

Fixed-effect meta-analysis

$$\bar{E} = \frac{\sum w_i E_i}{\sum w_i} \quad (1)$$

with study weights determined by the inverse variance method:

$$w_i = \frac{1}{\sigma_i^2} \quad (2)$$

Random-effects meta-analysis

$$\bar{E} = \frac{\sum w'_i E_i}{\sum w'_i} \quad (3)$$

with study weights determined by the inverse variance method incorporating τ^2 , the between-study variance component derived from the random-effects model:

$$w'_i = \frac{1}{\sigma_i^2 + \tau^2} \quad (4)$$

In the fixed-effect meta-analysis, which assumes no between-study heterogeneity, $\tau^2 = 0$.

Rosenberg's FSN¹³

$$FSN_R = \frac{nW'}{\sum w_i} \quad (5)$$

n is the number of studies included in the existing meta-analysis

$$W' = \frac{(\sum w_i E_i)^2}{t_{\alpha(v)}^2} - \sum w_i \quad (6)$$

W' is the amount of additional weight needed to produce the desired α level, which was set to 0.05 in all calculations ($t^2 = 1.96$).

Orwin's FSN¹⁴

$$FSN_O = \frac{n(\bar{D}_o - \bar{D}_m)}{\bar{D}_m - \bar{D}_n} \quad (7)$$

D_o is the standardized mean of the studies included in the existing meta-analysis.

D_n is the standardized mean of the future (unobserved) studies; which was set to 0 to be consistent with the underlying approach to Rosenberg's FSN

D_m is the standardized mean in the combined meta-analysis, which was set to be equivalent to odds ratios of 1.05; 1.10; 1.25; 1.50; and 2.00.

$$\bar{D} = \log \bar{E} \left(\frac{\sqrt{3}}{\pi} \right) \quad (8)$$

Conditional power¹¹

Approach 1 (no between-study heterogeneity in observed and future studies):

$$CP = \phi \left(-\frac{C_{\alpha/2} \sqrt{\sum w_i + mw'}}{\sqrt{mw'}} + \frac{\sum w_i E_i}{\sqrt{mw'}} + \delta \sqrt{mw'} \right) \quad (9)$$

$$+ \phi \left(-\frac{C_{\alpha/2} \sqrt{\sum w_i + mw'}}{\sqrt{mw'}} - \frac{\sum w_i E_i}{\sqrt{mw'}} + \delta \sqrt{mw'} \right)$$

m is the number of future studies with a weight of w' set to be the average weight of the studies included in the observed meta-analysis:

$$w' = \frac{\sum w_i}{n} \quad (10)$$

δ , the alternative effect size, was set to the summary odds ratio for the existing meta-analysis:

$$\delta = \bar{E} \quad (11)$$

With $\alpha = 0.05$, the critical value, $C_{\alpha/2}$, was set to 1.96.

Approach 2 (between-study heterogeneity in future studies equivalent to between-study heterogeneity in observed):

$$CP = \phi \left(-\sqrt{\frac{w' \tau_{all}^2}{mw'}} \left(C_{\alpha/2} \sqrt{\sum w_{rev,i}^* + \frac{mw'}{w' \tau_{all}^2}} - \sum w_{rev,i}^* E_i \right) + \frac{m\delta}{\sqrt{\frac{m}{w'} + m \tau_{all}^2}} \right) \quad (12)$$

$$+ \phi \left(-\sqrt{\frac{w' \tau_{all}^2}{mw'}} \left(C_{\alpha/2} \sqrt{\sum w_{rev,i}^* + \frac{mw'}{w' \tau_{all}^2}} + \sum w_{rev,i}^* E_i \right) - \frac{m\delta}{\sqrt{\frac{m}{w'} + m \tau_{all}^2}} \right)$$

