SUPPLEMENTARY FILE 2 to "Environmental tobacco smoke exposure and lung cancer – a systematic review".

The relationship between lung cancer and ETS exposure

Adjustment for the potential confounding effects of multiple risk factors and for misclassification of active smoking status

Updated analyses

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EXECUTIVE SUMMARY

In 1997 Hackshaw *et al* [1] published a paper in the BMJ concluding that neither adjustment for confounding by diet nor correction for misclassification bias materially affects the observed association between ETS exposure and risk of lung cancer in lifelong nonsmokers, and concluded that breathing other people's tobacco smoke is a cause of lung cancer. In a series of five papers [2-6] published in 2000-2002 we concluded that Hackshaw *et al* [1] had severely underestimated the importance of confounding and misclassification bias and had also overstated the evidence on the strength of the dose-response relationship of lung cancer risk with the number of cigarettes smoked. We also concluded that a causal effect of ETS on risk of lung cancer had not been demonstrated.

The updated analyses presented in this report are now based on a total of 93 epidemiological studies relating ETS exposure from the spouse (or nearest equivalent) to risk of lung cancer in nonsmokers, and on currently available evidence on the relationship of potential confounding variables to nonsmoker lung cancer risk and to ETS exposure and on the intercorrelations between the various potential confounding variables. Compared with our previous work we have based our estimates on data for females and have used random-effects analyses to summarize all the main associations. We have also considered the effect of confounding and bias not only, as previously, on the estimated increase in lung cancer risk per 10 cigarettes per day smoked by the husband, but also on the more commonly cited increase in risk associated with the husband smoking regardless of amount. We attempted to extend the list of potential confounding variables for which data were extensive or reliable enough to include in our formal adjustment procedures, but were unsuccessful and our adjustments are based on the same four variables (fruit, vegetable and dietary fat consumption, and education) as used in 2001-2002.

As summarized in the table below, our updated analyses confirm that, in nonsmoking females, both lung cancer risk and ETS exposure are significantly reduced in relation to fruit consumption, vegetable consumption and education while being increased in relation to dietary fat consumption.

		Association with lung cancer risk		Association with ETS exposure at home	
Variable	Unit[a]	N[b]	RR (95% CI)[c]	N	δ (SE)[d]
Fruit consumption	SD	14	0.86 (0.78 to 0.96)	11	-0.073 (0.020)
Vegetable consumption	SD	16	0.88 (0.80 to 0.97)	16	-0.056 (0.021)
Dietary fat consumption	SD	6	1.22 (1.09 to 1.36)	12	+0.131 (0.032)
Education	Year	12	0.91 (0.88 to 0.95)	13	-0.534 (0.063)

[a] SD = standard deviation of the variable
[b] N = number of studies on which combined estimate of association is based
[c] RR (95% CI) = relative risk in nonsmoking females (95% confidence interval) per unit of the variable
[d] δ (SE) = difference in units (standard error) of the variable between nonsmoking females exposed and unexposed to ETS at home

Taking into account confounding by all these four factors (by a procedure which allowed for intercorrelations between them and whether or not the original ETS/lung cancer risk estimates for individual studies had already been adjusted for any of them) substantially reduced the estimated association between ETS exposure and lung cancer, and correction for misclassification, using techniques similar to those used in the 2000-2002 work, reduced the association further. The table overleaf summarizes the main results of the adjustments and corrections.

Studies	N[d]	Unadjusted and uncorrected[a] RR (95% CI)[e]	Adjusted for confounding[b] RR (95% CI)[e]	Also corrected for misclassification[c] RR (95% CI)[e]
Per 10 cigs/day smoked by the husband				
All	**93**	**1.102 (1.065 to 1.140)**	**1.062 (1.027 to 1.099)**	**1.032 (0.994 to 1.071)**
North America	29	1.037 (0.977 to 1.101)	1.006 (0.946 to 1.070)	0.957 (0.896 to 1.022)
Europe and New Zealand	20	1.060 (0.995 to 1.128)	1.020 (0.956 to 1.088)	1.003 (0.938 to 1.073)
Asia	44	1.158 (1.104 to 1.216)	1.113 (1.060 to 1.170)	1.089 (1.033 to 1.147)
Age adjustment	75	1.084 (1.046 to 1.123)	1.044 (1.008 to 1.082)	1.015 (0.976 to 1.056)
No age adjustment[f]	18	1.211 (1.101 to 1.331)	1.168 (1.061 to 1.285)	1.131 (1.018 to 1.256)
Husband smokes				
All	**93**	**1.219 (1.138 to 1.305)**	**1.139 (1.062 to 1.221)**	**1.077 (0.999 to 1.162)**
North America	29	1.074 (0.937 to 1.232)	1.004 (0.873 to 1.154)	0.898 (0.775 to 1.039)
Europe and New Zealand	20	1.174 (1.007 to 1.369)	1.092 (0.934 to 1.277)	1.062 (0.899 to 1.254)
Asia	44	1.314 (1.199 to 1.439)	1.229 (1.121 to 1.348)	1.181 (1.070 to 1.304)
Age adjustment	75	1.184 (1.100 to 1.274)	1.106 (1.027 to 1.191)	1.048 (0.966 to 1.136)
No age adjustment[f]	18	1.437 (1.194 to 1.728)	1.340 (1.110 to 1.618)	1.264 (1.026 to 1.556)

[a] Unadjusted for confounding and uncorrected for misclassification of smoking habits
[b] Adjusted for confounding by fruit, vegetables and dietary fat consumption and by education
[c] Assuming an additive model, a concordance ratio of 3 and misclassification rates of 2.5% for studies in North America and Europe and 10% for studies in Asia (see section 9.2.3 for interpretation of the misclassification rates)
[d] N = number of studies of ETS and lung cancer
[e] Relative risk of lung cancer (95% confidence intervals)
[f] 12 studies presented no analyses adjusted for age and did not match nonsmoking cases and controls on age

When adjustment for confounding and correction for misclassification is carried out the association between ETS and lung cancer is no longer statistically significant for North America, Europe or New Zealand or where all 93 studies are considered, but is significant for Asia. When attention is further restricted to those studies that had presented age-adjusted results, generally considered extremely important in epidemiology, the association, whether with husband smoking (RR 1.05, 95% CI 0.97 to 1.14) or with each 10 cigarettes per day smoked by the husband (RR 1.02, 95% CI 0.98 to 1.06), is close to 1 and non-significant. The lack of significance and closeness of the estimates to 1.0 would not have been affected by further adjustment for ETS exposure in the reference group ("background correction"), as carried out by Hackshaw *et al* [1].

While our estimates are subject to various uncertainties, as discussed in the report, the overall analyses have not shown an association. If an association does exist – and one cannot prove a negative – it is likely to be much weaker than that claimed by Hackshaw *et al* [1].

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Appendices

1. Background – The series of five papers

In a series of papers published between 2000 and 2002 [2-6], entitled "Revisiting the association between environmental tobacco smoke exposure and lung cancer risk", we examined in detail arguments put forward to support the claim that exposure to environmental tobacco smoke (ETS) increases the risk of lung cancer in lifelong nonsmokers.* The series of papers were produced partly in response to an analysis by Hackshaw *et al* in 1997 [1] of 37 epidemiological studies of risk in nonsmoking females according to smoking by the husband. Hackshaw *et al* [1] had obtained a relative risk (RR) by meta-analysis of the results from the 37 studies of 1.24 (95% confidence interval [CI] 1.13 to 1.36). They had adjusted this for three types of bias – due to misclassification of active smoking by the subject, confounding by diet and exposure to ETS in the reference group – and had ended up with a RR estimate of 1.26 (95% CI 1.06 to 1.47) which they took to be their best estimate of the excess risk of lung cancer in nonsmokers from all sources of ETS exposure. Taking into account evidence of risk of lung cancer from active smoking and evidence of tobacco-specific carcinogens in the blood and urine of nonsmokers exposed to ETS, Hackshaw *et al* [1] argued that their estimate provided compelling evidence that breathing other people's tobacco smoke is a cause of lung cancer.

Hackshaw *et al* [1] had also estimated that (without adjustment for the three sources of bias) the risk of lung cancer in nonsmoking females rises by 23% (95% CI 14 to 32%)† for every 10 cigarettes smoked by the husband, and much of the work in our series of papers [2-6] concerned assessing the validity of this claim and calculating the extent to which the estimate was affected by correction for bias.

1.1 Paper I

The first paper "I. The dose-response relationship with amount and duration of smoking" [2] concluded that Hackshaw *et al* [1] had overestimated the association by restricting attention to those studies that had specifically

* Referred to henceforward as nonsmokers or on occasion never smokers.
† Alternatively expressed as an RR of 1.23 (95% CI 1.14 to 1.32).

reported results by level of exposure, since such studies reported markedly higher exposed/unexposed RRs than did those studies which only reported exposed/unexposed results. Using results from both types of study, including results from some additional studies published since 1997, and also correcting confidence limits from one study [7] that had been shown [8] to be clearly erroneous and had led to substantial overweighting of its results, resulted in a lower estimate of the risk increase in lung cancer per 10 cigarettes/day smoked by the husband of 10% (95% CI 5 to 15%). This was substantially lower than the original estimate of 23% (95% CI 14 to 32%) of Hackshaw *et al* [1]. Given that men typically smoke of the order of 20 cigarettes a day (and the data generally relate to total smoking by the husband and not smoking in the presence of the wife), a lower estimate seems appropriate anyway, since a 23% increase in relation to the husband smoking 10 cigarettes/day does not align well with a 24% increase in relation to overall smoking.

1.2 Paper II

The second paper "II. Adjustment for the potential confounding effects of fruit, vegetables, dietary fat and education" [3] described the extent to which adjustment for confounding by dietary variables and education might affect the estimated increase in risk per 10 cigarettes/day. Hackshaw *et al* [1] had adjusted for a single (unclearly defined) variable of fruit/vegetable consumption but our paper considered the separate and combined effects of adjustment for four specific sources of potential confounding – fruit consumption, vegetable consumption, dietary fat consumption and education. The correction process required three types of information:

(i) estimates of the association of each potential confounding variable with lung cancer in nonsmokers,

(ii) estimates of the association of each potential confounding variable with ETS exposure in nonsmokers, and

(iii) estimates of the correlation between each pair of potential confounding variables in nonsmokers.

This was obtained by combining evidence from available studies that provided such information. There were problems in combining the data for the association of dietary fat and education with ETS exposure in that estimates weighted on sample size were dominated by one very large study (Cancer Prevention Study = CPS II) which provided results very different from those seen in multiple other studies. Accordingly, estimates were calculated based on both unweighted means and weighted means.

Paper II [3] described the methodology developed to account for confounding by multiple correlated variables. This methodology corrects the results of each of the ETS/lung cancer studies individually, taking account of whether the RRs had already been adjusted for any of the four confounding variables. After applying the methodology, we estimated that the increase in lung cancer risk per 10 cigarettes/day smoked reduced from 10% (95% CI 5 to 15%) to 6% (1 to 11%) using unweighted means or to 9% (5 to 14%) using weighted means.

1.3 Paper III

The third paper "III. Adjustment for the biasing effect of misclassification of smoking habits" considered the effects of bias due to some of the self-reported nonsmokers actually being true current or former smokers. We used a somewhat different method of correction [9] than did Hackshaw *et al* [1] but we showed, based on exposed/unexposed (rather than dose-response) data for smoking by the husband, that the two methods produced similar results. We also noted that the bias was increased if strong evidence of much higher misclassification rates in Asian females [10-13] was taken into account, and could then explain about half the observed association. We described an approach for misclassification correction of dose-response data and applied it to data relating risk to amount smoked by the husband. We showed that the estimate of risk increase per 10 cigarettes smoked by the husband adjusted for confounding using unweighted estimates reduced, following further adjustment for misclassification bias, from 6% (95% CI 1 to 11%) to 2% (-3 to 8%). Using weighted estimates reduced the estimate adjusted only for confounding from 9% (5 to 14%) to 5.5% (0 to 11%).

1.4 Paper IV

The fourth paper "IV. Investigating heterogeneity between studies" [5] noted that there is highly significant ($p<0.001$) heterogeneity between the lung cancer risk estimates from the 47 studies considered, whether in relation to the number of cigarettes/day smoked by the husband or the exposed/unexposed risk according to whether the husband smokes. Two major conclusions emerged from these analyses. First, there was a marked tendency for risk estimates to be higher in those studies that had not adjusted or matched for age, and there was a strong case for removing such studies from meta-analyses as being of unacceptable quality. Also, as noted above, studies which reported dose-response results for smoking by the husband also reported higher risks. There was also some evidence that risk estimates tended to be lower in larger studies, in studies published in the 1990s, in studies not requiring histological confirmation of all cases, and in studies where the proportion of proxy responders was no higher in cases than in controls, though these associations were not independent. We also concluded that variation in risk by study characteristics largely explained the apparently low RR in one large Chinese study [14], arguing against the view that it is an outlier which should be excluded from meta-analyses.

1.5 Paper V

The final paper in the series "V. Overall conclusions" [6] brought together all this material and added discussion on such issues as existence of a threshold, low-dose extrapolation, publication bias, systematic differences between cases and controls, diagnostic inaccuracy, errors in determining ETS exposure, bias due to exposure to ETS in the reference group, other indices of ETS exposure, histological type of lung cancer and expression of uncertainty. The abstract of the paper [6], repeated below for convenience, summarizes our main results and arguments:

"We examine in detail arguments put forward to support the claim that exposure to environmental tobacco smoke (ETS) increases risk of lung cancer in nonsmokers. Hackshaw et al.

[1] have estimated that the risk increases by 23% (95% CI 14% to 32%) per 10 cigarettes/day smoked by the husband. The estimated increase essentially disappears if proper adjustment is made for smoking misclassification bias, if correction is made for the joint effects of confounding by fruit, vegetables, dietary fat and education, if errors in published data in one study are corrected, and if results from all pertinent studies are included (and not just those which report risk by level of smoking by the husband). Taking account of all these factors and using unweighted estimates of the association between ETS exposure and the confounding variables (as one very large study reported results discrepant from those for numerous smaller studies), the risk increase per 10 cigarettes/day was found to be 2% (95% CI -3% to +7.5%), based on data from 47 ETS/lung cancer studies. Using weighted estimates, the risk increase was 5.5% (95% CI 0% to +11%). Restricting attention to the 36 studies that had adjusted for age, the increase reduced further to -2% (95% CI -6% to +3%) using unweighted estimates, or to +1% (95% CI -4% to +6%) using weighted estimates.

These estimates are not materially affected by bias due to the reference group (nonsmokers married to nonsmokers) having some ETS exposure from other sources. Other sources of potential upward and downward bias, not formally taken account of in the analysis, are discussed.

Based on extrapolation from the known lung cancer risk in smokers, Hackshaw et al. [1] estimate that environmental tobacco smoke exposure would be expected to increase the risk of lung cancer in nonsmokers by 19%. Using more appropriate assumptions (for the relative exposure to smoke constituents of passive and active smokers, for the lung cancer risk in those who have ever smoked and for the dose-response model) leads to a much lower estimate of about 0.5%. Even this estimate is open to question as a threshold might exist for the effects of tobacco smoke constituents on lung cancer risk.

Whether or not a true risk exists, it is clear that this is not demonstrated by the overall evidence. The true increase in risk per 10 cigarettes/day smoked by the husband is very unlikely to be as large as 23%. It might be as much as 5%, but it could well be 1% or less, or even zero."

2. Objectives and differences from our earlier work

The work published in our five papers [2-6] is now out of date, being based on publications up to about 1999. One objective of the updated analyses described in the present report is to produce more recent estimates including more current papers. To this end, we have extended the literature used on the association of lung cancer with ETS exposure and the four potential confounding variables considered previously (fruit, vegetables, fat, education) and on the association of the four potential confounders with ETS and with each other. Although we have updated our misclassification-corrected estimates, we have not attempted to search for additional literature on the extent of misclassification, partly because in any event the misclassification rates assumed are based already on a quite extensive literature [15].

Another objective is to improve our estimation in various ways. One is to use, where possible, estimates based on data for females. In our original work the ETS/lung cancer data related to risk in females associated with smoking by the husband. Although we included a limited number of estimates based on studies where only results for sexes combined had been presented (see Table 1 in section 4), these were typically studies where the great majority of the lung cancer cases in nonsmokers were females. However, our estimates of associations of potential confounders with lung cancer, ETS and with each other were often derived from data ignoring gender. Given there are sufficient data specifically for females, it seems more scientific to base all our calculations, as far as possible, on data for females.

Another possible method of improving our estimation is to add to the list of potential confounding variables. With that in mind, we have reviewed evidence relating lung cancer and ETS to various other potential confounders.

In our previous work, we had used random-effects analyses to summarize data relating lung cancer to ETS and to the potential confounders. However, we had summarized differences in potential confounding variables between ETS exposed and unexposed individuals by either weighted or unweighted means. Here we use random-effects analysis for consistency and also to avoid problems of presenting multiple answers allowing selective citation of specific results, e.g. by IARC [16]. We do, however, include some results of analyses using weighted and unweighted means to illustrate the effect the different approaches make.

