Letter to the editor

Hast thou slain the *Jabberwock* of funnel plot asymmetry? From the meta-analysis of smoking bans for reduction of acute myocardial infarction

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*Meyers et al. [1] performed a systematic review and a meta-analysis in 2009 to determine the association between public smoking bans and risk for hospital admission for acute myocardial infarction (AMI). The authors included only AMI cases (some investigators supplied additional data), except where the case definition was acute coronary syndrome (ACS), which required an elevated serum troponin. More recently (in 2010), Mackay et al. [2] undertook another meta-analysis of the effects of smoke-free legislation. The case definitions used in the studies included in the meta-analysis [2], however, varied: e.g. myocardial infarction, ACS, coronary heart disease including angina and heart failure, and myocardial infarction plus ischemic heart disease. Thus, the study by Meyers et al. [1] has been the most comprehensive meta-analysis of smoking bans for reduction in exclusive AMI incidence to date.*

*Using 11 reports from 10 study locations in the meta-analysis by Meyers et al. [1], AMI risk decreased by 17% overall (random-effects rate ratio [RR], 0.83; 95% confidence interval [CI], 0.75 to 0.92). A serious statistical concern in the meta-analysis, however, is the funnel plot asymmetry shown graphically, indicating either publication bias or heterogeneity that cannot be explained by a random-effects meta-analysis. Therefore, we assessed the funnel plot asymmetry not only graphically but also mathematically using an adjusted rank-correlation test without continuity correction, according to the method of Begg and Mazumdar [3]. All analyses were conducted using Comprehensive Meta-Analysis version 2 (Biostat, Englewood, NJ). There was marginally nonsignificant funnel plot asymmetry (*p = 0.064*). Because of this, we undertook a sensitivity analysis using the trim and fill method [4], which conservatively imputes hypothetical negative unpublished studies to mirror the positive studies that cause funnel plot asymmetry. The imputed 3 studies produce a symmetrical funnel plot (Fig. 1). The pooled analysis incorporating the hypothetical studies showed a statistically nonsignificant 3% reduction in AMI risk in the random-effects model (RR, 0.97; 95% CI, 0.87 to 1.08).*  

*A funnel plot is a simple scatter plot of the intervention effect estimates from individual studies against some measure of each study's size or precision. In the absence of bias the plot should approximately resemble a symmetrical (inverted) funnel [5]. When there is bias, this would lead to an asymmetrical appearance of the funnel plot with a gap in a bottom corner of the graph e.g. because smaller studies without statistically significant effects remain unpublished. The effect calculated in a meta-analysis would tend to overestimate the intervention effect in this situation [6,7]. The more pronounced the asymmetry, the more likely it is that the amount of bias would be substantial. Publication bias need not lead to asymmetry in funnel plots. In the absence of any intervention effect, selective publication based on the *p* value alone would lead to a symmetrical funnel plot in which studies on the extreme left or right are more likely to be published than those in the middle [5]. This could bias the estimated between-study heterogeneity variance. It has been argued that visual interpretation of funnel plots is inherently subjective. When review authors are concerned that small study effects are in the results of a meta-analysis, they may want to conduct sensitivity analyses subject to publication bias [8]. There remains a concern that visual interpretation of funnel plots is inherently subjective. When review authors are concerned that small study effects are influencing the results of a meta-analysis, they may want to conduct sensitivity analyses in order to explore the robustness of the meta-analyses’ conclusions to different assumptions about the causes of funnel plot asymmetry [5]. The ‘trim and fill’ method aims both to identify and correct for funnel plot asymmetry arising from publication bias [4]. The basis of the method is to (1) ‘trim’ (remove) the smaller studies causing funnel plot asymmetry, (2) use the trimmed funnel plot to estimate the true ‘centre’ of the funnel, then (3) replace the omitted studies and their missing ‘counterparts’ around the centre (filling). Performing a meta-analysis including the filled studies derives an adjusted intervention effect as well as providing an estimate of the number of missing studies.*
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The authors of this manuscript have certified that they comply with the Principles of Ethical Publishing in the International Journal of Cardiology (Shewan and Coats 2010; 144:1–2).

References