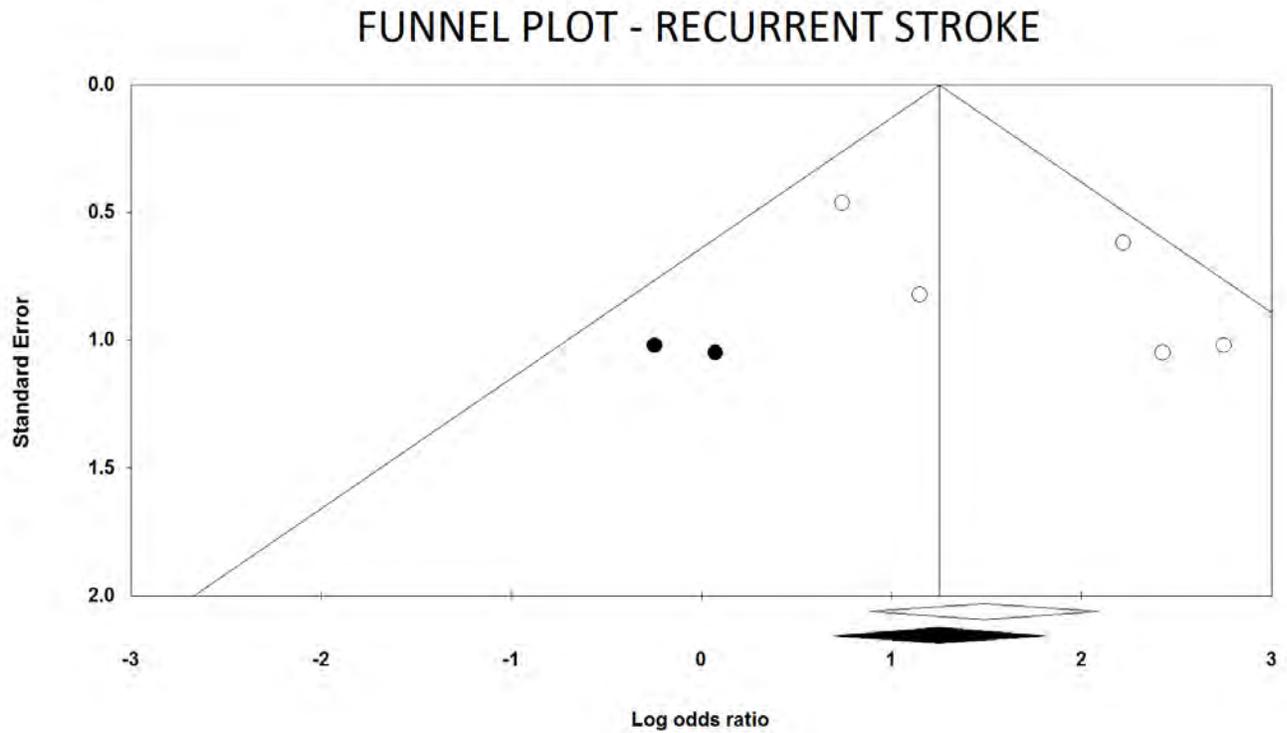


**Supplementary Figure 1:** Selection of clinical studies included in the systematic review and meta-analysis

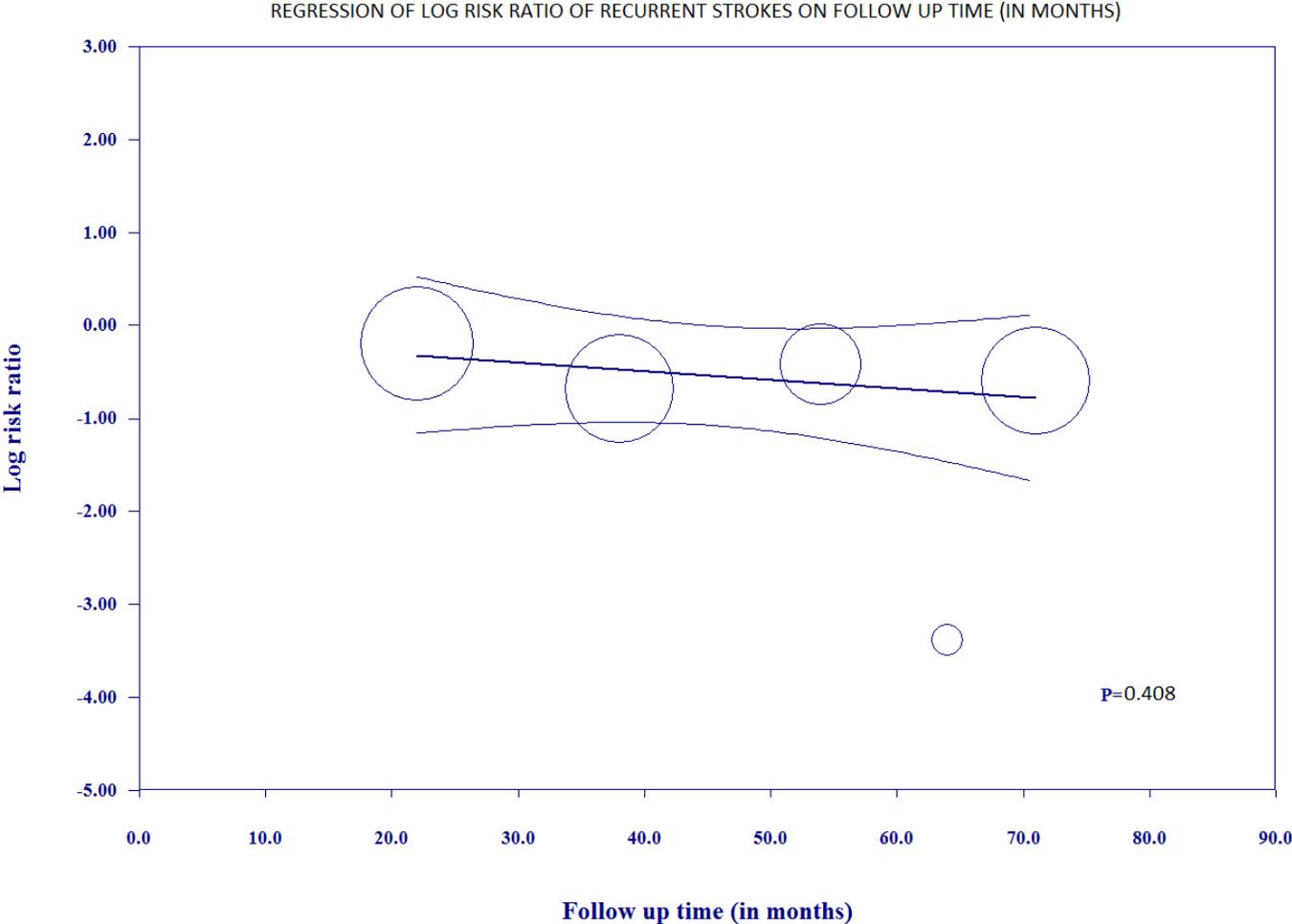


**Supplementary Figure 2:** Funnel plot for assessment of publication bias for recurrent stroke

\*Each dot represents a study; y-axis represents the size of the study and the x-axis shows the study results