Previously, our analyses correcting for the effect of confounding and misclassification bias concerned the increase in risk per 10 cigarettes/day smoked by the husband. Though we again carry out analyses for this exposure index, we also carry out analyses for the simpler index of whether the spouse smokes or not. The latter analyses should be more readily explicable to ETS researchers who are used to this traditional index.

Our previous work included extensive analyses of heterogeneity [5]. We do not report such extensive analyses here, but we do present some results separated by region, year of publication, number of lung cancer cases in the study, whether the study actually provided dose-response results, whether adjustment had been made for age, and whether the study was of case-control or prospective design.

3. Structure of the rest of the report

We start by considering the dose-response results. Section 4 presents the ETS/lung cancer data uncorrected for confounding or misclassification bias, and gives meta-analysis results. Section 5 summarizes the data relating lung cancer risk to the various potential confounders considered and presents the combined estimates of the associations used in the adjustments. Similarly, section 6 summarizes the data relating ETS to the potential confounders. Section 7 then presents some additional information needed to carry out the confounder adjustments (including the intercorrelations between the potential confounders), after which section 8 then presents confounder-adjusted risk estimates. Section 9 summarizes the basis of the misclassification correction method used and presents the results of the risk estimates adjusted for both confounding and misclassification. Section 10 then turns to the exposed/unexposed index. Following a discussion of the findings in Section 11 the results are summarized in Section 12. The tables then follow, and then the references. Additional material is presented in a series of separate appendices, each with their own reference section where required.

4. The relationship between lung cancer risk and the number of cigarettes smoked by the husband

Table 1 shows for each study the data used in the dose-response analyses relating risk of lung cancer in lifelong nonsmoking females to the number of cigarettes smoked by the husband. Data relating risk in nonsmoking men to smoking by the wife are sparser and are not considered. Ninety-three studies [7,14,16-105] are included, as compared to forty-seven in our earlier analyses [2]. The 45 studies published from 1999 onwards are additional, as are two earlier studies [82,104]. One study included earlier [106] has been superseded by updated results published in 2000 [66]. Appendix 1 explains why results from certain other publications, which might have been thought to cite relevant data, are not included. Reasons include the results already being given in another paper or being superseded by a later publication, the study being a single centre of a multicentre study published elsewhere, no results being presented separately for lifelong nonsmokers, the control group being inappropriate (typically patients with other smoking-related diseases), and the number of lung cancer cases considered being less than five.

Of the 93 studies, the first was published in 1981 [40], with a further 25 published in the 1980s, 27 in the 1990s, 26 in the 2000s and 14 from 2010 to the end of 2014. 29 studies were conducted in North America (USA, Canada and Mexico), 18 in Europe, 26 in China (including Hong Kong) and 18 in other parts of Asia. One of the Asian studies was of Chinese women in Singapore, and this has been included in the subset of China studies. A further two studies were from New Zealand. As these were principally of people of European descent they have been included in the European subset of studies. Sixteen were prospective studies and 77 case-control. The studies varied in the number of lung cancer cases in lifelong nonsmokers, with 22 involving less than 50 cases (smallest 4 cases) and nine over 400 cases (largest 1907 cases).

Twenty-four of the studies provided data on risk of lung cancer by the number of cigarettes per day smoked by the husband while, for the remaining

69 studies, estimates were only available for overall exposure. For most of the studies, the index of exposure used was smoking by the husband, but in some the nearest equivalent index was used (typically smoking by other household members but sometimes ETS exposure at home and/or at work, general ETS exposure or urinary cotinine). The term "relative risk" is taken to include direct estimates of the relative risks (RRs) from prospective studies and indirect estimates (odds ratios) from case-control studies.

RRs and 95% confidence limits in Table 1 are adjusted for covariates if adjusted data are available, and otherwise are unadjusted. In 18 studies [7,19,25,28-31,38,58,62,63,67,68,71,72,93,94,98], the RRs were not adjusted for age, either directly in analysis or by matching in design. (In some of these 18 studies, the whole set of cases and controls, regardless of smoking habits, were matched on age, but the lifelong nonsmoking cases and controls were not.)

Where studies present appropriate data on numbers of cases and controls (or populations at risk) unadjusted RRs and 95% CIs are calculated, or checked using standard software [107]. Some studies reported adjusted RRs and CIs only by a level of exposure other than cigarettes per day smoked by the husband. These adjusted RRs and CIs were used to estimate corresponding "effective numbers" of cases and controls (or subjects at risk) at each level, which could then be combined to allow estimation of RRs and CIs for overall exposure, as described elsewhere [2,108]. Note that the CIs for the Geng *et al* study [7] are not the erroneously narrow ones given in the source paper but have been corrected as described elsewhere [2,8].

For the 46 studies considered earlier [2], the RRs and CIs in Table 1 are identical to those presented in Table 1 of that paper, except for the CIs for the study by Gao *et al* [39], which were found to be slightly in error and were corrected from (0.89 to 1.91) to (0.87 to 1.94).

To each RR and CI given in Table 1, a cigarettes/day midpoint is attached, using the methods and rationale described in paper I of our series [2].

Note that the number of cigarettes per day smoked by husbands in US studies is about 5 more than that smoked by husbands in non-US studies.

The final column in Table 1 contains the estimate of β, the slope of the relationship of log RR to dose (in units of 10 cigarettes per day smoked by the husband), together with its standard error (SE). For each study, β is derived from the available RRs using the model

$$RR\ (d_2,d_1) = (\exp\ (\beta(d_2\text{-}d_1))$$

where RR (d_2,d_1) is the RR for exposure to dose d_2 compared to d_1. Where d_1 is the unexposed group ($d_1 = 0$), the RR is given by

$$RR\ (d_2,0) = \exp\ (\beta d_2) \text{ or}$$
$$\log RR\ (d_2,0) = \beta d_2$$

The method for deriving β and SE(β) is as used previously [2,109]. It takes account of the fact that a set of RRs by number of cigarettes smoked for a given study is not independent, being based on a common control group. The method requires the data to be available in the form of counts of exposed and unexposed cases and controls (or populations at risk) at each level of exposure. For a set of RRs and CIs adjusted for age or other variables, corresponding hypothetical pseudo-numbers are estimated as described elsewhere [2,108]. The ratio, Z, of β to SE(β) can be taken to be an approximate normal deviate, and can be used to assess the significance of β in an individual study.

The individual study estimates of β and SE(β) can then be combined to give overall estimates using inverse-variance weighted random-effects or fixed-effects meta-analysis [110].

Appendix 2 contains the individual study estimates of β, SE(β) and Z, as well as the counts (or pseudo-numbers), and the results of the various meta-analyses conducted. It also contains listings and distributions of various other relevant variables.

The results of the meta-analyses are summarized in Table 2. Overall, the estimated increase in risk of lung cancer per 10 cigarettes/day smoked by the husband is equal to 9% (95% CI 7 to 11%) using fixed-effects meta-analysis or 11% (7 to 14%) using random-effects meta-analysis. This increase is consistent with only three studies [14,18,22] of the 93 showing a significantly ($p<0.05$) reduced slope as against 18 studies [7,35,36,41,42,49,53,62,63,66,67,69,71,74,93,94,100,104] showing a significantly increased slope. The heterogeneity chisquared is 169.93 on 92 degrees of freedom ($p<0.001$). Table 2 includes meta-analyses by region, year of publication, study size, availability of specific dose-response data by cigarettes/day smoked by the husband, adjustment (or matching) for age, and study design. The most notable differences seen were the tendency for the increases to be greater ($p<0.01$) for lack of age adjustment, with the 18 studies that did not adjust for age [7,19,25,28-31,38,58,62,63,67,68,71,72,93,94,98]* having a high estimate of 21% (10 to 33%, random-effects), and for the increases to vary by study size, with the nine studies of over 400 cases [14,20,24,36,42,49,68,80,105] showing no increase (4%, -2% to +11%, random-effects). There was also a tendency ($p<0.01$) for estimates to be higher in Asian studies, where the random-effects estimate was 16% (10% to 22%) than in other studies where ii was 5% (0% to 9%). Variation by decade of publication, though significant ($p<0.01$) did not show any time-related trend, while variation by study type, and whether the study reported dose-response data was not significant.

In the next section we will discuss the effect of adjustment for fruit, vegetable and dietary fat consumption and for education. It should be noted however that, as summarized below, there were a very limited number of

* These were studies that did not present any age-adjusted analyses. There were three further studies [48,57,64] where the exposed/unexposed RR estimates used in section 10 were age-adjusted, but the dose-response estimates used in sections 4 to 9 were not. These three studies have been included as having age-adjusted data for consistency with earlier work [5], and in order to make the analyses by age adjustment comparable for the dose-response and exposed/unexposed RRs.

estimates that were already adjusted for diet and rather more that were adjusted for education.

Thus, the RR was adjusted for fruit consumption in nine studies [33,34,36,53,54,76,97,101,105], for vegetable consumption in eleven [27,34-36,52-54,76,82,97,101] and for dietary fat consumption in four [27,34,44,76]. This includes one study [105] that adjusted for vitamin C, taken as equivalent to adjusting for fruit; one study [34] that adjusted for energy intake, taken as equivalent to adjusting for dietary fat; one study [76] that adjusted for meat, also taken as equivalent to adjusting for dietary fat; and one study [44] that adjusted for cholesterol, also taken as equivalent to adjusting for dietary fat. Some other studies, e.g. [57,81] had recorded data on fruits, vegetables or dietary fat, but the RRs in Table 1 were not adjusted for these.

There were 32 studies that adjusted for education [14,18,23,27,33-36,39,42-45,52,54,56,59,61,66,69,71,75,82,87,89,90,96,97,101-103,105], or a variable related to it, such as income, socioeconomic status or, in the case of one study [96], ownership of a colour TV.

5. The relationship between lung cancer risk and potential confounding variables

5.1 Introduction

As described in our paper II [3], the correction for potential confounding of estimates of the relationship between lung cancer risk and the number of cigarettes smoked by the husband requires *inter alia* estimates of the relationship between lung cancer risk and the various potential confounding variables considered. Paper II [3] obtained estimates of the increase in risk per standard deviation of fruit, vegetable and dietary fat consumption and of the increase in risk per year of education. Data on social class and income and on occupational exposure to specific lung carcinogens were also studied, but were much sparser and more difficult to combine and no attempt was made to correct for these.

For this report we reviewed papers published between 2000 and 2006 on fruit, vegetable and dietary fat consumption and on education and also on various other potential confounding variables – air pollution, alcohol, income, obesity, occupation, physical activity and socioeconomic status. The intent was to update our estimates for fruit, vegetable and dietary fat consumption and for education and to review our original decision not to adjust for additional potential confounding variables.

Appendix 3 gives details of each paper considered as potentially relevant from our literature search. For some of the papers, it explains why useful information could not be obtained and for the others it gives details of the relevant data from which the estimate was obtained.

While data were extracted from the relevant studies for males and for sexes combined, for never and exsmokers combined, and for certain other indices of exposure, it was decided to restrict attention to data for females, for never smokers (occasionally including long-term exsmokers) and for the specific indices for which results are given in Tables 3, 5 and 7.

5.2 Fruit and vegetable consumption

Table 3 presents data relating fruit and vegetable consumption to lung cancer risk in lifelong nonsmoking females. The table shows β, the logarithm of the estimated risk increase per SD of exposure, and Z, the ratio of β to its standard error. The table corresponds to Table 1 in our paper II [3] except that some earlier results are excluded due to the restrictions discussed in the previous paragraph. There are now 16 independent estimates of β for vegetable consumption (10 of which are the same as in paper II Table 1) and 14 independent estimates of β for fruit consumption (eight of which were included previously). Five of the 16 vegetable estimates are significantly below 0 (Z < 1.96), as are six of the 14 fruit estimates. None are significantly increased.

Appendix 4, similar in layout to Appendix 2, gives additional results including limited meta-analyses. Table 4 summarizes relevant results for random-effects meta-analyses. The combined RR estimate of 0.88 (95% CI 0.80 to 0.97) per SD of vegetable consumption is almost identical to that used in paper II (0.88, 0.81 to 0.95). The combined RR estimate of 0.86 (0.78 to 0.96) per SD of fruit consumption is also similar to the earlier estimate (0.84, 0.76 to 0.93). As found previously, the RRs for vegetable and for fruit consumption did not vary significantly by location, and were essentially unaffected if two studies which included long-term exsmokers were excluded.

5.3 Dietary fat consumption

Table 5 presents data relating dietary fat consumption to lung cancer risk and is laid out similarly to Table 3 of this report and to Table 2 of our 2001 paper [3]. Again we exclude results for males or for sexes combined, and restrict attention to results for never smokers or never smokers plus long term exsmokers. Of the six independent estimates of β in Table 5, two are significantly above one (Z > 1.96) and one almost so. None are significantly decreased.

For some of the studies considered in our paper II [3] results are available for alternative exposure indices (such as cholesterol rather than saturated fat [111,112], or animal fat or plant fat rather than total fat [113]), but we selected the one in Table 5 using the same order of preference we described earlier. For the first study in Table 5 [111,112] four sets of results were presented. Although we have calculated β for each set, our corrections will be based on the one given in Table 5, with adjustment for energy made using the "multivariate nutrient density" method, considered by the study authors [112] to be the most appropriate.

Appendix 5 gives additional results as well as meta-analyses, and Table 6 summarizes the meta-analyses. The combined RR estimate of 1.22 (95% CI 1.09 to 1.36) is slightly greater than that of 1.17 (1.08 to 1.26) used in our paper II [3]. There is no significant variation by region, but the data are rather limited. The estimate is little affected by excluding the two studies which included long-term exsmokers.

5.4 Education

Table 7 presents data (similar to Table 3 of our paper II [3]) relating education to lung cancer risk. Unlike for fruit, vegetable, and dietary fat where the results are expressed per SD, risks are quantified per year of education. Again we excluded results for males and for sexes combined. Results are generally for never smokers, but we include results for never plus occasional smokers in two studies. Of the 12 estimates of β in Table 7, seven show a significant ($Z < -1.96$) decrease in risk with increasing education, and none a significant increase.

Appendix 6 gives additional results as well as meta-analyses, and Table 8 summarizes the meta-analyses. The combined estimate of 0.91 (95% CI 0.88 to 0.95) is similar to that of 0.92 (0.89 to 0.96) used in our paper II [3]. Estimates are very similar by region and are unaffected by omitting the two studies which included results for never plus occasional smokers.

5.5 Other factors

As noted earlier, Appendix 3 reviews papers relating to a larger number of factors considered than fruit, vegetable and dietary fat consumption and education. Although we considered the possibility of including air pollution, alcohol, income, obesity, occupation, physical activity and socioeconomic factors as additional potential confounding variables to adjust for, we decided in the end not to extend the list. Reasons for this decision are given in Appendix 3.

6. The relationship between at home ETS exposure and the potential confounding variables

6.1 Introduction

We now turn to some further information required to correct for confounding estimates of the relationship between lung cancer risk and the number of cigarettes smoked by the husband, namely estimates of the difference in levels of the confounders of interest between nonsmokers who were ETS exposed and those who were not.

We reviewed apparently relevant papers published from 2000 to 2006 relating ETS exposure to fruit, vegetable and dietary fat consumption and to education. Appendix 7 gives details of each paper considered as potentially relevant from our literature search, explaining why useful information could not be obtained or presenting the relevant data where it could be.

In addition to the publications considered in Appendix 7, we also looked for additional publicly available databases that could provide useful data. In our previous work [3], we had used data from the UK Health and Lifestyle Study 2 (HALS2) [114], the 1993 Health Survey for England (HSE) [115] and the unpublished Hungarian Lifestyle Survey, all the estimates being provided by J Hamling as a personal communication. Here we investigated the possibility of additional databases and were successful in obtaining useful data from two.

One was the National Health Interview Survey (NHIS) [116], a leading source of information on the civilian non-institutionalised population of the US. Although surveys have been conducted since 1960, individuals were not asked about smoking in the household in almost all of them, and since only one adult from each household was surveyed, household smoking information could not be obtained by linkage. In 2000, however, a direct question was asked which enabled one to distinguish those where someone smoked for 1-7 days per week inside the home and those where exposure was less than 1 day per week, rarely or not at all. Hence we could obtain estimates of differences between ETS exposed and non-exposed individuals for vegetable and fruit consumption, for an estimate of dietary fat based on eating bacon, fried potatoes or chips, and for years of education.

The other publicly available source to provide useful data was the National Health and Nutrition Examination Survey III (NHANES III) [117], earlier surveys not having data on smoking within the household. NHANES III, however, included questions on cigarettes smoked in the home by household members. From this, we were able to derive estimates of differences between ETS exposed and non-exposed individuals for consumption of vegetables and fruit, for an estimate of dietary fat based on consumption of bacon, sausages, processed meats and eggs and for years of education.

Using techniques developed for our earlier work [3], the new data from the publications and the publicly available databases were transformed to differences per SD for dietary variables or per year of education for education.

Although our initial review (Appendix 7) was more wide-ranging, the actual estimates of difference we used are restricted to data for females and for never smokers, and to ETS exposure from the spouse or cohabitant.

