at high risk of death. Thereafter the value of adjuvant chemotherapy should be tested in a randomised, prospective trial.

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# Passive smoking and lung cancer: a publication bias?

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## Abstract

**To assess the likelihood of publication bias in a recent review of the effect of passive smoking on lung cancer the evidence from the reviewed papers was visualised on a "funnel" plot. In such a plot if the relative risks from various studies are plotted according to sample size they should scatter round some underlying true value, the scatter being greatest where the studies have the lowest statistical power—thus showing a "funnel" pattern. If there is publication bias and studies with non-significant results are not being published there should be a "gap" in the plot. The logarithm of the relative risks was plotted against the standard error of the logarithm of the relative risk (which was used instead of sample size as a measure of statistical uncertainty). The resulting plot was compatible with a publication bias but only in studies on men.**

**Further studies of passive smoking and lung cancer in men seem to be warranted.**

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## Introduction

A recent review on passive smoking and lung cancer by Wald *et al* concluded, in line with other reviews, that passive smoking causes a 30% extra risk of lung cancer—that is, a relative risk of 1·30.[1] This conclusion was challenged by Mantel, who held, among others, that publication bias was responsible for this result and concluded, "Whether or not the risk is raised remains to be taken as a matter of faith according to one's choice."[2]

The objection of publication bias is interesting, since it is amenable to statistical analysis by the use of "funnel plotting."[3]

## Methods and results

The principle is straightforward. When a diverse number of estimates of some value exist one expects some scatter around the underlying truth. The scatter will be largest, however, for the studies which contain the smallest number of subjects—that is, those which have lowest statistical power.

So, ideally, if some value X, which has the true underlying value $X_T$, has to be estimated and we plot the estimates from different studies according to sample size we expect to see a "funnel." Results will scatter around the truth and the more so in the regions of low statistical power. In figure 1 the borders of the imaginary scatter plot are given by the dashed lines.

When publication bias exists we also expect something else. A publication bias occurs when papers with non-significant results are either not submitted or not accepted for publication.[3] Non-significant results are most likely when the statistical power is low—that is, when the numbers are small. So in the event of a positive true effect $X_T$ and the existence of a publication bias we would expect to find few if any published papers within the lower left bottom of the funnel display—that is, around the null effect, indicated by the word "gap" in figure 1.

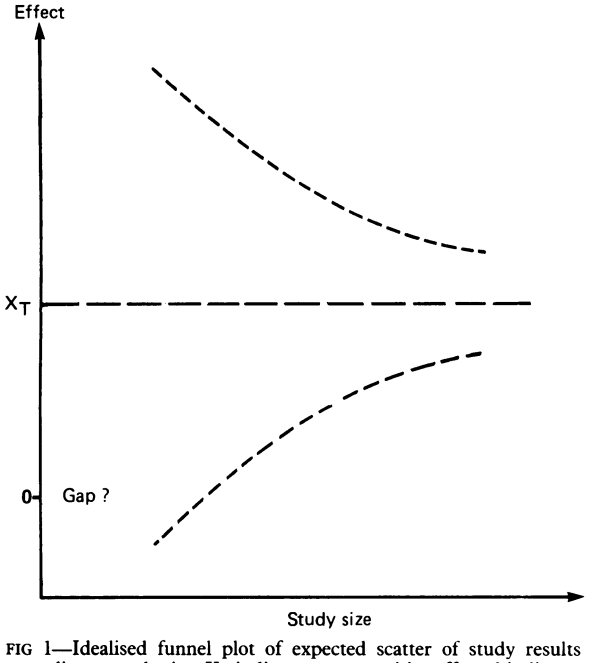


FIG 1—Idealised funnel plot of expected scatter of study results according to study size. $X_T$ indicates a true positive effect; 0 indicates the null-effect; and "Gap" indicates the expected lack of published results in the event of publication bias.

Following this line of thinking, I set out to plot the studies reviewed by Wald *et al*[1] according to their degree of statistical uncertainty (see references 2-14 from that paper). Simply plotting the relative risk (RR) by study size would not do. Firstly, the plain relative risk does not have a symmetrical distribution and will thus never yield a funnel unless transformed logarithmically. Thus on the Y axis I plotted the logarithm of the relative risk (ln(RR)). Secondly, ranking the reviewed studies by size was not feasible since they contained both cohort and case-control studies, and among the latter there were studies with different case to control ratios. Therefore, I sought some measure of statistical uncertainty independent of the type of study. I used the standard error of the logarithm of the relative risk, which could be calculated from the relative risk and its 95% confidence interval as given by Wald *et al*[1] (see table I of that paper). This was accomplished by logarithmic transformation of these three quantities, calculation of the average distance between upper and lower limits and (ln)RR, and division by 1·96. After an initial inspection I judged it better to present the points for studies in men and women separately. The result is shown in figure 2.

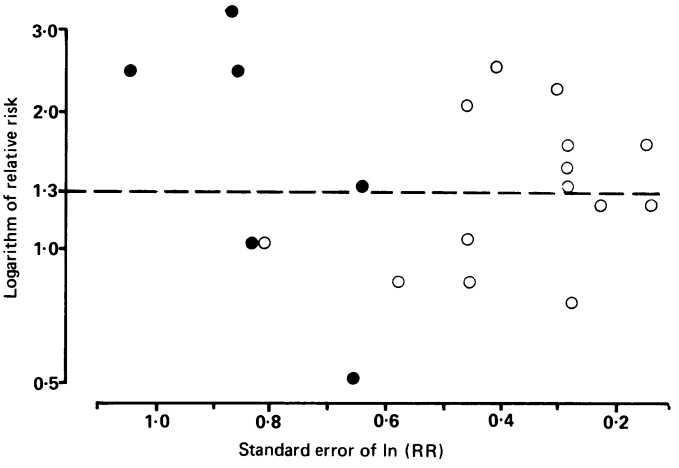


FIG 2—Funnel plot of relative risk (on logarithmic scale) according to standard error of ln(RR) for men (●) and women (○) calculated on 13 studies reviewed by Wald *et al*.[1] Dashed line indicates proposed passive smoking effect of 1.30.

## Discussion

An overall view of figure 2 is consistent with a pattern brought about by publication bias. The lower left of the funnel plot, the "non-significant relative risks around unity" is empty. On closer inspection, however, we see that studies with a larger standard error—that is, those with lower statistical power—are predominantly those in men and that it is among these studies that the possibility of publication bias seems most likely. The pattern of the studies in women is much more symmetrical around the value of 1.30, the average relative risk.

In summary, the funnel plot, used to verify the charge of publication bias by Mantel, shows us that for review purposes the published papers on passive smoking and lung cancer ought to be separated on the basis of sex—as so often in epidemiology—and that for studies in men the objection of publication bias seems reasonable.

The mechanism of such a bias can be imagined. Given the near unanimity in medical circles about the risk of active smoking, epidemiologists will have difficulty in exonerating the smoking habit from causing harm. Confronted with weak data on men alongside stronger data on women, authors or reviewers might be inclined to drop the former in favour of the latter. Theoretically two possible remedies for this unsatisfactory situation exist: either call for a new and large study on men only or invite researchers to submit their unpublished low power studies to accumulate their hidden information. In practice, this aim might be frustrated because the number of men who are passive smokers—for example, through being married to a smoker—is likely to be much lower than among women.

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