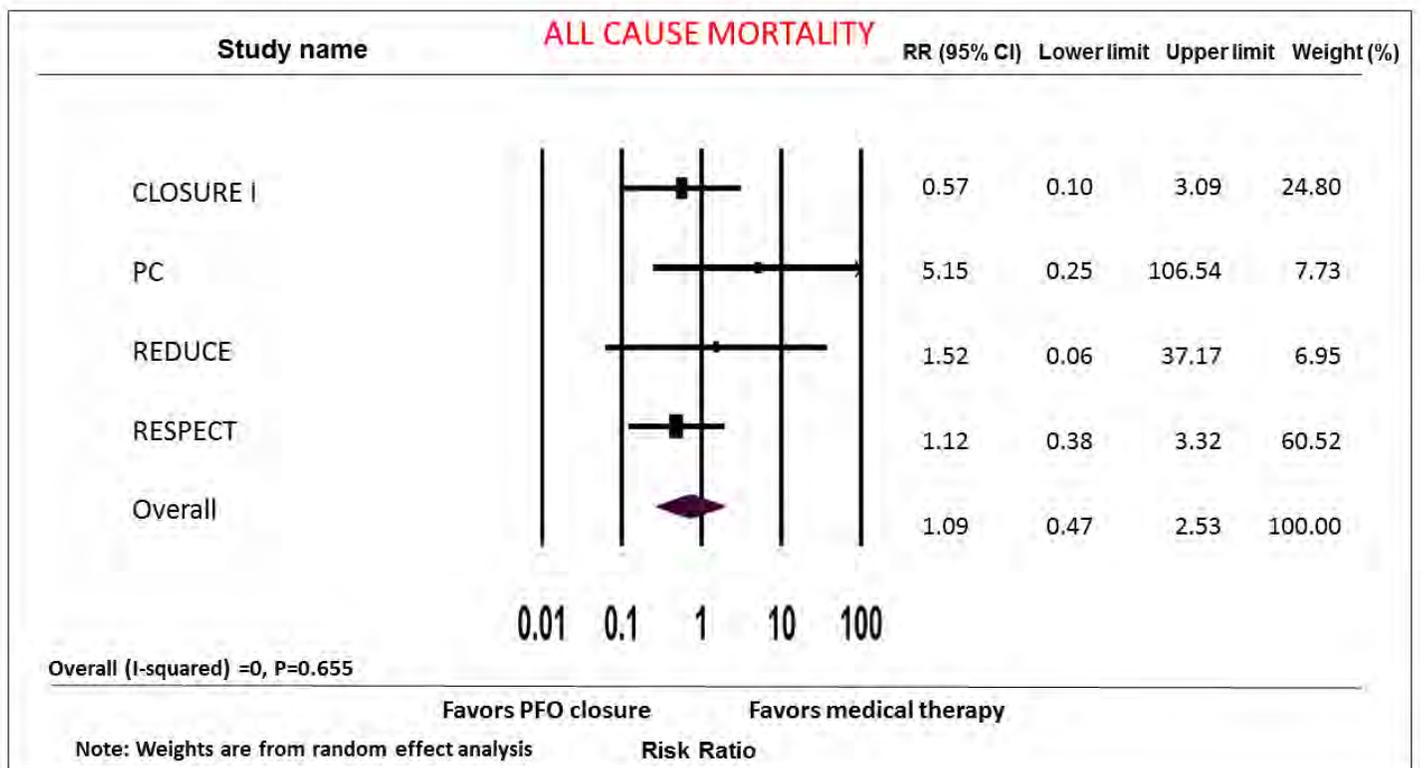


**Supplementary Figure 3:** Meta regression of follow up time on log risk ratio of recurrent stroke events



**Supplementary Figure 4:** Forest plot and pooled analysis for all-cause mortality (N=3,341) in cryptogenic stroke patients (PFO closure vs. medical therapy alone)

RR: relative risk; CI: confidence interval



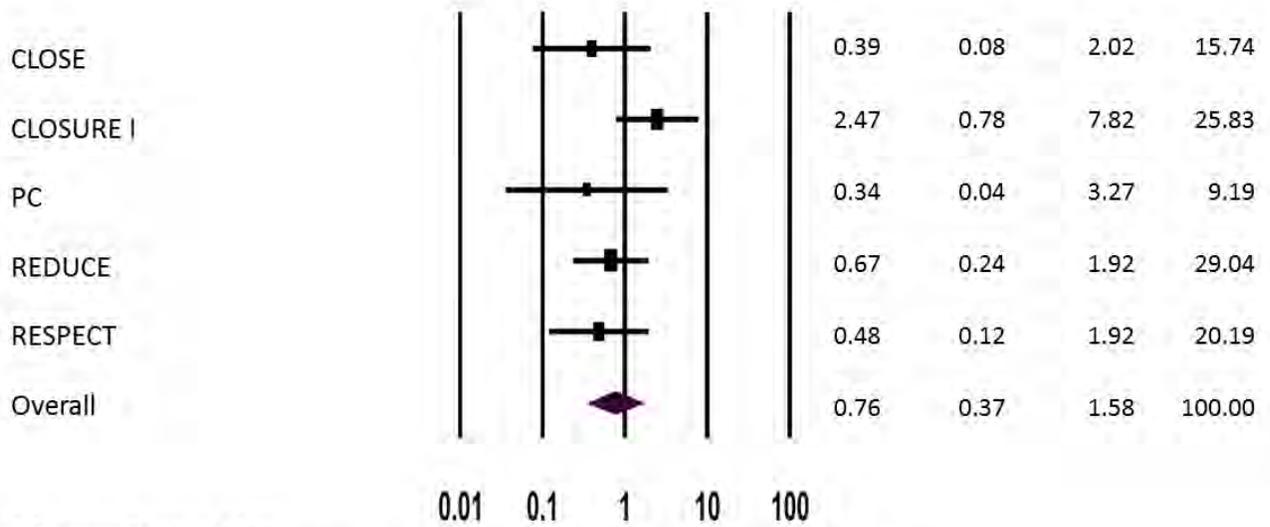
**Supplementary Figure 5:** Forest plot and pooled analysis for major bleeding (N=3,283) in cryptogenic stroke patients (PFO closure vs. medical therapy alone)

RR: relative risk; CI: confidence interval

## MAJOR BLEEDING EVENTS

Study name

RR (95% CI) Lower limit Upper limit Weight (%)



Overall (I-squared) =28, P=0.233

Favors PFO closure

Favors medical therapy

Note: Weights are from random effect analysis

Risk Ratio

**Supplementary Figure 6:** Forest plot and pooled analysis for adverse events (N=2,918) in cryptogenic stroke patients (PFO closure vs. medical therapy alone)

RR: relative risk; CI: confidence interval