In our earlier work [3], we had combined the meta-analysis estimates using either weighted or unweighted means. Here our main estimates, to be consistent with the estimates for lung cancer risk, are based on random-effects meta-analysis. However, we also present estimates based on unweighted and weighted means for comparison.

6.2 Fruit and vegetable consumption

Table 9 presents the available estimates for lifelong nonsmoking females of δ, the difference (in SDs) in fruit or vegetable consumption associated with ETS exposure at home. Table 9 also presents the number of females exposed (N_e) or unexposed (N_u) to ETS at home. The table corresponds to Table 4 in our paper II [3] except that results for males have been excluded. There are now 16 independent estimates of δ for vegetable consumption (12 of which were included previously) and 11 independent estimates of δ for fruit consumption (seven of which were included previously). Within the estimates for vegetable consumption 11 were negative and five were positive, while for fruit consumption only one estimate was positive, that from Italy [118], while the other 10 were negative. The study sizes on which the estimate were based varied considerably, especially between those of the very large prospective cohort studies of Cardenas and Hirayama and the small case control studies reported by Koo.

As shown in more detail in Appendix 8 and summarized in Table 10, various combined estimates were calculated:

(a) unweighted for study sizes,

(b) weighted on the combined sample size, $N_u + N_e$, or

(c) using random-effects analysis, using weights which were the inverse of the variance. The variance was estimated as $\sigma^2 ((1/N_u) + (1/N_e))$ where σ is 1 for the dietary variables and is estimated as 2.435 years for education (Appendix 9).

The estimates from the random-effects models of the differences for vegetables and for fruit are quite similar for the USA and Europe, with values of -0.0866 and -0.0892 for vegetables and -0.0862 and -0.0581 for fruit respectively. The estimates for the Asian studies of +0.0185 for vegetables and –0.1661 for fruit were less similar, but they have larger standard errors and are not significantly different from the results for the USA and Europe. We will take the overall values of -0.0559 and -0.0733 for vegetables and fruit respectively for our main analyses.

6.3 Dietary fat consumption

Table 11 presents estimates of δ for dietary fat consumption, together with the associated values of N_u and N_e. These estimates are all for lifelong nonsmoking females, and only those estimates for the most appropriate index of fat have been included. See Table 5 of our paper II [3] for estimates of δ using alternative indices (e.g. don't use low fat spread rather than fried foods for HALS2 and HSE93). One estimate previously included in Table 5 of our paper II [3] based on an analysis of NHANES III by Butler [119] is not now included as it is superseded by our own analysis.

There are now 12 estimates of δ for dietary fat. 10 of these are positive with only that based on the very large CPS II study [27] and the Italian study [118] being negative. Results of various combined analyses are given in Table 12, with further detail in Appendix 10. Because of the very large size of the CPS II study we get very different results depending on the type of model used. Thus when using all the studies we see estimates ranging from 0.2089 when using unweighted analysis to 0.0001 when using simple weighted analysis, with the random-effects model giving us an estimate lying between these of 0.1310. As the random-effects models are being used throughout our analyses this is the main value we will use in our subsequent work. The random-effects estimates are similar for USA (0.1188) and Europe (0.1302). The single estimate from Asia is rather higher (0.3532).

6.4 Education

Table 13 presents the estimates of δ for education (here expressed in years rather than SDs), together with the associated values of N_u and N_e. Again, the estimates are all for lifelong nonsmoking females. Table 6 of our paper II [3] previously included results from the Butler analysis of NHANES III [119] but we exclude that now to avoid overlap with our own analysis.

There are now 13 estimates of δ for education. All of them show less years of education in the ETS exposed females. This was also true for our previous analysis, though an association in the opposite direction was noted for men in the very large CPS II study [27]. Results of combined analyses are given in Table 14, with further detail in Appendix 11.

The overall random-effects estimate is –0.5337 and estimates for the USA (-0.6083), Europe (-0.4752) and Asia (-0.5000) are all consistent with this. Bearing in mind the quite small standard error of the random-effects estimate, the data are quite consistent in showing that nonsmokers with ETS exposure at home have about half a year less education on average than do unexposed nonsmokers.

(Note that the estimate given for the Thornton study [120] shown in Table 13 differs from that given in Table 6 of our paper II [3]. This was due to an error in presenting Table 6, and the correct estimate, as used in our analyses then and now, is that shown in Table 13.)

7. Additional information required to carry out the adjustment for confounding

7.1 The method for confounder adjustment

It is helpful to repeat the part of our earlier paper [3] which describes the method:

"Suppose that lung cancer risk, L, is related to n factors x_1, $x_2 \ldots x_n$ by the linear equation

$$\log L = \beta_0^* + \sum_i^n \beta_i^* x_i$$

where exp (β_0^*) is the expected background risk in someone with zero exposure to each factor and exp (β_i^*) is the expected multiplication in risk associated with a unit increase in exposure to factor i.

Suppose that, instead of having direct estimates of β_i^*, data relating lung cancer risk to the factors are only available on a univariate basis, i.e. assuming that the relationship can be described by the equation

$$\log L = \beta_0 + \beta_i x_i$$

Here, exp (β_i) is the observed relative risk associated with a unit increase in dose of the factor unadjusted for other risk factors.

Now it can be readily be demonstrated that, provided log L is normally distributed, the β_i and the β_i^* are related by the matrix equation

$$\underline{B}^* = S^{-1}C^{-1}S\underline{B}$$

where $\underline{B}^*$ and $\underline{B}$ are the n x 1 column vectors of, respectively, β_i^* and β_i , S is the diagonal n x n matrix of the standard deviations of the factors s_i and C is the n x n matrix of correlations of the risk factors c_{ij}.

Assuming data on $\underline{B}$, C and S can be obtained, this gives a method for estimating $\underline{B}^*$. In our principal context there would be n = 5 factors, with i = 1 representing the factor ETS exposure, and i = 2, 3, 4 and 5 representing, respectively, fruit, vegetables, dietary fat and education. Exp (β_1) would be the unadjusted increase in risk associated with unit increase in ETS exposure (e.g. per 10 cigarettes/day smoked by the husband) and exp (β_i^*) would be the increase adjusted for the other four factors, so that the joint confounding effect would be estimated as $\exp(\beta_1)/\exp(\beta_i^*)$."

7.2 Availability of the relevant data

7.2.1 Relationships of lung cancer risk to the factors (β_1)

Estimates for each study of β_1, which quantifies the relationship of lung cancer to the number of cigarettes smoked by the husband (in units of 10 cigarettes/day), are generally those given in table 1 (as β). However, the method assumes that β_1 is an estimate of the relationship unadjusted for any of the other risk factors of interest which, as discussed in section 4, and as is clear from pages A-3 and A-4 of Appendix 2, is not always so. Where the estimates were already adjusted for one or more of the risk factors, the β_1 values were first back-corrected to remove the effect of the adjustment (and avoid erroneous double-adjustment) as described earlier [3].

Based on the data (for all studies given in Appendices 4, 5 and 6), we used the following estimates of β_2 to β_5:

β_2	Fruit	-0.1452	(14 studies)
β_3	Vegetables	-0.1264	(16 studies)
β_4	Dietary fat	+0.1960	(6 studies)
β_5	Education	-0.0917	(12 studies)

These correspond to relative risks, respectively, of 0.86, 0.88, 1.22 and 0.91 [and 0.73] as given in Tables 4, 6 and 8.

7.2.2 *Standard deviations (s_i)*

s_1, the SD for the ETS variable, can be estimated directly for each study (in units of 10 cigarettes/day smoked by the husband) from the data for controls by level of exposure given in Appendix 2, as discussed in our paper I [2].

The SDs for the dietary variables, s_2, s_3 and s_4 [and s_6] are equal to 1 as they are measured in SDs.

The SD for education is taken as 2.435 years (see section 6.2 and Appendix 9).

7.2.3 Correlations (c_{ij})

Clearly, when i = j, $c_{ij} = 1$.

When quantifying the association between ETS exposure and the other risk factors ($c_{12} \ldots c_{16}$) we have derived (see tables 10, 12 and 14) combined estimates of δ_j, the difference in exposure to risk factor j associated with living with a smoker:

δ_2	Fruit	-0.0733	(11 studies)
δ_3	Vegetables	-0.0559	(16 studies)
δ_4	Dietary fat	+0.1310	(12 studies)
δ_5	Education	-0.5337	(13 studies)

The variables δ_j and c_{1j} are related by the formula

$$c_{1j} = \delta_j s_1/(\bar{d}_1 s_j)$$

where $\bar{d}_1$ is the mean ETS exposure for exposed never smokers (see section 7.3 below). c_{1j} was derived separately for each study using a common estimate of δ_j and study-specific estimates of $\bar{d}_1$ and s_1.

When quantifying the correlations between the potential confounding variables, we used the data described below (in section 7.4).

7.3 Mean ETS exposure for exposed never smokers

For each study, Table 1 gives the mean exposure in cigarettes/day by level of exposure. For studies with only one level of exposure, this is (when divided by 10) the estimate of $\bar{d}_1$. For studies with more than one level of exposure, $\bar{d}_1$ is estimated by weighting the exposures by level by the corresponding numbers of exposed controls.

7.4 Intercorrelations between the potential confounding factors

Appendix 12 presents data from seven studies, four conducted in the UK (HALS, HALS2, HSE93, HSE94), one in Hungary (HULS) and two in the USA (NHIS2000, NHANES III). Averaging the data over the seven studies for females, we have the following correlations:

	Fruit	Vegetables	Dietary fat	Education
Fruit	1 (c_{22})	+0.3136 (c_{23})	-0.1036 (c_{24})	+0.1428 (c_{25})
Vegetables		1 (c_{33})	-0.0538 (c_{34})	+0.1303 (c_{35})
Dietary fat			1 (c_{44})	-0.0393 (c_{45})
Education				1 (c_{55})

7.5 Problems with adjusting for potential confounding factors

One study, Lopez-Cima [72] did have problems with the procedure for allowing for confounding. This was due to the very small number of cases that had been assigned to it by the process of generating pseudo numbers that would generate the proposed adjusted relative risks. In such cases where infeasible solutions would have resulted from the procedure, no adjustment has been made to the original RRs.

8. Confounder-corrected estimates of the relationship between lung cancer risk and number of cigarettes smoked by the husband

8.1 Results

Table 15 shows which studies had already been corrected for fruit, vegetables, dietary fat and education. Table 16 shows the results of simultaneous adjustment for fruit, vegetables, dietary fat and education. When the study-specific estimates of δ given in Tables 9, 11 and 13 were combined by random-effects analysis into a single mean, the unadjusted estimate of the increase in lung cancer risk per 10 cigarettes/day smoked by the husband was reduced from 1.102 (95% CI 1.065 to 1.140) to 1.062 (1.027 to 1.099). This suggests that uncontrolled confounding by the four risk factors biased the estimated increase upward by 1.1019/1.0622 = 1.037, or equivalently that about 40% of the observed excess risk may be due to confounding by these four variables alone.

Using unweighted rather than random-effects means of δ increased the estimated bias from 1.037 to 1.1019/1.0531 = 1.046, while using weighted means decreased it to 1.1019/1.0816 = 1.019.

Table 16 also breaks down the analyses into subgroups of region, date published, numbers of cases used, whether or not dose response data was used, whether age adjustment was used and whether the studies were case-control or prospective. The results for North America and for Europe and New Zealand were quite similar and neither of these was significant after correcting for the confounding, giving a combined value of 1.01 (0.97 to 1.06). The results for Asia were higher both for China and for the rest of Asia, with the combined result being marginally significant at 1.11 (1.06 to 1.17). There was evidence that estimates were: larger in the studies published in the 1980s than in those published later; lower in studies with large numbers of cases; larger for studies with dose response data than for those without; and lower for studies where age adjustment had been carried out than for those with no age adjustment (1.05 versus 1.17). There seemed to be no difference between the case control and the prospective studies.

Fuller details of the data used and results summarized in Table 15, including the effects of adjustment in individual studies, are given in Appendix 13.

Table 17 gives more details of the analysis showing how the estimate of the increase in risk per 10 cigarettes/day smoked by the husband varied following adjustment for only one of the four factors (fruit, vegetables, dietary fat and education and for all four factors. Also shown are the bias estimates. Results are shown overall and also separately for North America, Europe and New Zealand combined and for Asia. All the estimates are based on the same common random-effects combined estimates of δ for all studies given in Tables 10, 12 and 14.

The biggest effects were seen when the effects of education were controlled for. It was responsible for a bias correction of 1.024 on its own. Dietary fat could account for about half this amount of bias, with fruit and vegetables having only about a quarter of the effect of education, with fruit correcting for a bias of 1.005 and vegetables of 1.004. When the four main confounding variables were taken together, the combined bias corrected for was 1.039.

Fuller details of the results relating to the findings summarised in Table 17 are given in Appendix 14.

8.2 Discussion

There are a number of sources of uncertainty in our adjusted estimates of the relationship of lung cancer risk to the number of cigarettes/day smoked by the husband (β_1^*). These include:

(i) lack of data specific for each study to allow estimation of the required elements of B, S and C to correct the unadjusted relationship, β_1, so that estimates combined from those (usually separate) studies which did have relevant data had to be used instead;

(ii) uncertainties in the method of obtaining the combined estimates from the individual studies, especially where the available study estimates vary markedly;

(iii) statistical variability in these combined estimates, not reflected in the 95% CI of the adjusted estimates which essentially reflect the variability of the unadjusted estimates of β_1; and

(iv) failure to take into account other possibly relevant sources of confounding (e.g. occupation).

These are discussed further in our 2001 paper [3]. Nevertheless, we feel that the restriction of data specifically to females, and the use of random-effects analysis to combine estimates of δ for the confounding variables, has improved our original work. Taking into account the fact that the associations of fruit, vegetables, dietary fat and education with both lung cancer risk and with ETS exposure are generally statistically significant and quite consistent, we feel that the results presented in Tables 15 and 16 are a reasonable indication of the extent of bias arising from failure to adjust for these factors.

As noted in our earlier paper [3], the direct evidence available from those epidemiological studies of ETS and lung cancer that have presented results by varying extent of adjustment for confounding is of very limited value, and does not rule out the possibility of relevant uncontrolled confounding existing by fruit, vegetables, dietary fat or education.

9. Adjustment for bias due to misclassification of smoking habits

9.1 Introduction

Studies of the potential effects of environmental tobacco smoke (ETS) on lung cancer risk usually compare risk in never smoking females according to whether or not the husband smokes. If in fact a proportion of the females are actually current or exsmokers, bias may result. While random errors in determining exposure typically tend to dilute any true relationships, random errors in misclassifying ever smokers as never smokers tend to increase the observed association between lung cancer risk and smoking by the spouse. This 'misclassification bias' arises because smokers tend to be more likely to marry smokers than would be expected by chance, so that misclassified smokers are likely to be more frequent among those with a spouse who smokes. The size of the misclassification bias depends mainly on the following parameters – the misclassification rate, the excess risk associated with active smoking, the degree of smoking concordance between husband and wife, and the true proportions of subjects and of spouses who smoke [9].

Our paper [4] described in detail two methods for bias correction, the 'Hackshaw method' and the 'Lee and Forey method'. We showed that the choice of method was not crucial, but the choice of misclassification rates was, noting that the original analysis by Hackshaw *et al* [1] did not, but should have, taken into account strong evidence of much higher misclassification rates in Asian females. Our paper described an extension of the Lee and Forey method to apply the correction to data relating risk to the number of cigarettes/day smoked by the husband. It also presented a variety of results using differing misclassification rate estimates and values of other parameters required for the analysis. For the purpose of the current work, we have used the extended method and have restricted attention to what we regarded as the most appropriate model parameters, and have used the same methods as described earlier [4]. Apart from input of some data specific to the new studies (see section 9.2), and starting with different confounder-adjusted estimates of risk associated with smoking by the husband, there are no differences from what we did previously.

9.2 Assumptions

9.2.1 Model

We use an additive rather than a multiplicative model for the joint effects of active smoking and ETS exposure.

9.2.2 Concordance ratio

The concordance (or aggregation) ratio expresses the tendency for husbands and wives to have similar smoking habits. It is the ratio of the odds of the husband smoking given the wife ever smoked to the odds of the husband smoking given the wife never smoked. Here we use an estimate of 3.0 based on an earlier review [121].

9.2.3 Misclassification rates

Both the Hackshaw method and the Lee and Forey method take into account the fact that misclassified smokers tend to have lower lung cancer risks than do non-misclassified smokers [4]. In the Hackshaw method, this is achieved by inclusion of a parameter which represents the risk for *misclassified* ever smokers (relative to all reported never smokers), the value taken for it being substantially less than typically observed for the ever/never smoking relative risk. In the Lee and Forey method, the actual ever/never smoking relative risk is used, but a lower misclassification rate. The lower rate is than interpreted as the proportion of *average risk* ever smokers denying smoking that would produce equivalent bias. In other words, although the actual misclassification rate is higher than this, the below average risk of misclassified smokers is taken into account by assuming a lower misclassification rate.