A revised weight, accounting for the additional weight contributed by the future studies, was attributed to studies included in the observed meta-analysis:

$$w_{rev,i}^* = \frac{1}{1/w_i + \tau_{all}^2} \quad (13)$$

For the between-study heterogeneity in the updated meta-analysis (existing meta-analysis plus the future studies), we used the formula used by Roloff et al.¹¹:

$$\tau_{all}^2 = \frac{n}{n+m} \tau_{observed}^2 + \frac{m}{n+m} \tau_{future}^2 \quad (14)$$

under our original assumption that the future studies (m) had equivalent between-study heterogeneity as the studies included in the observed meta-analysis (n) such that:

$$\tau_{future}^2 = \tau_{observed}^2 \quad (15)$$

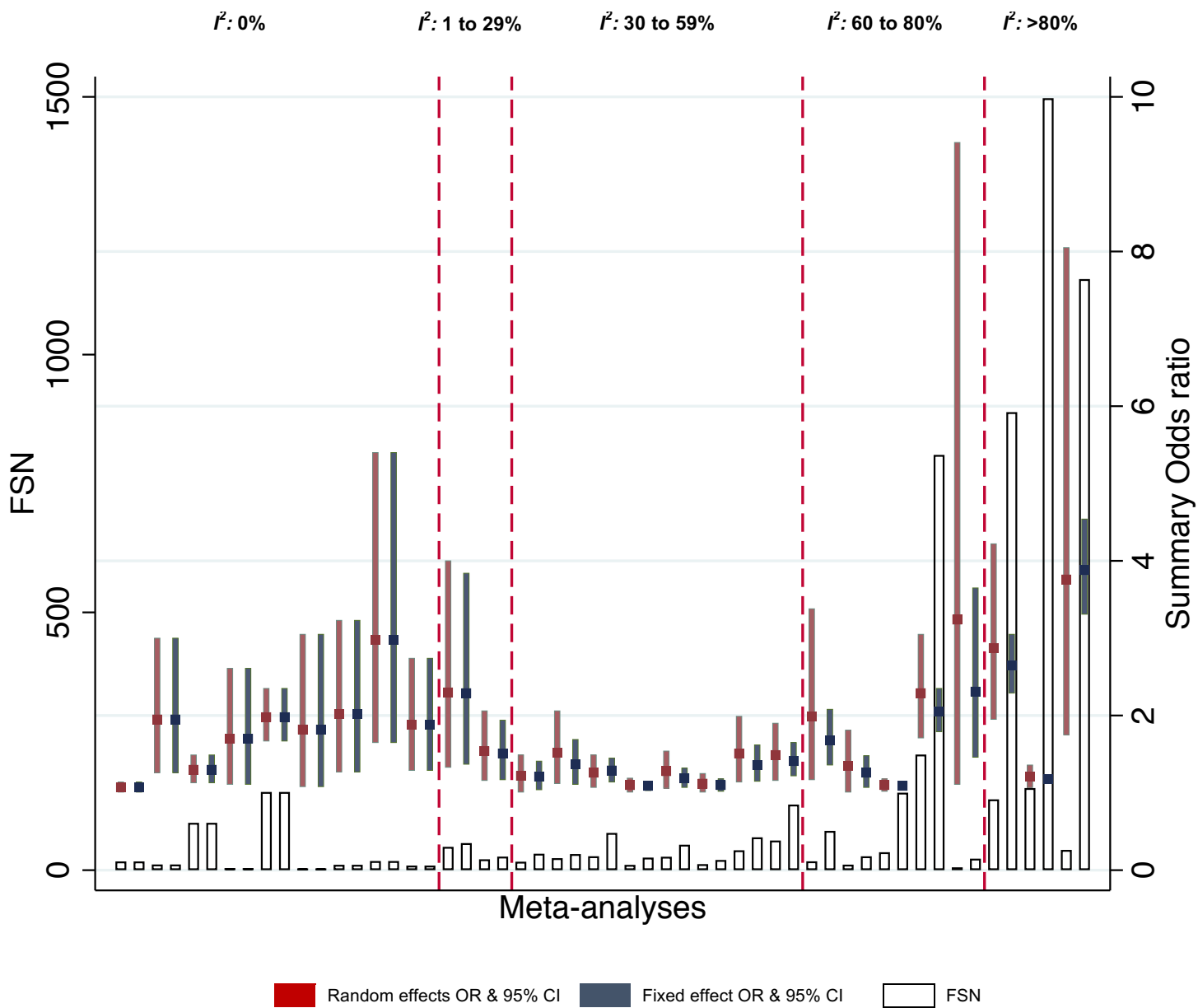
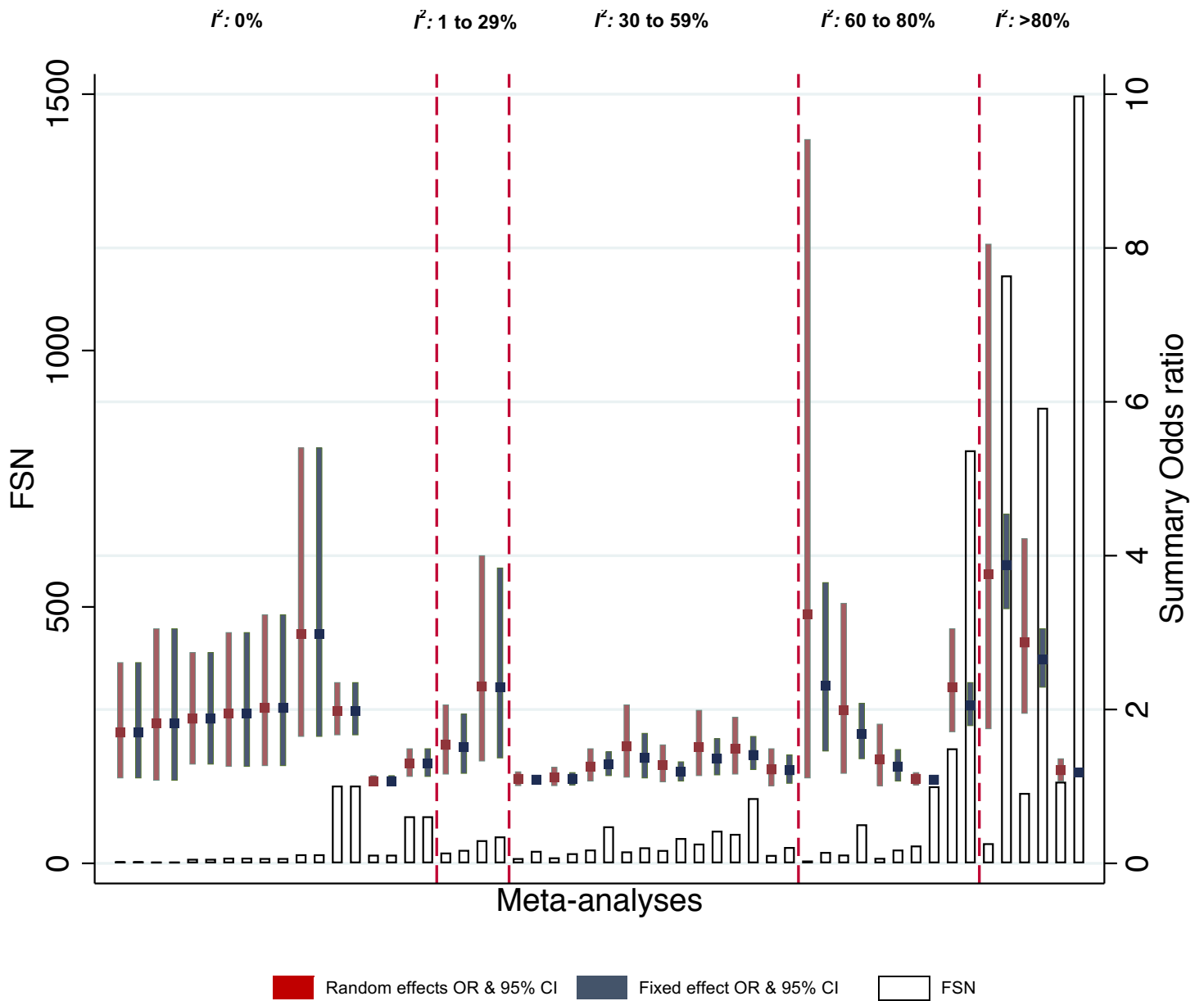