Here we used a misclassification rate of 2.5% for North American and European studies and of 10.0% for Asian studies. The interested reader can refer to our paper III [4] and to various papers cited there [9,13,121,122] and to reasons why we believe that the claim of Hackshaw *et al* [123] that the misclassification rates for Asian females are "implausibly high" is based on a specious argument. In fact, 10.0% seems to be quite a conservative estimate given the available data [13].

9.2.4 *Study-specific data on active smoking RRs*

The Lee and Forey method requires an estimate of the ever smoking/never smoking RR for each of the studies included. Table 18 shows these estimates as well as giving information on the percentage of smokers among controls, required by the Hackshaw method. As explained in the table, which corresponds in part to Table 1 of our paper III [4], some of these data were not available directly from the source paper and had to be estimated by other means.

9.2.5 *Studies with problems on allowing for misclassification*

The Lee and Forey method can sometimes not produce a feasible solution for allowing for misclassification rates. Thus, the relative risk for the Al-Zoughool study [18] started from such a low level (0.390) that allowing for a misclassification rate based on the suggested %ever smoking rate of 50% would lead to a proposed relative risk less than zero. In this case the relative risk was not reduced due to the misclassification. Fortunately this was the only study where this correction could not be applied, apart from the Lopez-Cima study [72], which had already had problems when applying the confounding correction.

9.3 Results

Table 19 shows the results of the meta-analyses corrected for misclassification and confounding by fruit, vegetables, dietary fat and education, comparing them with the results (previously shown in Table 16) adjusted for confounding only, and showing the bias by failing to correct for misclassification.

The overall result is now just not quite significant, with the estimate being 1.032 (0.994 to 1.071). The estimate is somewhat higher for Asia (1.089, 1.033 to 1.147) and is still significant, while that for North America, Europe and New Zealand is actually less that 1 (0.974, 0.928 to 1.023).

Studies published in the 1980s still show effects that are significant, as do studies that are without age adjustment, but the more up-to-date studies and studies which adjust for age show no significant effect, with the estimate for age adjusted studies at 1.015 (0.976 to 1.056).

Fuller details of the results (including those adjusted for specific confounding variables) are shown in Appendices 15 and 16 corresponding to Appendices 13 and 14 which are uncorrected for misclassification.

10. The effect of adjustment for confounding and correction for misclassification on the exposed/unexposed lung cancer relative risk

10.1 Introduction

So far, we have followed most of our previous work [2-4] in concentrating mainly on the effect of adjustment for confounding and correction for misclassification on the estimated relative risk per 10 cigarettes/day smoked by the husband. The same methodology can also be applied to the simple relative risk according to whether the husband smokes or not, as demonstrated in this section.

10.2 Relative risk estimates

The exposed/unexposed ETS risk estimates in Table 20 correspond to the dose-response ETS risk estimates in Table 1. The RR estimates are the same as in Table 1 for the studies which only have results by level of exposure and are only different for the other studies. We have entered a dose level of 1 to represent the effect of the exposure to ETS by a spouse for all studies. This compares to the value of around 2 which was used in the previous work as beta there referred to the increase in risk from 10 cigarettes and the average number of cigarettes smoked is around 20 cigarettes per day. The betas and their standard errors are therefore around twice the value we had in the dose response work, thus increasing the estimates of RR and the 95% confidence limits accordingly.

10.3 Results

Table 21 presents the results of various meta-analyses of the risk of lung cancer according to whether the spouse smokes. Three sets of analyses are shown:

(a) unadjusted for confounding and uncorrected for misclassification,

(b) adjusted for confounding only, and

(c) adjusted for confounding and corrected for misclassification. Fuller details of these analyses are shown in Appendices 17, 18 and 19.

The results are essentially the same as seen for the dose-response analysis, except that the estimates of beta and standard errors of beta are approximately twice as large. Thus the estimates of RR across all 93 studies now starts at a quite significant value of 1.219 (1.138 to 1.305), the excess then decreases by 37% to 1.139 (1.062 to 1.221) when allowing for the confounding by fruit, vegetables, dietary fat and education, and then decreases by another 44% to a just not significant value of 1.077 (0.999 to 1.162) when misclassification is corrected for. Values for North America, Europe and New Zealand reduce from 1.112 (1.004 to 1.231) to a non-significant 1.037 (0.935 to 1.150) allowing for the multiple confounders and then to 0.959 (0.858 to 1.072) when misclassification is corrected for. The estimate for studies that had age adjustment had a much lower value than those that had no such adjustment, 1.184 compared to 1.437. Their estimate was only marginally significant when the multiple confounders were allowed for and was a non-significant 1.048 when misclassification was corrected for. There was some evidence that studies published early had larger estimates than the later studies, and that studies with very large numbers of cases had a very low estimate of risk – 0.957 (0.826 to 1.108) where more than 400 cases were seen.

11. Discussion

11.1 Background

In their 1997 paper, Hackshaw *et al* [1] found a significantly increased risk of lung cancer in nonsmokers who lived with a smoker, considered that neither adjustment for confounding nor correction for misclassification bias had a material effect, and noted a significant dose-response relationship of lung cancer risk with the number of cigarettes smoked by the spouse. Based on these findings, and the supporting evidence of tobacco specific carcinogens in the blood and urine of ETS-exposed nonsmokers, they regarded it as compellingly demonstrated that breathing other people's tobacco smoke is a cause of lung cancer.

In our series of five papers [2-6] published in 2000-2002, we concluded that Hackshaw *et al* [1]:

(i) overstated the strength of the dose-response relationship of lung cancer risk with the number of cigarettes smoked by the spouse because they failed to consider studies which reported results only as exposed/unexposed and because the results from one study [7] were considerably overweighted;

(ii) underestimated the misclassification bias, by failing to account for the demonstrated high misclassification rates in Asian women [7]; and

(iii) inadequately considered confounding, by limiting attention only to fruit and vegetable consumption as potential confounding variables.

The original work of Hackshaw *et al* [1] only considered the effects of bias from misclassification or confounding on the simple association between lung cancer and whether or not the spouse smoked. They did not consider the effects such biases might have on the dose-response relationship.

The work we published in 2000-2002 [2-6], on the other hand, was mainly concerned with the effect adjustment for bias had on the dose-response relationship. Hackshaw *et al* [1] had estimated that the risk increases by 23% (95% CI 14-32%) per 10 cigarettes/day smoked by the husband. The various estimates we calculated were substantially less than this (see section 1.1.5) and we concluded that a true risk is not demonstrated by the overall evidence, stating that "the true increase in risk per 10 cigarettes/day smoked by the husband is very unlikely to be as large as 23%. It might be as much as 5%, but it could well be 1% or less, or even zero."

The work we present here had a number of objectives:

1) To update the evidence on the association of lung cancer with ETS exposure and with the four potential confounding variables considered previously (fruit, vegetables, fat and education) and on the association of the four potential confounders with ETS and with each other.

2) If possible, to add to the list of potential confounding variables considered previously (fruit, vegetables, fat and education).

3) Where possible, to base estimates of the associations investigated on data for females. In our earlier work [3], estimates of the associations of potential confounders with lung cancer, with ETS and with each other were often derived from data ignoring gender.

4) Use random-effects analyses to summarize data relating to all the main associations. Previously [3], though we had used random-effects analyses to summarise data relating lung cancer to ETS and to the potential confounding variables, we had summarized differences in potential confounding variables between ETS exposed and unexposed individuals by either weighted or unweighted means, which was inconsistent and led to selective citation of results (see section 1.2.2).

5) To carry out analyses adjusting for confounding and correcting for misclassification bias not only, as before, on the estimated increase in risk per 10 cigarettes/day smoked by the husband, but also on the estimated increase in risk associated with smoking by the husband.

These objectives have largely been achieved, though we were unable to find any additional potential confounding variables for which data were extensive or reliable enough to include in our formal adjustment procedures.

11.2 Findings

The results in section 5 (Tables 3-8) confirmed that, in nonsmoking females, lung cancer risk is reduced in relation to fruit consumption (by a factor of 0.86 per SD, 95% CI 0.78 to 0.96), vegetable consumption (0.88 per SD, 95% CI 0.80 to 0.97), education (0.91 per year, 95% CI 0.88 to 0.95), and increased in relation to dietary fat consumption (1.22 per SD, 95% CI 1.09 to 1.36).

The results in section 6 (Tables 9-14) also confirmed that, in nonsmoking females, ETS exposure at home is associated with decreased fruit consumption (-0.073 SDs), vegetable consumption (-0.056 SDs), education (-0.534 years), and increased dietary fat consumption (+0.131 SDs).

Taking into account confounding by all these four factors (by a procedure which allowed for intercorrelations between them and whether or not the original ETS/lung cancer risk estimates for individual studies had already been adjusted for any of them) substantially reduced the estimated association between ETS exposure and lung cancer. Fuller details are given in tables 16 and 21 for subsets of the data, but for all 93 studies the main findings are as follows:

	Unadjusted	Adjusted*
	RR (95% CI)	RR (95% CI)
Husband smokes	**1.219 (1.138 to 1.305)**	**1.139 (1.062 to 1.221)**
Per 10 cigs/day	**1.102 (1.065 to 1.140)**	**1.062 (1.027 to 1.099)**

* For fruit, vegetable and dietary fat consumption, and for education

In both analyses, adjustment explained about 40% of the excess risk.

Further correction for misclassification (see Tables 19 and 21 for fuller details) reduced the confounder-adjusted estimates further to non-significant levels.

	Uncorrected	Corrected*
	RR (9% CI)	RR (95% CI)
Husband smokes	**1.139 (1.062 to 1.221)**	**1.077 (0.999 to 1.162)**
Per 10 cigs/day	**1.062 (1.027 to 1.099)**	**1.032 (0.994 to 1.071)**

* Assuming an additive model, a concordance ratio of 3 and misclassification rates of 2.5% for studies in North America and Europe and 10% for studies in Asia

The results for North America, Europe and New Zealand showed a non-significant estimate of risk when the multiple confounders were allowed for, 1.037 (0.935 to 1.150) for husband smoking and 1.012 (0.967 to 1.059) for 10 cigs/day. This turned into a risk estimate of slightly less than 1 when misclassification was also allowed for, with estimates of 0.959 (0.858 to 1.072) for husband smoking and 0.974 (0.928 to 1.023) for 10 cigs/day.

Similarly, the results restricted to those studies which allowed for age-adjustment showed only a marginally significant estimate of risk when the multiple confounders were allowed for, 1.106 (1.027 to 1.191) for husband smoking and 1.044 (1.008 to 1.082) for 10 cigs/day. This then turned into non-significant estimates when misclassification was also allowed for, with estimates of 1.048 (0.966 to 1.136) for husband smoking and 1.015 (0.976 to 1.056) for 10 cigs/day.

11.3 Interpretation

Uncertainties in relation to our adjustment for confounding have been discussed earlier in section 8.2, while issues relating to adjustment for misclassification bias are no different from before and were discussed earlier [4,6].

One important point to note is that, whereas Hackshaw *et al* [1] adjusted for ETS exposure in the reference group ("background correction"), we have not done so. There are good reasons for this. Firstly, background correction makes no sense in the context of estimation of risk per cigarette/day smoked by the spouse. Second, while it is possible to correct estimates of risk of a nonsmoker with a smoking spouse calculated relative to that of a nonsmoker with a nonsmoking spouse so that they are calculated relative to a nonsmoker completely unexposed to ETS, this only seems appropriate when the original estimate of risk is significant. Third, even if one were to make such a correction, the effect would only be small. Assuming, as did Hackshaw *et al* [1], that total ETS exposure is three times higher in a nonsmoking female if married to a smoker, background correction would only increase RRs in the range 1.01 to 1.05 by a factor of about 1.5 (to 1.015 to 1.075) and would not affect the interpretation.*

All our analyses have been based on the available published data, with no attempt to take into account the possibility that studies showing stronger relationships may be more likely to be published. A number of attempts have been made to adjust the ETS/lung cancer data for publication bias [124-128] which are generally consistent in suggesting that the published evidence may overstate the association somewhat. However, there is no consensus on what is an appropriate method for adjustment, and there is recognition that many strong and largely untestable assumptions are often made, and that many approaches have shortcomings [129-131]. In any event, it seems unlikely that failure to publish has led to any underestimation of the true association.

Other potential sources of bias include recall bias (with knowledge of disease by patients in cases and controls affecting their reported answers on ETS exposure), systematic differences between cases and controls (e.g. cases interviewed in hospital, controls interviewed at home, or data obtained from next-of-kin more for cases than controls) and diagnostic inaccuracy. These have been discussed earlier [6], and seem unlikely to alter the interpretation of a lack of association of ETS with lung cancer risk once confounding and misclassification of active smoking are taken account of.

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* If Z is the ratio of cotinine in nonsmokers married to smokers compared to nonsmokers married to nonsmokers, the background corrected RR is RR(Z-1) / (Z-RR) [6]

We have also discussed earlier [6] the argument put forward by Hackshaw *et al* [1] that extrapolation from the known lung cancer risk in smokers would lead one to expect a 19% increased risk of lung cancer in ETS exposed nonsmokers. Using more appropriate assumptions (for the relative exposure to smoke constituents of passive and active smokers, for the lung cancer risk in those who have ever smoked, and for the dose-response model) leads to a much lower estimate of about 0.5%. Even this estimate, equivalent to a RR of 1.005, is open to question as a threshold might exist for the effects of tobacco smoke constituents on lung cancer risk [6].

While our analyses are clearly affected by considerable uncertainties, they do allow conclusions to be reached. We certainly do not share the views of Hackshaw *et al* [1] that the evidence "provides compelling confirmation that breathing other people's tobacco smoke is a cause of lung cancer." Our detailed assessment shows that an association has *not* been demonstrated. Such an association might exist, but if so is likely to be far weaker than that claimed by Hackshaw *et al* [1].

12. Summary

In 1997 Hackshaw *et al* [1] published a paper in the BMJ concluding that neither adjustment for confounding by diet nor correction for misclassification bias materially affects the observed association between ETS exposure and risk of lung cancer in lifelong nonsmokers, and concluded that breathing other people's tobacco smoke is a cause of lung cancer. In a series of five papers [2-6] published in 2000-2002 we concluded that Hackshaw *et al* [1] had severely underestimated the importance of confounding and misclassification bias and had also overstated the evidence on the strength of the dose-response relationship of lung cancer risk with the number of cigarettes smoked. We also concluded that a causal effect of ETS on risk of lung cancer had not been demonstrated.

The updated analyses presented in this report are now based on a total of 93 epidemiological studies relating ETS exposure to risk of lung cancer in nonsmokers, and on currently available evidence on the relationship of potential confounding variables to nonsmoker lung cancer risk and to ETS exposure and on the intercorrelations between the various potential confounding variables. Compared with our previous work we have generally based our estimates on data for females and have used random-effects analyses to summarize all the main associations. We have also considered the effect of confounding and bias not only, as previously, on the estimated increase in lung cancer risk per 10 cigarettes per day smoked by the husband, but also on the more commonly cited increase in risk associated with the husband smoking regardless of amount. We attempted to extend the list of potential confounding variables for which data were extensive or reliable enough to include in our formal adjustment procedures, but were unsuccessful and our adjustments are based on the same four variables (fruit, vegetable and dietary fat consumption, and education) as used in 2001-2002.

As summarized in the table below, our updated analyses confirm that, in nonsmoking females, both lung cancer risk and ETS exposure are significantly reduced in relation to fruit consumption, vegetable consumption and education while being increased in relation to dietary fat consumption.

		Association with lung cancer risk		Association with ETS exposure at home	
Variable	Unit[a]	N[b]	RR (95% CI)[c]	N	δ (SE)[d]
Fruit consumption	SD	14	0.86 (0.78 to 0.96)	11	-0.073 (0.020)
Vegetable consumption	SD	16	0.88 (0.80 to 0.97)	16	-0.056 (0.021)
Dietary fat consumption	SD	6	1.22 (1.09 to 1.36)	12	+0.131 (0.032)
Education	Year	12	0.91 (0.88 to 0.95)	13	-0.534 (0.063)

[a] SD = standard deviation of the variable
[b] N = number of studies on which combined estimate of association is based
[c] RR (95% CI) = relative risk in nonsmoking females (95% confidence interval) per unit of the variable
[d] δ (SE) = difference in units (standard error) of the variable between nonsmoking females exposed and unexposed to ETS at home

Taking into account confounding by all these four factors (by a procedure which allowed for intercorrelations between them and whether or not the original ETS/lung cancer risk estimates for individual studies had already been adjusted for any of them) substantially reduced the estimated association between ETS exposure and lung cancer, and correction for misclassification, using techniques similar to those used in the 2000-2002 work, reduced the association further. The table overleaf summarizes the main results of the adjustments and corrections.

Studies	N[d]	Unadjusted and uncorrected[a] RR (95% CI)[e]	Adjusted for confounding[b] RR (95% CI)[e]	Also corrected for misclassification[c] RR (95% CI)[e]
Per 10 cigs/day smoked by the husband				
All	**93**	**1.102 (1.065 to 1.140)**	**1.062 (1.027 to 1.099)**	**1.032 (0.994 to 1.071)**
North America	29	1.037 (0.977 to 1.101)	1.006 (0.946 to 1.070)	0.957 (0.896 to 1.022)
Europe and New Zealand	20	1.060 (0.995 to 1.128)	1.020 (0.956 to 1.088)	1.003 (0.938 to 1.073)
Asia	44	1.158 (1.104 to 1.216)	1.113 (1.060 to 1.170)	1.089 (1.0331.289 to 1.147)
Age adjustment	75	1.084 (1.046 to 1.123)	1.044 (1.008 to 1.082)	1.015 (0.976 to 1.056)
No age adjustment[f]	18	1.211 (1.101 to 1.331)	1.168 (1.061 to 1.285)	1.131 (1.018 to 1.256)
Husband smokes				
All	**93**	**1.219 (1.138 to 1.305)**	**1.139 (1.062 to 1.221)**	**1.077 (0.999 to 1.162)**
North America	29	1.074 (0.937 to 1.232)	1.004 (0.873 to 1.154)	0.898 (0.775 to 1.039)
Europe and New Zealand	20	1.174 (1.007 to 1.369)	1.092 (0.934 to 1.277)	1.062 (0.899 to 1.254)
Asia	44	1.314 (1.199 to 1.439)	1.229 (1.121 to 1.348)	1.181 (1.070 to 1.304)
Age adjustment	75	1.184 (1.100 to 1.274)	1.106 (1.027 to 1.191)	1.048 (0.966 to 1.136)
No age adjustment[f]	18	1.437 (1.194 to 1.728)	1.340 (1.110 to 1.618)	1.264 (1.026 to 1.556)

[a] Unadjusted for confounding and uncorrected for misclassification of smoking habits
[b] Adjusted for confounding by fruit, vegetables and dietary fat consumption and by education
[c] Assuming an additive model, a concordance ratio of 3 and misclassification rates of 2.5% for studies in North America and Europe and 10% for studies in Asia (see section 9.2.3 for interpretation of the misclassification rates)
[d] N = number of studies of ETS and lung cancer
[e] Relative risk of lung cancer (95% confidence intervals)
[f] 12 studies presented no analyses adjusted for age and did not match nonsmoking cases and controls on age

When adjustment for confounding and correction for misclassification is carried out the association between ETS and lung cancer is no longer statistically significant for North America, Europe or New Zealand or where all 93 studies are considered, but is marginally significant for Asia. When attention is further restricted to those studies that had presented age-adjusted results, generally considered extremely important in epidemiology, the association, whether with husband smoking (RR 1.05, 95% CI 0.97 to 1.14) or with each 10 cigarettes per day smoked by the husband (RR 1.02, 95% CI 0.98 to 1.06), is close to 1 and non-significant. The lack of significance and closeness of the estimates to 1.0 would not have been affected by further adjustment for ETS exposure in the reference group ("background correction"), as carried out by Hackshaw *et al* [1].

While our estimates are subject to various uncertainties, as discussed in the report, the overall analyses have not shown an association. If an association did exist – and one cannot prove a negative – it is likely to be much weaker than that claimed by Hackshaw *et al* [1].

Table 1 Lung cancer risk in lifelong nonsmokers in relation to the number of cigarettes smoked per day by the husband (or nearest equivalent)

Study [ref]	Year	Location	Type[a]	Number of lung cancers[b]	Cigarettes/day Group	Midpoint	RR (95% CI)[c]	β (SE(β))[d]
Akiba *et al* [17]	1986	Japan	CC	94	1-19	10.00	1.30 (0.62 to 2.57)	0.19 (0.14)
					20-29	21.35	1.50 (0.71 to 3.16)	
					30+	38.39	2.10 (0.57 to 8.07)	
Al-Zoughool *et al*[18]	2013	Canada	CC	31	Any	18.18	0.37 (0.14 to 0.92)	-0.55 (0.26)–
Asomaning[19]	2008	USA	CC	82	Any	23.16	0.84 (0.28 to 2.52)	-0.03 (0.24)
Boffetta *et al* [20]	1998	West Europe	CC	509	0.1-10.0[e]	13.38	1.00 (0.77 to 1.31)	0.01 (0.05)
					10.1-18.0[e]	25.88	0.57 (0.34 to 0.93)	
					18.1+[e]	43.06	1.34 (0.83 to 2.17)	
Boffetta *et al* [21]	1999	Europe	CC	66	Any	18.18	1.00 (0.50 to 1.90)	0.00 (0.19)
Brenner *et al*[22]	2010	Canada	CC	110	Any	18.18	0.40 (0.25 to 0.63)	-0.50 (0.13) ---
Brownson *et al* [23]	1987	USA	CC	19	Any	23.16	1.68 (0.39 to 6.90)	0.22 (0.32)
Brownson *et al* [24]	1992	USA	CC	432	Any	23.16	1.00 (0.80 to 1.20)	0.00 (0.04)
Buffler *et al* [25]	1984	USA	CC	41	Any	23.16	0.80 (0.34 to 1.90)	-0.10 (0.19)
Butler [26]	1988	USA	P	8	Any	23.16	2.02 (0.48 to 8.56)	0.30 (0.32)
Cardenas *et al* [27]	1997	USA	P	246	1-19	10.04	1.10 (0.50 to 2.20)	0.14 (0.07)
					20-39	22.67	1.20 (0.70 to 2.20)	
					40+	43.14	1.90 (1.00 to 3.60)	
Chan and Fung [28]	1982	Hong Kong	CC	84	Any	18.18	0.75 (0.43 to 1.30)	-0.16 (0.16)
Choi *et al* [29]	1989	Korea	CC	75	Any	18.18	1.63 (0.92 to 2.87)	0.27 (0.16)
Correa *et al* [30]	1983	USA	CC	25	Any	23.16	2.07 (0.81 to 5.25)	0.31 (0.21)+
de Waard *et al* [31]	1995	Netherlands	CC	23	Any	18.18	2.57 (0.84 to 7.85)	0.52 (0.31)+
Du *et al* [32]	1993	China	CC	75	1-19	10.00	0.67 (0.33 to 1.39)[f]	0.17 (0.12)
					20+	26.03	1.49 (0.82 to 2.70)[f]	
Enstrom and Kabat [33]	2003	USA	P	177	Any	23.16	0.94 (0.66 to 1.33)	-0.03 (0.08)
EPIC Adulthood [34]	2005	Western Europe	P	43	Any	18.18	0.84 (0.33 to 2.17)	-0.10(0.26)
Fang *et al* [35]	2006	China	CC	157	Any	18.18	1.77 (1.07 to 2.92)	0.31 (0.14)
Fontham *et al* [36]	1994	USA	CC	653	Any	23.16	1.29 (1.04 to 1.60)	0.11 (0.05)
Franco-Marina *et al* [37]	2006	Mexico	CC	72	Any	18.18	1.80 (0.95 to 3.42)	0.32 (0.18)
Gallegos *et al* [38]	2008	Mexico	CC	13	Any	18.18	8.00 (0.85 to 75.31)	1.14 (0.63)
Gao *et al* [39]	1987	China	CC	246	Any	18.18	1.30 (0.87 to 1.94)	0.15 (0.11)
Garfinkel [40]	1981	USA	P	153	1-19	10.04	1.27 (0.86 to 1.89)	0.03 (0.07)
					20+	27.52	1.10 (0.76 to 1.59)	
Garfinkel *et al* [41]	1985	USA	CC	134	1-19	10.04	0.84 (0.40 to 1.77)	0.15 (0.06)+
					20-39	22.67	1.08 (0.64 to 1.82)	
					40+	43.14	1.99 (1.13 to 3.49)	
GELAC [42]	2013	Taiwan	CC	1221	Any	18.18	1.30 (1.09 to 1.56)	0.34 (0.10)++
Geng *et al* [7]	1988	China	CC	54	1-9	4.85	1.40 (0.49 to 4.02)	0.38 (0.15)+
					10-19	12.73	1.95 (0.60 to 6.33)	
					20+	26.03	2.73 (1.23 to 6.08)	
Gorlova *et al* [43]	2006	USA	CC	130	Any	23.16	1.15 (0.63 to 2.10)	0.06 (0.13)
He *et al* [44]	2012	China	P	6	Any	18.18	2.07 (0.23 to 18.34)	0.40 (0.61)
Hill (Study 1) [45]	2007	New Zealand	P	63	Any	18.18	1.00 (0.49 to 2.01)	0.00 (0.20)
Hill (Study 2) [45]	2007	New Zealand	P	123	Any	18.18	1.38 (0.78 to 2.41)	0.18 (0.16)
Hirayama [46]	1984	Japan	P	200	1-19[g]	8.60	1.35 (0.92 to 1.99)	0.15 (0.08)
					20+	26.03	1.59 (1.03 to 2.46)	
Hole *et al* [47]	1989	Scotland	P	6	1-14[g]	2.08	1.30 (0.12 to 14.3)	0.37 (0.36)
					15+	24.09	2.71 (0.28 to 26.0)	
Humble *et al* [48]	1987	USA	CC	20	1-20	15.82	1.80 (0.49 to 6.96)	0.11 (0.25)
					21+	33.92	1.20 (0.23 to 6.89)	
IARC (Kreuzer) [16]	2004	Germany	CC	100	Any	18.18	0.80 (0.50 to 1.30)	-0.12 (0.13)
ILCCO [49]	2014	International	CC	1907	Any	18.18	1.20 (1.06 to 1.36)	0.10 (0.04)++
Inoue and Hirayama [50]	1988	Japan	CC	28	1-19	10.00	2.58 (0.31 to 6.63)	0.35 (0.27)
					20+	26.03	3.09 (0.84 to 15.3)	
Janerich *et al* [51]	1990	USA	CC	146	Any	23.16	0.75 (0.47 to 1.20)[h]	-0.12 (0.10)
Jee *et al* [52]	1999	Korea	P	79	1-19	10.00	2.00 (1.10 to 3.90)	0.09 (0.15)
					20+	26.03	1.50 (0.70 to 3.30)	
Jiang *et al* [53]	2010	China	CC	98	Any	18.18	2.27 (1.13 to 4.53)	0.45 (0.19)+
Johnson *et al* [54]	2001	Canada	CC	71	Any	18.18	1.20 (0.62 to 3.30)	0.10 (0.18)
Kabat and Wynder [55]	1984	USA	CC	53	Any	23.16	0.79 (0.25 to 2.45)	-0.10 (0.25)
Kabat *et al* [56]	1995	USA	CC	69	1-10[j]	16.54	0.82 (0.42 to 1.61)	0.00 (0.11)
					11+[j]	36.38	1.06 (0.49 to 2.30)	
Kalandidi *et al* [57]	1990	Greece	CC	91	1-20	13.38	1.54 (0.79 to 3.00)	0.11 (0.09)
					21-40	29.02	1.77 (0.83 to 3.79)	

					41+	53.35	1.57 (0.54 to 4.57)	
Kiyohara *et al* [58]	2011	Japan	CC	49	Any	18.18	1.01 (0.47 to 2.17) [ℓ]	0.00 (0.22)
Koo *et al* [59]	1987	Hong Kong	CC	88	1-10	7.08	2.33 (0.92 to 5.92)	0.09 (0.14)
					11-20	17.67	1.74 (0.81 to 3.75)	
					21+	31.83	1.19 (0.46 to 3.03)	
Kurahashi *et al* [60]	2008	Japan	P	109	1-19	10.00	1.02 (0.51 to 2.04)	0.16 (0.10)
					20+	26.03	1.47 (0.87 to 2.49)	
Lagarde *et al* [61]	2001	Sweden	CC	242	Any	18.18	1.15 (0.84 to 1.58)[h]	0.08 (0.09)
Lam [62]	1985	Hong Kong	CC	75	Any	18.18	2.01 (1.09 to 3.72)	0.38 (0.17)+
Lam *et al* [63]	1987	Hong Kong	CC	202	1-10	7.08	2.18 (1.14 to 4.15)	0.27 (0.09)++
					11-20	17.67	1.85 (1.19 to 2.87)	
					21+	31.83	2.07 (1.07 to 4.03)	
Layard [64]	1994	USA	CC	39	1-14	8.19	0.60 (0.23 to 1.59)	-0.18 (0.15)
					15+	26.64	0.63 (0.28 to 1.40)	
Lee *et al* [65]	1986	UK	CC	32	Any	18.18	1.00 (0.37 to 2.71)	0.00 (0.28)
Lee *et al* [66]	2000	Taiwan	CC	268	Any	18.18	1.87 (1.29 to 2.71)	0.34 (0.10)+++
Liang *et al* [67]	2009	China	CC	226	Any	18.18	1.45 (1.01 to 2.07)	0.20 (0.10)+
Lim *et al* [68]	2012	Chinese women in Singapore	CC	433	Any	18.18	1.12 (0.90 to 1.40)	0.06 (0.06)
Lin *et al* [69]	2012	China	CC	226	Any	18.18	2.50 (1.66 to 3.77)	0.50 (0.12)+++
Liu *et al* [70]	1991	China	CC	54	Any	18.18	0.77 (0.30 to 1.96)	-0.14 (0.26)
Liu *et al* [71]	1993	China	CC	38	1-19	10.00	0.70 (0.23 to 2.20)	0.44 (0.18)+
					20+	26.03	2.90 (1.20 to 7.30)	
López-Cima *et al* [72]	2007	Spain	CC	4	Any	18.18	0.99 (0.00 to 509.87)	-0.00 (1.75)
Malats *et al* [73]	2000	Europe/Brazil	CC	105	Any	18.18	1.50 (0.77 to 2.91)[h]	0.22 (0.19)
Masjedi *et al* [74]	2013	Iran	CC	55	Any	18.18	2.01 (1.01 to 4.00) [m]	0.38 (0.19)+
McGhee *et al* [75]	2005	Hong Kong	CC	179	Any	18.18	1.38 (0.94 to 2.04)	0.18 (0.11)
Nishino *et al* [76]	2001	Japan	P	24	Any	18.18	1.80 (0.67 to 4.60)	0.32 (0.27)
Ohno *et al* [77]	2002	Japan	CC	191	Any	18.18	1.00 (0.67 to 1.49)[k]	0.00 (0.11)
Pershagen *et al* [78]	1987	Sweden	CC	83	Any	18.18	1.20 (0.70 to 2.10)	0.10 (0.15)
Rapiti *et al* [79]	1999	India	CC	41	Any	18.18	1.20 (0.50 to 2.90)	0.10 (0.25)
Ren *et al* [80]	2013	China	CC	764	Any	18.18	1.20 (0.99 to 1.46)	0.10 (0.05)
Rylander and Axelsson [81]	2006	Sweden	CC	31	Any	18.18	1.37 (0.57 to 3.30)[h]	0.17 (0.25)
Schoenberg *et al* [82]	1989	USA	CC	116	Any	23.16	1.07 (0.70 to 1.64)[h]	0.03 (0.09)
Schwartz *et al* [83]	1996	USA	CC	185	Any	23.16	1.10 (0.72 to 1.68)[h]	0.04 (0.09)
Seow *et al* [132]	2002	Singapore	CC	176	Any	18.18	1.29 (0.93 to 1.80)	0.14 (0.09)
Seki *et al* [84]	2013	Japan	CC	292	Any	18.18	1.31 (0.99 to 1.72)	0.15 (0.08)
Shen *et al* [85]	1998	China	CC	70	1-9	4.85	0.65 (0.21 to 2.07)	-0.09 (0.16)
					10-19	12.73	1.05 (0.32 to 3.38)	
					20+	26.03	0.70 (0.28 to 1.76)	
Shimizu *et al* [86]	1988	Japan	CC	90	Any	18.18	1.08 (0.64 to 1.82)	0.04 (0.15)
Sobue [87]	1990	Japan	CC	144	Any	18.18	1.13 (0.78 to 1.63)	0.07 (0.10)
Speizer *et al* [88]	1999	USA	P	35	Any	23.16	1.50 (0.30 to 6.30)	0.18 (0.34)
Stockwell *et al* [89]	1992	USA	CC	210	Any	23.16	1.60 (0.80 to 3.00)	0.20 (0.15)
Sun *et al* [90]	1996	China	CC	230	Any	18.18	1.16 (0.80 to 1.69)	0.08 (0.11)
Svensson *et al* [91]	1989	Sweden	CC	38	Any	18.18	1.36 (0.53 to 3.49)	0.17 (0.26)
Torres-Duran *et al* [92]	2014	Spain	CC	153	Any	18.18	0.71 (0.46 to 1.10)	-0.19 (0.12)
Trichopoulos *et al* [93]	1983	Greece	CC	77	1-10	7.08	0.57 (0.12 to 2.63)	0.26 (0.11)+
					11-20	17.67	2.50 (1.26 to 4.94)	
					21-30	25.88	3.97 (1.31 to 12.0)	
					31+	43.06	1.87 (0.70 to 5.01)	
Wang *et al* [94]	1996	China	CC	82	Any	18.18	2.53 (1.26 to 5.10)	0.51 (0.20)++
Wang *et al* [95]	1996	China	CC	135	1-9	4.85	0.35 (0.11 to 1.16)	0.17 (0.12)
					10-19	12.73	1.35 (0.74 to 2.45)	
					20+	26.03	1.40 (0.76 to 2.57)	
Wang *et al* [96]	2000	China	CC	200	Any	18.18	1.03 (0.60 to 1.70)	0.02 (0.15)
Wen *et al* [97]	2006	China	P	106	Any	18.18	1.09 (0.74 to 1.61)	0.05 (0.11)
WHI-OS [98]	2013	USA	P	200	Any	23.16	0.88 (0.52 to 1.49)	-0.06 (0.12)
Wu *et al* [99]	1985	USA	CC	31	Any	23.16	1.20 (0.50 to 3.30)	0.08 (0.21)
Wu-Williams *et al* [14]	1990	China	CC	417	Any	18.18	0.70 (0.60 to 0.90)	-0.20 (0.06)---
Yang *et al* [100]	2008	USA	CC	74	Any	23.16	2.00 (1.10 to 3.63)	0.30 (0.13)+
Yu *et al* [101]	2006	Hong Kong	CC	213	Any	18.18	1.35 (0.70 to 2.63)	0.17 (0.19)
Zaridze *et al* [102]	1998	Russia	CC	189	1-10	7.08	1.66 (1.09 to 2.52)	0.13 (0.11)
					11+	22.93	1.35 (0.84 to 2.18)	
Zatloukal *et al* [103]	2003	Czech Republic	CC	84	Any	18.18	0.48 (0.21 to 1.09)[ℓ]	-0.40 (0.23)
Zheng *et al* [104]	1997	China	CC	69	Any	18.18	2.52 (1.09 to 5.85)	0.51 (0.24)+
Zhong *et al* [105]	1999	China	CC	504	1-10	7.08	1.40 (0.90 to 2.20)	-0.01 (0.09)
					11-20	17.67	0.90 (0.60 to 1.40)	
					21+	31.83	1.40 (0.70 to 2.60)	