Figure 1. Rosenberg's Fail-Safe Number (FSN) for statistically significant fixed and random effects meta-analyses with summary odds ratios between 1.00 and 4.00 by increasing level of between-study heterogeneity (I^2).



SFigure 2. Rosenberg's Fail-Safe Number (FSN) for statistically significant fixed and random effects meta-analyses with summary odds ratios between 1.00 and 4.00 by number of studies included in each meta-analysis within strata of between-study heterogeneity (I^2).

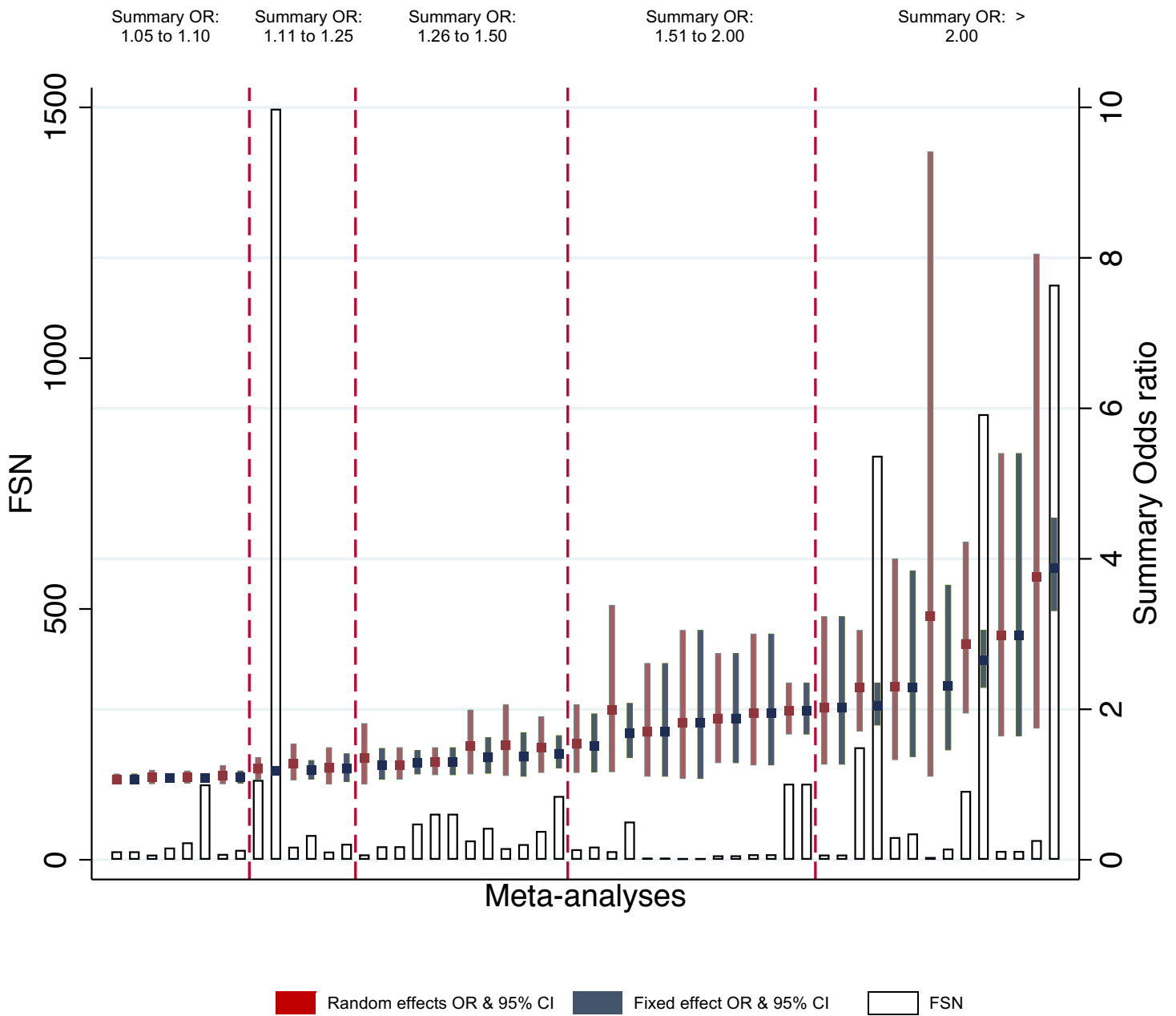


Figure 3. Rosenberg's Fail-Safe Number (FSN) for statistically significant fixed and random effects meta-analyses with summary odds ratios between 1.00 and 4.00 by total number of cases and controls within levels of summary effect estimates.