[a] P = prospective; CC = case-control
[b] Number of lung cancer cases in female lifelong nonsmokers; numbers with data by amount smoked may total less than this
[c] RR = Relative risk of lung cancer in nonsmoking females (baseline = husband nonsmoker); 95% CI = 95% confidence interval for RR
[d] β = Slope of relationship of log RR to dose (in units of 10 cigarettes/day by the husband); SE(β) = standard error of β,
Significance is shown by –,+: P<0.05; --,++: P<0.01; ---,+++: P<0.001, with – representing a negative relationship, + representing a positive relationship
[e] Smoked in presence of the spouse
[f] Based on data for two control groups combined
[g] Lowest level includes exsmokers
[h] Relative risks were presented for sexes combined and assumed to apply to each sex separately, with confidence intervals weighted according to number of subjects by sex
[j] Smoked in marriage (including exsmokers)
[k] Based on data for hospital controls. Data for population controls not used as non-response rate very high
[ℓ] Based on data for two pathological groups of lung cancer combined
[m] Based on data from earlier publication by Hosseini et al [133]

Table 2 Meta-analyses of the relationship of the number of cigarettes smoked per day by the husband (or near equivalent) to risk of lung cancer in lifelong nonsmoking females (without adjustment for confounding[a] or correction for misclassification of active smoking by the subject)

		Fixed-effects meta-analysis		Random-effects meta-analysis
Studies	N	RR (95% CI)[b]	Heterogeneity chisquared (d.f.)p[c]	RR (95% CI)[b]
All	93	1.09 (1.07 to 1.11)	169.93 (92) ***	1.10 (1.07 to 1.14)
North America	29	1.04 (1.01 to 1.08)	50.82 (28) **	1.04 (0.98 to 1.10)
Europe and New Zealand	20	1.06 (1.00 to 1.12)	20.42 (19) NS	1.06 (1.00 to 1.13)
China (including Hong Kong and Lim[68])	27	1.11 (1.06 to 1.16)	75.70 (26) ***	1.17 (1.08 to 1.26)
Rest of Asia	17	1.14 (1.09 to 1.19)	11.54 (16) NS	1.14 (1.09 to 1.19)
Heterogeneity between levels			11.45 (3) **	
North America, Europe and NZ	49	1.05 (1.02 to 1.08)	71.34 (48) *	1.05 (1.00 to 1.09)
Asia	44	1.12 (1.09 to 1.16)	88.19 (43) ***	1.16 (1.10 to 1.22)
Heterogeneity between levels			10.40 (1) **	
Published in 1980s	26	1.15 (1.09 to 1.21)	21.75 (25) NS	1.15 (1.09 to 1.21)
Published in 1990s	27	1.04 (1.00 to 1.08)	51.27 (26) **	1.06 (1.00 to 1.12)
Published in 2000s	26	1.12 (1.06 to 1.18)	30.46 (25) NS	1.12 (1.06 to 1.19)
Published in 2010s	14	1.10 (1.06 to 1.14)	54.15 (13) ***	1.07 (0.97 to 1.19)
Heterogeneity between levels			12.30 (3) **	
<100 cases	49	1.14 (1.08 to 1.20)	58.57 (48) NS	1.14 (1.08 to 1.21)
100-199 cases	22	1.07 (1.02 to 1.11)	48.48 (21) ***	1.06 (0.99 to 1.14)
200-399 cases	13	1.17 (1.11 to 1.24)	18.35 (12) NS	1.18 (1.10 to 1.26)
400+ cases	9	1.05 (1.02 to 1.09)	29.04 (8) ***	1.04 (0.98 to 1.11)
Heterogeneity between levels			15.50 (3) **	
With dose-response data[d]	24	1.12 (1.07 to 1.16)	27.81 (23) NS	1.12 (1.07 to 1.18)
Without dose-response data	69	1.08 (1.05 to 1.11)	139.99 (68) ***	1.09 (1.04 to 1.14)
Heterogeneity between levels			2.13 (1) NS	
With age adjustment[e]	75	1.08 (1.05 to 1.10)	132.83 (74) ***	1.08 (1.05 to 1.12)
Without age adjustment	18	1.18 (1.11 to 1.26)	29.70 (17) *	1.21 (1.10 to 1.33)
Heterogeneity between levels			7.39 (1) **	
Case-control studies	77	1.09 (1.06 to 1.11)	160.69 (76) ***	1.11 (1.06 to 1.15)
Prospective studies	16	1.08 (1.02 to 1.15)	9.18 (15) NS	1.08 (1.02 to 1.15)
Heterogeneity between levels			0.06 (1) NS	

[a] Other than the adjustments made for confounding by the authors of the studies
[b] Relative risk per 10 cigarettes/day smoked by the husband
[c] d.f. = degrees of freedom; p is coded as *** p<0.001, ** p<0.01, * p<0.05, (*) p<0.1, NS p≥0.1
[d] Specifically for number of cigarettes smoked by the husband
[e] Or matching (within nonsmokers)

Table 3 Relationship of fruit and vegetable consumption to lung cancer risk in lifelong nonsmoking females

Study [ref]	Location	Smoking habits	Exposure index	β[a]	Z[b]
Agudo *et al* [134]	Spain	never	vegetables	-0.1293	-0.7839
Alavanja *et al* [111]	USA	never/ex 15+y	vegetables	-0.0071	-0.1232
			fruit	+0.0124	+0.0607
Candelora *et al* [135]	USA	never	vegetables	-0.4937	-3.6284
			fruit	-0.2512	-1.9734
Feskanich *et al* [136]	USA	never	vegetables	-0.0284	-0.1704
			fruit	-0.4945	-2.8116
Hirayama [46]	Japan	never	vegetables	-0.1608	-1.7378
Hu *et al* [137]	Canada	never	vegetables	+0.1246	+0.8696
			fruit	+0.0417	+0.3536
Kalandidi *et al* [57]	Greece	never	vegetables	+0.1166	+0.7738
			fruit	-0.2598	-1.7132
Ko *et al* [106]	Taiwan	never	vegetables	-0.5116	-2.5910
			fruit	0.0000	0.0000[c]
Koo [138]	China	never	vegetables	-0.2189	-1.3982
			fruit	-0.4413	-2.7219
Kreuzer *et al* [139]	Germany	never	vegetables	-0.2398	-2.5065
			fruit	-0.0577	-0.5616
Mayne *et al* [140]	USA	never/ex 10+y	vegetables	-0.2712	-2.3748
			fruit	-0.2381	-2.2463
Ozasa *et al* [141]	Japan	never	vegetables	+0.1388	+1.0966
			fruit	+0.1051	+0.6633
Rachtan [142]	Poland	never	vegetables[d]	-1.3832	-2.0906
			fruit	-0.5812	-2.0208
Seow *et al* [132]	Singapore	never	vegetables	-0.1111	-1.1287
			fruit	-0.2357	-2.3706
Shimizu *et al* [86]	Japan	never	vegetables	-0.0630	-0.3154
			fruit	+0.0895	+0.4230
Steinmetz *et al* [143]	Japan	never	vegetables	+0.0848	+0.3146
			fruit	+0.0229	+0.0811

[a] Slope of dose relationship; exp (β) is the increase in risk per SD of exposure
[b] Z = β/SE(β) and is an approximate normal deviate
[c] SE(β) = 0.1858
[d] Data for other vegetables used rather than data for carrots (β = -1.4429, Z = -3.6324)

Table 4 Random-effects meta-analyses of the relationship of vegetable and fruit consumption to risk of lung cancer in lifelong nonsmoking females[a]

Exposure	Studies	N	RR (95% CI)[b]
Vegetable consumption	All	16	0.88 (0.80 to 0.97)
	North America and Europe	10	0.88 (0.77 to 1.02)
	Asia	6	0.88 (0.76 to 1.01)
	Excluding studies of never smokers plus long-term exsmokers	14	0.88 (0.78 to 0.98)
Fruit consumption	All	14	0.86 (0.78 to 0.96)
	North America and Europe	9	0.86 (0.76 to 0.97)
	Asia	5	0.89 (0.73 to 1.08)
	Excluding studies of never smokers plus long-term exsmokers	12	0.85 (0.76 to 0.96)

[a] Includes two studies of never smokers plus long-term exsmokers (see Table 3)
[b] Relative risk per standard deviation of exposure

Table 5 Relationship of dietary fat consumption to lung cancer risk in lifelong nonsmoking females

Study [ref]	Country	Smoking habits	Exposure index	β[a]	Z[b]
Alavanja *et al* [111], Swanson *et al* [112]	USA	never/ ex 15+ years	saturated fat	+0.2666	+2.9136
Hu *et al* [144]	Canada	never	French fries or fried potatoes	+0.2543	+2.0330
Kalandidi *et al* [57]	Greece	never	fats and oils	-0.0796	-0.4742
Ozasa *et al* [141]	Japan	never	fried foods	+0.2567	+1.8884
Swanson *et al* [145]	USA	never/ ex 15+ years	saturated fat	-0.0376	-0.1849
Wu *et al* [113]	USA	never	total fat	+0.1989	+1.1231

[a] Slope of dose-relationship; exp(β)
[b] Z = β/SE(β) and is an approximate normal deviate

Table 6 Random-effects meta-analyses of the relationship of dietary fat consumption to risk of lung cancer in lifelong nonsmoking females[a]

Studies	N	RR (95% CI)[b]
All	6	1.22 (1.09 to 1.36)
USA and Canada	4	1.25 (1.10 to 1.42)
Other countries	2	1.11 (0.80 to 1.54)
Excluding studies of never smokers plus occasional smokers	4	1.20 (1.04 to 1.39)

[a] Includes two studies of never smokers plus long-term exsmokers (see Table 5)
[b] Relative risk per standard deviation of exposure

Table 7 Relationship of years of education to lung cancer risk in lifelong nonsmoking females

Study [ref]	Country	Smoking habits	β[a]	Z[b]
Boffetta *et al* [20]	West Europe	never	-0.2257	-5.0111
Fontham *et al* [36]	USA	never	-0.1390	-6.0108
Kabat and Wynder [55]	USA	never	-0.0227	-0.3781
Kabat *et al* [56]	USA	never	-0.0274	-0.4661
Kalandidi *et al* [57]	Greece	never	+0.0478	0.8327
Ko *et al* [106]	Taiwan	never	-0.0484	-1.1503
Mao *et al* [146]	Canada	never	-0.0653	-2.0365
Sobue *et al* [87]	Japan	never	-0.1172	-3.7846
Stockwell *et al* [89]	USA	never	-0.0902	-2.1399
Wichmann *et al* [147][c]	Germany	never/occasional	+0.0212	+0.1352
Wichmann *et al* [147][d]	Germany	never/occasional	-0.1280	-2.3385
Zaridze *et al* [102]	Russia	never	-0.1425	-2.3243

[a] Slope of dose-response relationship; exp(β) is the increase in risk per year of education
[b] Z = β/SE(β) and is an approximate normal deviate
[c] Data for study BIPS
[d] Data for study GSF

Table 8 Random-effects meta-analysis of the relationship of education to risk of lung cancer in lifelong nonsmoking females[a]

Studies	N	RR (95% CI)[b]
All	12	0.91 (0.88 to 0.95)
USA and Canada	5	0.92 (0.88 to 0.96)
Europe	5	0.90 (0.81 to 1.00)
Asia	2	0.92 (0.86 to 0.98)
Excluding studies of never smokers plus occasional smokers	10	0.91 (0.88 to 0.95)

[a] Includes two studies of never smokers plus occasional smokers (see Table 7)
[b] Relative risk per additional year of education

Table 9 Differences in fruit and vegetable consumption in SDs between lifelong nonsmoking females exposed or unexposed to ETS at home

Study [ref]	Location	ETS source	Fruit or vegetables	δ[a]	N_u[b]	N_e[c]
Published papers						
Cardenas *et al* [27]	USA	spouse	vegetables	-0.0852	71,634	104,686
Forastiere *et al* [118]	Italy	spouse	vegetables[d]	-0.2022	725	1,208
			fruit	+0.1043	722	1,229
Hirayama [46]	Japan	spouse	vegetables	+0.0245	21,895	69,645
Hirayama [148]	Japan	spouse	vegetables	-0.0240	456	1,512
Koo *et al* [149]	Hong Kong	spouse	vegetables	+0.3532	419	111
			fruit	-0.3009	419	111
	Japan	spouse	vegetables	-0.0863	8,146	4,901
			fruit	-0.0818	8,146	4,901
	Sweden	spouse	vegetables	-0.9022	69	18
			fruit	-0.6795	69	18
	USA	spouse	vegetables	+0.2859	60	84
Matanoski *et al* [150]	USA	spouse	vegetables	-0.0449	1,214	2,124
Reynolds *et al* [151]	USA	cohabitant	vegetables	-0.0582	8,388[l]	20,413[l]
			fruit	-0.0871	9,665[l]	22,848[l]
Thornton *et al* [120][e]	UK	cohabitant	vegetables	+0.0527	1673	678
			fruit	-0.0561	1673	678
Public databases						
HALS2[f]	UK	cohabitant	vegetables	+0.0447	974	291
			fruit	-0.1256	974	291
HSE93[g]	UK	cohabitant	vegetables	-0.0851	3007	657
			fruit	-0.0887	3007	657
HULS[h]	Hungary	cohabitant	vegetables	-0.0718	643	305
			fruit	-0.0446	643	305
NHIS2000[j]	USA	cohabitant	vegetables	-0.1170	4564	532
			fruit	-0.0846	4567	533
NHANES III[k]	USA	cohabitant	vegetables	-0.2238	2555	616
			fruit	-0.0760	2555	616

[a] δ = SD difference in fruit or vegetable consumption associated with ETS exposure at home
[b] N_u = number of lifelong nonsmokers unexposed to ETS
[c] N_e = number of lifelong nonsmokers exposed to ETS
[d] Data for fresh vegetables rather than for cooked vegetables (δ = -0.1294)
[e] The source reference presented results for sexes combined; results for females were provided by J Hamling [personal communication]
[f] UK Health and Lifestyle Study 2 [114]. Estimates provided by J Hamling [personal communication]
[g] Health Survey for England 1993 [115]. Estimates provided by J Hamling [personal communication]
[h] Hungarian Lifestyle Survey. Estimates provided by J Hamling [personal communication]
[j] National Health Interview Survey 2000 [116]
[k] National Health and Nutrition Examination Survey III [117]
[l] Estimated

Table 10 Combined estimates of the differences, δ, in vegetable and fruit consumption (in SDs) between lifelong nonsmoking females exposed or unexposed to ETS at home

			δ (SE(δ))		
Dietary index	Studies	N	Random-effects	Unweighted	Weighted
Vegetable consumption	All	16	-0.0559 (0.0211)	-0.0712 (0.0672)	-0.0525 (0.0149)
	USA	6	-0.0866 (0.0191)	-0.0405 (0.0703)	-0.0835 (0.0101)
	Europe	6	-0.0892 (0.0596)	-0.1940 (0.1468)	-0.0653 (0.0535)
	USA+Europe	12	-0.0813 (0.0195)	-0.1173 (0.0810)	-0.0827 (0.0102)
	Asia	4	0.0185 (0.0471)	0.0669 (0.0981)	0.0117 (0.0252)
Fruit consumption	All	11	-0.0733 (0.0197)	-0.1382 (0.0610)	-0.0812 (0.0142)
	USA	3	-0.0862 (0.0113)	-0.0826 (0.0034)	-0.0859 (0.0021)
	Europe	6	-0.0581 (0.0481)	-0.1484 (0.1110)	-0.0503 (0.0427)
	USA+Europe	9	-0.0634 (0.0249)	-0.1264 (0.0725)	-0.0788 (0.0160)
	Asia	2	-0.1661 (0.1066)	-0.1913 (0.1096)	-0.0904 (0.0424)