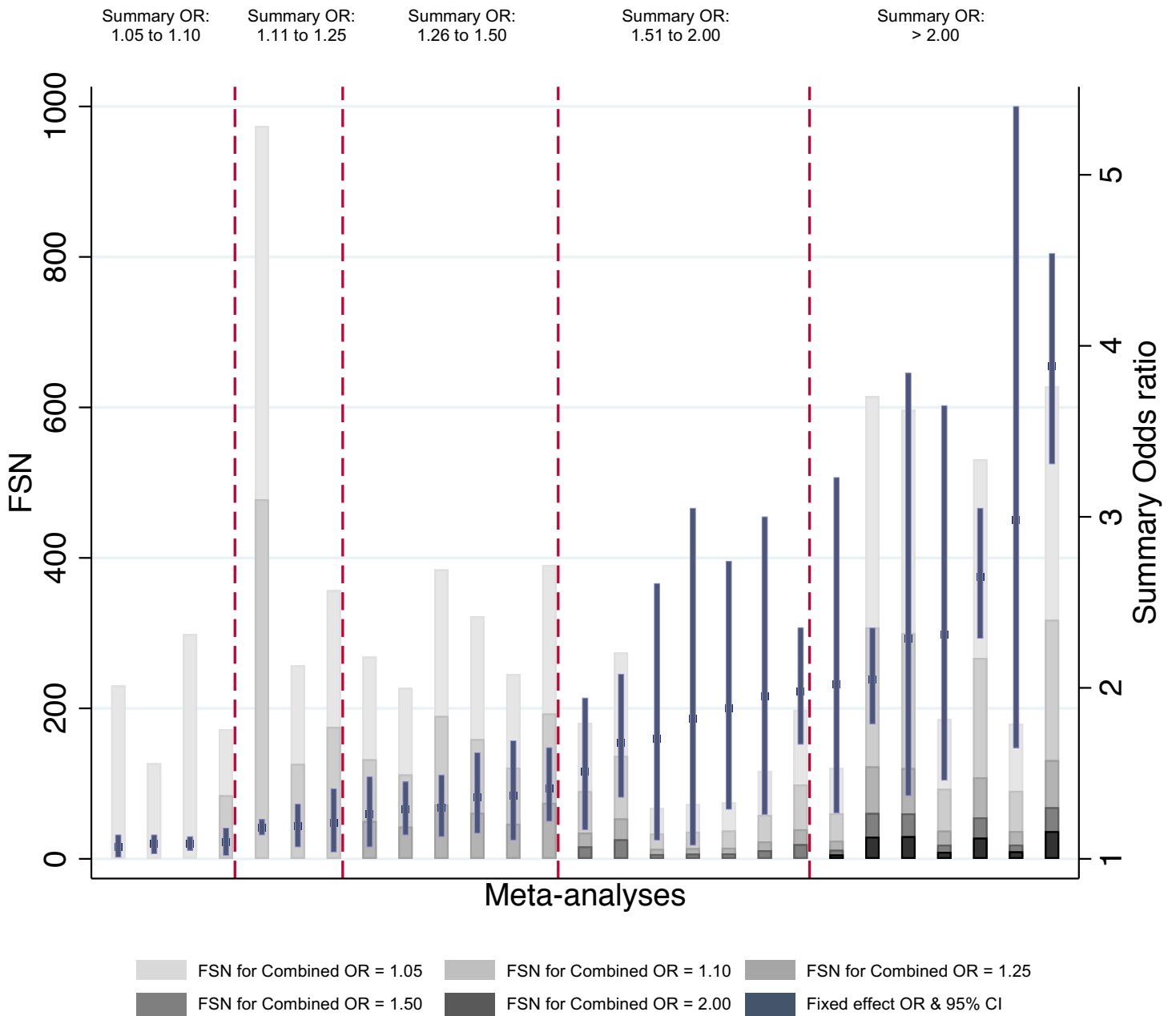


Figure 4. Orwin's Fail-Safe number (FSN) for an average null effect (OR = 1) in future studies reducing the combined fixed effect meta-analysis to an odds ratio of 1.05; 1.10; 1.25; 1.50; and 2.00 in fixed effect meta-analyses with an observed effect size 1.00 to 4.00.

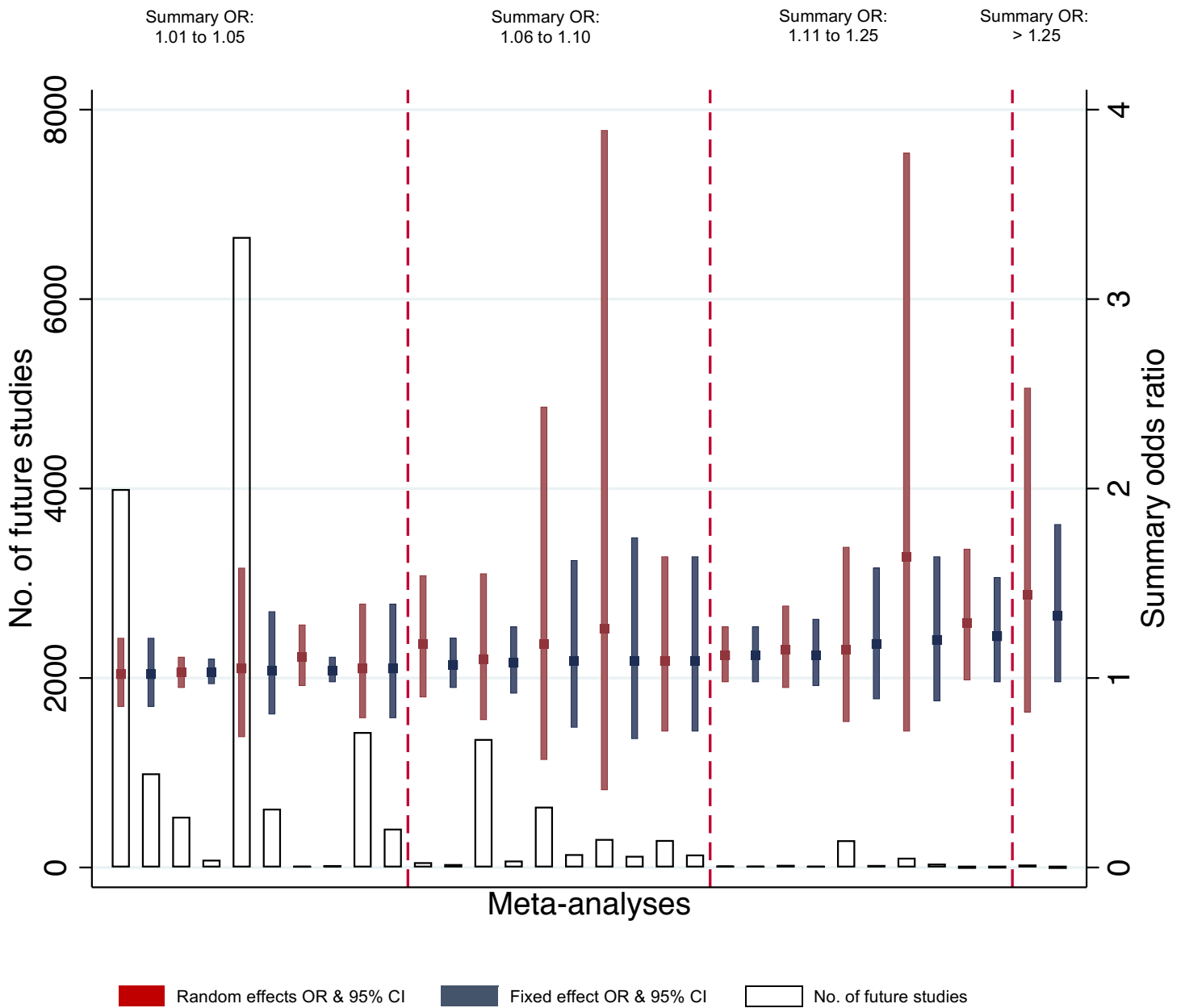


Figure 5. Number of future studies required to achieve 80% power to detect the observed summary odds ratio for statistically non-significant fixed and random effects meta-analyses with summary odds ratios between 1.01 and 4.00.