Table 11 Differences in dietary fat consumption in SDs between lifelong nonsmoking females exposed or unexposed to ETS at home

Study [ref]	Location	ETS source	Index of fat consumption	δ^a	N_u[b]	N_e[c]
<u>Published papers</u>						
Cardenas *et al* [27]	USA	spouse	dietary fat	-0.0307	71,634	104,686
Forastiere *et al* [118]	Italy	spouse	meat	-0.0837	722	1,210
Koo *et al* [149]	Hong Kong	spouse	fried food	+0.3532	419	111
	Sweden	spouse	fried potatoes, french fries	+0.8087	69	18
	USA	spouse	fat	+0.3578	60	84
Reynolds *et al* [151]	USA	cohabitant	meat	+0.0570	20,950[k]	21,287[k]
Thornton *et al* [120][d]	UK	cohabitant	fried foods	+0.1898	1,673	678
<u>Public databases</u>						
HALS2[e]	UK	cohabitant	fried foods	+0.0782	974	291
HSE93[f]	UK	cohabitant	fried foods	+0.0660	3007	657
HULS[g]	Hungary	cohabitant	fried foods	+0.2551	643	305
NHIS2000[h]	USA	cohabitant	bacon,fried potatoes,chips	+0.2218	4538	525
NHANESIII[j]	USA	cohabitant	bacon,sausages, processed meats and eggs	+0.2337	2555	616

[a] δ = SD difference in dietary fat consumption associated with ETS exposure at home
[b] N_u = number of lifelong nonsmokers unexposed to ETS
[c] N_e = number of lifelong nonsmokers exposed to ETS
[d] The source reference presented results for sexes combined; results for females were provided by J Hamling [personal communication]
[e] UK Health and Lifestyle Study 2 [114]. Estimates provided by J Hamling [personal communication]
[f] Health Survey for England 1993 [115]. Estimates provided by J Hamling [personal communication]
[g] Hungarian Lifestyle Survey. Estimates provided by J Hamling [personal communication]
[h] National Health Interview Survey 2000 [116]
[j] National Health and Nutrition Examination Survey III [117]
[k] Estimated

Table 12 Combined estimates of the differences, δ, in dietary fat consumption (in SDs) between lifelong nonsmoking females exposed or unexposed to ETS at home

		δ (SE(δ))		
Studies	N	Random-effects	Unweighted	Weighted
All	12	0.1310 (0.0317)	0.2089 (0.0680)	0.0001 (0.0200)
USA	5	0.1188 (0.0420)	0.1679 (0.0689)	-0.0048 (0.8745)
Europe	6	0.1302 (0.0633)	0.2190 (0.1271)	0.0917 (0.0549)
USA+Europe	11	0.1179 (0.0319)	0.1958 (0.0730)	-0.0006 (0.0204)
Asia	1	0.3532	0.3532	0.3532

Table 13 Differences in years of education between lifelong nonsmoking females exposed or unexposed to ETS at home

Study [ref]	Location	ETS source	δ[a]	N_u[b]	N_e[c]
Published papers					
Cardenas *et al* [152]	USA	cohabitant	-0.3160	71,892	141,262
Curtin *et al* [153]	Switzerland	cohabitant	-0.1920	698	81
Enstrom and Kabat [33]	USA	spouse	-0.3300	7,339	18,603
Forastiere *et al* [118]	Italy	spouse	-0.6422	724	1,209
Koo *et al* [149]	Hong Kong	spouse	-0.5000	419	111
	USA	spouse	-0.4000	60	84
Matanoski *et al* [150]	USA	spouse	-0.5032	1,380	2,411
Thornton *et al* [120][d]	UK	cohabitant	-0.3950	1,673	678
Public databases					
HALS2[e]	UK	cohabitant	-0.3200	974	291
HSE93[f]	UK	cohabitant	-0.5150	3007	657
HULS[g]	Hungary	cohabitant	-0.4600	643	305
NHIS2000[h]	USA	cohabitant	-0.9940	4515	523
NHANES III[j]	USA	cohabitant	-1.1239	2543	612

[a] δ = years difference in education associated with ETS exposure at home
[b] N_u = number of lifelong nonsmokers unexposed to ETS
[c] N_e = number of lifelong nonsmokers exposed to ETS
[d] The source reference presented results for sexes combined; results for females were provided by J Hamling [personal communication] – see also text in section 6.4
[e] UK Health and Lifestyle Study 2 [114]. Estimates provided by J Hamling [personal communication]
[f] Health Survey for England 1993 [115]. Estimates provided by J Hamling [personal communication]
[g] Hungarian Lifestyle Survey. Estimates provided by J Hamling [personal communication]
[h] National Health Interview Survey 2000 [116]
[j] National Health and Nutrition Examination Survey III [117]

Table 14 Combined estimates of the difference, δ, in years of education between lifelong nonsmoking females exposed or unexposed to ETS at home

		δ (SE(δ))		
Studies	N	Random-effects	Unweighted	Weighted
All	13	-0.5337 (0.0634)	-0.5147 (0.0744)	-0.3493 (0.0384)
USA	6	-0.6083 (0.0946)	-0.6112 (0.1451)	-0.3441 (0.0586)
Europe	6	-0.4752 (0.0548)	-0.4207 (0.0639)	-0.4614 (0.0551)
USA+Europe	12	-0.5331 (0.0651)	-0.5159 (0.0809)	-0.3490 (0.0401)
Asia	1	-0.5000	-0.5000	-0.5000

Table 15 Confounder Data used for adjustment

STUDY	Fruit[a]	Vegetable[a]	Fat[a]	Education[a]	Age	[Ref]	Adjustments
Akiba	0	0	0	0	1	17	City, vital status, participation in medical examinations.
Al-Zoughool	0	0	0	1	0	18	Median income, and proxy (if applicable).
Asomaning	0	0	0	0	0	19	
Boffetta	0	0	0	0	1	20	Study centre.
Boffetta 2	0	0	0	0	1	21	centre
Brenner	0	0	0	0	0	22	
Brownson 1	0	0	0	1	1	23	Education.
Brownson 2	0	0	0	0	1	24	History of lung disease.
Buffler	0	0	0	0	0	25	
Butler	0	0	0	0	1	26	
Cardenas	0	1	1	2	1	27	Race, education, blue collar employment, vegetable consumption, fat consumption, occupational exposure to asbestos, history of chronic lung disease.
Chan	0	0	0	0	0	28	
Choi	0	0	0	0	0	29	
Correa	0	0	0	0	0	30	
De Waard	0	0	0	0	0	31	
Du	0	0	0	0	1	32	Residence.
Enstrom	1	0	0	2	1	33	race; education; exercise; body mass index; urbanisation; fruit or fruit juice intake; health status
EPIC Adulthood	1	1	1	2	1	34	country; school years; energy intake; fruit and vegetable consumption; physical activity
Fang	0	1	0	1	1	35	Consumption of internal organs of animals, occupational exposure to dust, bad ventilation at work, consumption of vegetables, taking vitamins, income level, age of first procreation.
Fontham	1	1	0	2	1	36	Race, area, education, fruits, vegetables and supplemental vitamin index, family history of not available for DR lung cancer, employment in high risk occupations.
Franco-Marina	0	0	0	0	0	37	Access to health care.
Gallegos	0	0	0	0	0	38	
Gao	0	0	0	2	1	39	Ethnicity.
Garfinkel 1	0	0	0	0	1	40	
Garfinkel 2	0	0	0	0	1	41	Hospital.
GELAC study	0	0	0	2	1	42	Exposure from spouse: Education, ETS exposure from father, ETS exposure from mother.
Geng	0	0	0	0	0	7	
Gorlova	0	0	0	1	1	43	Race, education, socio-economic status.
He	0	0	2	2	1	44	Education, marital status, occupation, alcohol, BMI, diastolic BP, triglycerides, cholesterol
Hill (study 1)	0	0	0	0	1	45	Ethnicity.
Hill (study 2)	0	0	0	3	1	45	Ethnicity, marital status, SES, household car access, tenure, small-area deprivation index.
Hirayama	0	0	0	0	1	46	
Hole	0	0	0	0	1	47	
Humble 1	0	0	0	0	2	48	not available for DR
IARC: Kreuzer	0	0	0	0	1	16	region
ILCCO	0	0	0	0	1	49	Race, study.
Inoue	0	0	0	0	1	50	
Janerich	0	0	0	0	1	51	Years of schooling, interviewer, total energy intake, fruit consumption.
Jee	0	1	0	3	1	52	socioeconomic, residence, husbands veg consumption & occupation
Jiang	1	1	0	0	1	53	BMI, moved to a renovated home, family history of cancer: first degree relatives and second/third degree relatives, eating fruit and/or vegetables, exercise, mental/psychological factors: lack of emotional regulation, heavy work pressure, poor sleep quality.

Johnson	1	1	0	2	1	54	province; education; total fruit and vegetables
Kabat 1	0	0	0	0	1	55	Race, hospital.
Kabat 2	0	0	0	2	1	56	Race, hospital, date of interview, years of education.
Kalandidi	0	0	0	0	2	57	
Kiyohara	0	0	0	0	0	58	
Koo	0	0	0	2	1	59	Live births, years since exposure ceased, schooling.
Kurahashi	0	0	0	0	1	60	Study area, alcohol, family history of lung cancer, menopausal status.
Lagarde	0	0	0	3	1	61	z radon; SES; occupation; residence; urban/rural
Lam W	0	0	0	0	0	62	
Lam T	0	0	0	0	0	63	
Layard	0	0	0	0	2	64	Race.
Lee	0	0	0	0	1	65	Income, occupation.
Lee C-H	0	0	0	2	1	66	residential area; education; occupation; tuberculosis; cooking fumes; fume extractor status.
Liang	0	0	0	0	0	67	
Lim	0	0	0	0	0	68	
Lin	0	0	0	2	0	69	Education, eggs, fruit, tea, cooking oil fumes, age at menarche, physical activity.
Liu Z	0	0	0	0	1	70	Age of starting to cook, years of cooking.
Liu Q	0	0	0	2	0	71	Education, occupation, living area.
Lopez-Cima	0	0	0	0	0	72	
Malats	0	0	0	0	1	73	Centre
Masjedi	0	0	0	0	0	74	
McGhee	0	0	0	2	1	75	Education
Nishino	1	1	1	0	1	76	Alcohol; green and yellow vegetables; fruit; meat; study area; history of respiratory disease
Ohno	0	0	0	0	1	77	Research institution (region)
Pershagen	0	0	0	0	1	78	Vital status.
Rapiti	0	0	0	0	1	79	Residence; religion
Ren	0	0	0	0	1	80	Family history of cancer, fuel smoke exposure, cooking oil fume exposure, interaction of p53 and MDM2 genotypes
Rylander	0	0	0	0	1	81	
Schoenberg	0	1	0	2	1	82	Race, education, occupation, vegetables, vital status
Schwartz	0	0	0	0	1	83	Race.
Seki	0	0	0	0	1	84	Year of recruitment, area of residence, referral status, occupation, alcohol, family history of lung cancer.
Shen	0	0	0	0	1	85	
Shimizu	0	0	0	0	1	86	Hospital.
Sobue	0	0	0	2	1	87	Education.
Spieze	0	0	0	0	1	88	
Stockwell	0	0	0	2	1	89	Race, education.
Sun	0	0	0	2	1	90	Education.
Svensson	0	0	0	0	1	91	Residence, direct/surrogate interview.
Torres-Duran	0	0	0	0	1	92	Radon.
Trichopoulos	0	0	0	0	0	93	
Wang S	0	0	0	0	0	94	
Wang T	0	0	0	0	1	95	
Wang L	0	0	0	1	1	96	Ownership of colour TV; number of cattle; prefecture; childhood ETS exposure
Wen	1	1	0	2	1	97	Education, occupation, income, physical activity, BMI, intake of meat, vegetables, fruit.
WHI-OS	0	0	0	0	0	98	
Wu	0	0	0	0	1	99	
Wu-Williams	0	0	0	2	1	14	Education, study area.
Yang	0	0	0	0	1	100	Any exposure: COPD, a1ATD carrier
Yu	1	1	0	2	1	101	Education, employment, history of lung diseases, family history of lung cancer, radon, kerosene use, firewood use, incense burning, mosquito coil use, years of cooking, orange/yellow vegetables, dark green vegetables, meats, citrus fruits, salted fish, pickled vegetables, multivitamins, coffee, tea.
Zaridze	0	0	0	2	1	102	Education.
Zatloukal	0	0	0	2	1	103	Residence; education

Zheng	0	0	0	0	1	104	
Zhong	1	0	0	1	1	105	Income; vitamin C; respondent status; smokiness of kitchen; family history of lung cancer; potentially high risk occupation

a NOTES:

FRU = 1 DOSE-RESPONSE ANALYSIS ADJUSTED FOR FRUIT

VEG = 1 " " " " VEGETABLES

FAT = 1 " " " " FAT

= 2 " " " " CHOLESTEROL

EDU = 1 " " " " INCOME

= 2 " " " " EDUCATION

= 3 " " " " SOCIO-ECONOMIC STATUS

AGE = 0 NO ADJUSTMENT FOR AGE

= 1 ADJUSTMENT FOR AGE IN DOSE-RESPONSE ANALYSIS

= 2 ADJUSTMENT FOR AGE IN 2 x 2 ANALYSIS BUT NOT DOSE RESPONSE ANALYSIS

CON = 1 US/CANADA

= 2 EUROPE

= 3 ASIA

Table 16 Random-effects meta-analyses of the relationship of the number of cigarettes smoked per day by the husband (or nearest equivalent) to risk of lung cancer in lifelong nonsmoking females (with and without adjustment for confounding by fruit, vegetable and dietary fat consumption and by education, but with no correction for misclassification of active smoking by the subject)

Studies	N	Unadjusted for confounding RR (95% CI)[a]	Adjusted for confounding RR (95% CI)[a]	Bias[b]
All	93	**1.102 (1.065 to 1.140)**	**1.062 (1.027 to 1.099)**	1.037
North America	29	1.037 (0.977 to 1.101)	1.006 (0.946 to 1.070)	1.031
Europe and New Zealand	20	1.060 (0.995 to 1.128)	1.020 (0.956 to 1.088)	1.039
China (including Hong Kong and Lim[68])	27	1.169 (1.082 to 1.263)	1.127 (1.041 to 1.219)	1.038
Rest of Asia	17	1.142 (1.095 to 1.191)	1.094 (1.050 to 1.141)	1.043
North America, Europe and New Zealand	49	1.046 (1.001 to 1.094)	1.012 (0.967 to 1.059)	1.034
Asia	44	1.158 (1.104 to 1.216)	1.113 (1.060 to 1.170)	1.040
Published in 1980s	26	1.148 (1.092 to 1.207)	1.105 (1.052 to 1.162)	1.038
Published in 1990s	27	1.063 (1.004 to 1.125)	1.025 (0.967 to 1.087)	1.036
Published in 2000s	26	1.123 (1.056 to 1.194)	1.085 (1.020 to 1.155)	1.034
Published in 2010s	14	1.073 (0.970 to 1.188)	1.032 (0.932 to 1.143)	1.040
<100 cases	49	1.143 (1.077 to 1.213)	1.101 (1.036 to 1.169)	1.038
100-199 cases	22	1.062 (0.993 to 1.137)	1.025 (0.957 to 1.098)	1.036
200-399 cases	13	1.176 (1.097 to 1.261)	1.134 (1.058 to 1.216)	1.037
400+ cases	9	1.041 (0.976 to 1.111)	1.002 (0.938 to 1.070)	1.040
With dose-response data[c]	24	1.123 (1.072 to 1.176)	1.082 (1.032 to 1.134)	1.038
Without dose-response data	69	1.091 (1.044 to 1.139)	1.053 (1.007 to 1.100)	1.036
With age adjustment[d]	75	1.084 (1.046 to 1.123)	1.044 (1.008 to 1.082)	1.038
Without age adjustment	18	1.211 (1.101 to 1.331)	1.168 (1.061 to 1.285)	1.037
Case-control studies	77	1.106 (1.064 to 1.150)	1.066 (1.025 to 1.109)	1.037
Prospective studies	16	1.081 (1.021 to 1.145)	1.043 (0.985 to 1.105)	1.036

[a] Relative risk per 10 cigarettes/day smoked by the husband
[b] Bias = RR unadjusted for confounding/RR adjusted for confounding (RRs to 4 decimal places)
[c] Specifically for number of cigarettes smoked by the husband
[d] Or matching (within nonsmokers)

Table 17 Effect of adjustment for specific confounding variables on the relationship of the number of cigarettes smoked per day by the husband (or nearest equivalent) to risk of lung cancer in lifelong nonsmoking females

Studies	N	Adjustment	RR (95% CI)[a]	Bias[b]
All	93	None[c]	**1.103 (1.067 to 1.141)**	1
		Fruit	1.097 (1.061 to 1.135)	1.005
		Vegetables	1.099 (1.063 to 1.137)	1.004
		Dietary fat or cholesterol	1.089 (1.053 to 1.127)	1.013
		Education	1.077 (1.041 to 1.114)	1.024
		All four factors	1.062 (1.027 to 1.099)	1.039
North America, Europe and New Zealand	49	None[c]	1.049 (1.004 to 1.097)	1
		Fruit	1.044 (0.998 to 1.091)	1.005
		Vegetables	1.046 (1.000 to 1.093)	1.003
		Dietary fat or cholesterol	1.036 (0.991 to 1.084)	1.012
		Education	1.025 (0.980 to 1.073)	1.023
		All four factors	1.012 (0.967 to 1.059)	1.037
Asia	44	None[c]	1.159 (1.104 to 1.216)	1
		Fruit	1.152 (1.097 to 1.209)	1.006
		Vegetables	1.154 (1.100 to 1.211)	1.004
		Dietary fat or cholesterol	1.143 (1.089 to 1.200)	1.014
		Education	1.130 (1.076 to 1.186)	1.025
		All four factors	1.113 (1.060 to 1.170)	1.041

[a] Relative risk per 10 cigarettes/day smoked by the husband
[b] Bias = RR adjusted for no confounders/RR with adjustment shown
[c] 'Back-corrected' to remove effect of adjustment for those studies which reported estimates adjusted for fruit, vegetables, dietary fat and education

Table 18 Active smoking data used in misclassification analyses

Study [ref]	Year	Location	Type[a]	Smokers among controls (%)	RR active smoking	Source[b]
Akiba *et al* [17]	1986	Japan	CC	20.59	2.38	1
Al-Zoughool *et al*[18]	2013	Canada	CC	50.81	12.70	7[154]
Asomaning[19]	2008	USA	CC	59.30	5.84	1
Boffetta *et al* [20]	1998	West Europe	CC	29.00	5.00	2
Boffetta *et al* [21]	1999	Europe	CC	29.00	5.00	2
Brenner *et al*[22]	2010	Canada	CC	42.88	1.53	1
Brownson *et al* [23]	1987	USA	CC	28.79	4.30	1
Brownson *et al* [24]	1992	USA	CC	43.00	8.00	4
Buffler *et al* [25]	1984	USA	CC	58.74	7.06	1
Butler [26]	1988	USA	P	14.00	4.00	3
Cardenas *et al* [27]	1997	USA	P	44.66	6.77	1
Chan and Fung [28]	1982	Hong Kong	CC	26.46	3.48	1
Choi *et al* [29]	1989	Korea	CC	13.68	1.68	1
Correa *et al* [30]	1983	USA	CC	47.22	12.40	1
de Waard *et al* [31]	1995	Netherlands	CC	25.68	5.79	1
Du *et al* [32]	1993	China	CC	18.84	3.12	2
Enstrom and Kabat [33]	2003	USA	P	22.00	6.00	5
EPIC Adulthood [34]	2005	Western Europe	P	29.00	5.00	6
Fang *et al* [35]	2006	China	CC	18.84	3.12	2
Fontham *et al* [36]	1994	USA	CC	43.00	8.00	3
Franco-Marina *et al* [37]	2006	Mexico	CC	20.58	2.95	1
Gallegos *et al* [38]	2008	Mexico	CC	20.58	2.95	2
Gao *et al* [39]	1987	China	CC	25.74	2.77	1
Garfinkel [40]	1981	USA	P	22.00	3.58	3
Garfinkel *et al* [41]	1985	USA	CC	34.00	6.00	3
GELAC [42]	2013	Taiwan	CC	3.39	2.19	7[155]
Geng *et al* [7]	1988	China	CC	40.76	2.77	1
Gorlova *et al* [43]	2006	USA	CC	36.00	8.00	4
He *et al* [44]	2012	China	P	12.41	1.86	7[156]
Hill (Study 1) [45]	2007	New Zealand	P	24.08	6.36	7[157]
Hill (Study 2) [45]	2007	New Zealand	P	14.81	7.65	7[157]
Hirayama [46]	1984	Japan	P	15.95	3.19	1
Hole *et al* [47]	1989	Scotland	P	55.81	3.33	1
Humble *et al* [48]	1987	USA	CC	40.66	16.27	1
IARC (Kreuzer) [16]	2004	Germany	CC	35.31	3.62	1
ILCCO [49]	2014	International	CC	36.83	3.96	1
Inoue and Hirayama [50]	1988	Japan	CC	12.96	2.14	1
Janerich *et al* [51]	1990	USA	CC	42.00	8.00	3
Jee *et al* [52]	1999	Korea	P	13.68	1.68	2
Jiang *et al* [53]	2010	China	CC	18.84	3.12	2
Johnson *et al* [54]	2001	Canada	CC	49.78	8.75	1
Kabat and Wynder [55]	1984	USA	CC	42.00	5.90	3
Kabat *et al* [56]	1995	USA	CC	42.00	8.00	4
Kalandidi *et al* [57]	1990	Greece	CC	17.73	3.25	1
Kiyohara *et al* [58]	2011	Japan	CC	18.02	2.65	2
Koo *et al* [59]	1987	Hong Kong	CC	31.50	2.77	1
Kurahashi *et al* [60]	2008	Japan	P	18.02	2.65	2
Lagarde *et al* [61]	2001	Sweden	CC	40.17	5.70	2
Lam [62]	1985	Hong Kong	CC	22.16	4.12	1
Lam *et al* [63]	1987	Hong Kong	CC	24.04	3.84	1
Layard [64]	1994	USA	CC	34.00	6.00	4
Lee *et al* [65]	1986	UK	CC	60.42	4.63	1
Lee *et al* [66]	2000	Taiwan	CC	2.56	4.20	1
Liang *et al* [67]	2009	China	CC	18.84	3.12	2
Lim *et al* [68]	2012	Chinese women in Singapore	CC	12.86	4.21	1
Lin *et al* [69]	2012	China	CC	0.37	4.83	1
Liu *et al* [70]	1991	China	CC	18.84	3.12	2
Liu *et al* [71]	1993	China	CC	25.00	4.26	1
López-Cima *et al* [72]	2007	Spain	CC	11.17	3.10	2[158]
Malats *et al* [73]	2000	Europe/Brazil	CC	29.00	5.00	6
Masjedi *et al* [74]	2013	Iran	CC	7.03	2.16	7[133]
McGhee *et al* [75]	2005	Hong Kong	CC	22.70	3.46	2
Nishino *et al* [76]	2001	Japan	P	18.02	2.65	2
Ohno *et al* [77]	2002	Japan	CC	18.02	2.65	2
Pershagen *et al* [78]	1987	Sweden	CC	37.00	4.20	3
Rapiti *et al* [79]	1999	India	CC	20.00	2.47	2[159]

Ren *et al* [80]	2013	China	CC	18.84	3.12	2
Rylander and Axelsson [81]	2006	Sweden	CC	40.94	6.80	1
Schoenberg *et al* [82]	1989	USA	CC	50.00	8.50	1
Schwartz *et al* [83]	1996	USA	CC	42.00	8.00	4
Seki *et al* [84]	2013	Japan	CC	16.60	2.58	1
Shen *et al* [85]	1998	China	CC	18.84	3.12	2
Shimizu *et al* [86]	1988	Japan	CC	21.00	2.80	3
Sobue [87]	1990	Japan	CC	21.00	2.81	3
Speizer *et al* [88]	1999	USA	P	56.59	7.08	1
Stockwell *et al* [89]	1992	USA	CC	42.00	8.00	4
Sun *et al* [90]	1996	China	CC	18.84	3.12	2
Svensson *et al* [91]	1989	Sweden	CC	42.58	6.10	1
Torres-Duran *et al* [92]	2014	Spain	CC	11.17	3.10	2[158]
Trichopoulos *et al* [93]	1983	Greece	CC	10.36	2.81	1
Wang *et al* [94]	1996	China	CC	5.05	3.90	1
Wang *et al* [95]	1996	China	CC	18.84	3.12	2
Wang *et al* [96]	2000	China	CC	10.55	1.27	1
Wen *et al* [97]	2006	China	P	18.84	3.12	2
WHI-OS [98]	2013	USA	P	47.88	5.36	1
Wu *et al* [99]	1985	USA	CC	61.27	2.71	1
Wu-Williams *et al* [14]	1990	China	CC	36.83	2.22	1
Yang *et al* [100]	2008	USA	CC	46.59	7.15	2
Yu *et al* [101]	2006	Hong Kong	CC	9.32	3.08	1
Zaridze *et al* [102]	1998	Russia	CC	10.38	1.53	2[160],[161]
Zatloukal *et al* [103]	2003	Czech Republic	CC	45.26	5.82	1
Zheng *et al* [104]	1997	China	CC	18.84	3.12	2
Zhong *et al* [105]	1999	China	CC	18.84	3.12	2

[a] P = prospective; CC = case-control

[b] Source of active smoking RR : 1 = Given in source paper or directly calculated from it; 2 = Estimated from other studies in the same country; 3 = As given by EPA Table B-11 [162]; 4 = Comparable to EPA estimates; 5 = Estimated from Garfinkel studies; 6 = Estimate from Boffetta studies; 7 = Secondary Paper on same study

Table 19 Random-effects meta-analyses of the relationship of the number of cigarettes smoked per day by the husband (or nearest equivalent) to risk of lung cancer in lifelong nonsmoking females (adjusted for confounding by fruit, vegetables and dietary fat consumption and by education, with and without correction for misclassification of active smoking by the subject)

Studies	N	Uncorrected for misclassification RR (95% CI)[b]	Corrected for misclassification[a] RR (95% CI)[b]	Bias[c]
All	93	**1.062 (1.027 to 1.099)**	**1.032 (0.994 to 1.071)**	1.030
North America	29	1.006 (0.946 to 1.070)	0.957 (0.896 to 1.022)	1.051
Europe and New Zealand	20	1.020 (0.956 to 1.088)	1.003 (0.938 to 1.073)	1.017
China (including Hong Kong and Lim[68])	27	1.127 (1.041 to 1.219)	1.094 (1.006 to 1.191)	1.029
Rest of Asia	17	1.094 (1.050 to 1.141)	1.079 (1.033 to 1.127)	1.014
North America, Europe and New Zealand	49	1.012 (0.967 to 1.059)	0.974 (0.928 to 1.023)	1.039
Asia	44	1.113 (1.060 to 1.170)	1.089 (1.033 to 1.147)	1.023
Published in 1980s	26	1.105 (1.052 to 1.162)	1.075 (1.019 to 1.134)	1.028
Published in 1990s	27	1.025 (0.967 to 1.087)	0.988 (0.926 to 1.053)	1.038
Published in 2000s	26	1.085 (1.020 to 1.155)	1.061 (0.995 to 1.132)	1.023
Published in 2010s	14	1.032 (0.932 to 1.143)	1.014 (0.912 to 1.128)	1.017
<100 cases	49	1.101 (1.036 to 1.169)	1.072 (1.005 to 1.144)	1.027
100-199 cases	22	1.025 (0.957 to 1.098)	0.994 (0.926 to 1.066)	1.032
200-399 cases	13	1.134 (1.058 to 1.216)	1.111 (1.027 to 1.202)	1.021
400+ cases	9	1.002 (0.938 to 1.070)	0.966 (0.895 to 1.042)	1.037
With dose-response data[d]	24	1.082 (1.032 to 1.134)	1.053 (1.005 to 1.103)	1.028
Without dose-response data	69	1.053 (1.007 to 1.100)	1.021 (0.973 to 1.071)	1.031
With age adjustment[e]	75	1.044 (1.008 to 1.082)	1.015 (0.976 to 1.056)	1.029
Without age adjustment	18	1.168 (1.061 to 1.285)	1.131 (1.018 to 1.256)	1.033
Case-control studies	77	1.066 (1.025 to 1.109)	1.034 (0.991 to 1.080)	1.031
Prospective studies	16	1.043 (0.985 to 1.105)	1.018 (0.957 to 1.083)	1.024

[a] Using the Lee and Forey method [4] with an additive model and assuming a concordance ratio of 3 and misclassification rates of 2.5% for studies in North America and Europe and 10% for studies in Asia
[b] Relative risk per 10 cigarettes/day smoked by the husband
[c] Bias = uncorrected RR/corrected RR
[d] Specifically for number of cigarettes smoked by the husband
[e] Or matching (within nonsmokers)

Table 20 Lung cancer risk in lifelong nonsmoking females in relation to smoking by the husband (or nearest equivalent)

Study [ref]	Year	Location	Type[a]	Number of lung cancers[b]	RR (95% CI)[c]	β (SE(β))[d]
Akiba *et al* [17]	1986	Japan	CC	94	1.50 (0.93 to 2.76)	0.41 (0.28)
Al-Zoughool *et al*[18]	2013	Canada	CC	31	0.39 (0.15 to 0.98)	-0.94 (0.48)
Asomaning[19]	2008	USA	CC	82	0.93 (0.31 to 2.78)	-0.07 (0.56)
Boffetta *et al* [20]	1998	West Europe	CC	509	1.00 (0.50 to 1.90)	0.00 (0.34)
Boffetta *et al* [21]	1999	Europe	CC	66	1.11 (0.88 to 1.39)	0.10 (0.12)
Brenner *et al*[22]	2010	Canada	CC	110	0.40 (0.25 to 0.63)	-0.92 (0.24)
Brownson *et al* [23]	1987	USA	CC	19	1.68 (0.39 to 6.90)	0.52 (0.73)
Brownson *et al* [24]	1992	USA	CC	432	1.00 (0.80 to 1.20)	0.00 (0.10)
Buffler *et al* [25]	1984	USA	CC	41	0.80 (0.34 to 1.90)	-0.22 (0.44)
Butler [26]	1988	USA	P	8	2.02 (0.48 to 8.56)	0.70 (0.74)
Cardenas *et al* [27]	1997	USA	P	246	1.20 (0.80 to 1.60)	0.18 (0.18)
Chan and Fung [28]	1982	Hong Kong	CC	84	0.75 (0.43 to 1.30)	-0.29 (0.28)
Choi *et al* [29]	1989	Korea	CC	75	1.63 (0.92 to 2.87)	0.49 (0.29)
Correa *et al* [30]	1983	USA	CC	25	2.07 (0.81 to 5.25)	0.73 (0.48)
de Waard *et al* [31]	1995	Netherlands	CC	23	2.57 (0.84 to 7.85)	0.94 (0.57)
Du *et al* [32]	1993	China	CC	75	1.09 (0.64 to 1.85)	0.09 (0.27)
Enstrom and Kabat [33]	2003	USA	P	177	0.94 (0.66 to 1.33)	-0.06 (0.18)
EPIC Adulthood [34]	2005	Western Europe	P	43	0.84 (0.33 to 2.17)	-0.17 (0.48)
Fang *et al* [35]	2006	China	CC	157	1.77 (1.07 to 2.92)	0.57 (0.26)
Fontham *et al* [36]	1994	USA	CC	653	1.29 (1.04 to 1.60)	0.25 (0.11)
Franco-Marina *et al* [37]	2006	Mexico	CC	72	1.80 (0.95 to 3.42)	0.59 (0.33)
Gallegos *et al* [38]	2008	Mexico	CC	13	8.00 (0.85 to 75.31)	2.08 (1.14)
Gao *et al* [39]	1987	China	CC	246	1.30 (0.87 to 1.94)	0.27 (0.20)
Garfinkel [40]	1981	USA	P	153	1.17 (0.85 to 1.61)	0.16 (0.16)
Garfinkel *et al* [41]	1985	USA	CC	134	1.23 (0.81 to 1.87)	0.21 (0.21)
GELAC [42]	2013	Taiwan	CC	1221	1.30 (1.09 to 1.56)	0.26 (0.09)
Geng *et al* [7]	1988	China	CC	54	2.16 (1.08 to 4.29)	0.77 (0.35)
Gorlova *et al* [43]	2006	USA	CC	130	1.15 (0.63 to 2.10)	0.14 (0.31)
He *et al* [44]	2012	China	P	6	2.07 (0.23 to 18.34)	0.73 (1.12)
Hill (Study 1) [45]	2007	New Zealand	P	63	1.00 (0.49 to 2.01)	0.00 (0.36)
Hill (Study 2) [45]	2007	New Zealand	P	123	1.38 (0.78 to 2.41)	0.32 (0.29)
Hirayama [46]	1984	Japan	P	200	1.45 (1.02 to 2.08)	0.37 (0.18)
Hole *et al* [47]	1989	Scotland	P	6	1.89 (0.22 to 16.12)	0.64 (1.10)
Humble *et al* [48]	1987	USA	CC	20	2.20 (0.76 to 6.56)	0.79 (0.55)
IARC (Kreuzer) [16]	2004	Germany	CC	100	0.80 (0.50 to 1.30)	-0.22 (0.24)
ILCCO [49]	2014	International	CC	1907	1.20 (1.06 to 1.36)	0.18 (0.06)
Inoue and Hirayama [50]	1988	Japan	CC	28	2.25 (0.77 to 8.85)	0.81 (0.62)
Janerich *et al* [51]	1990	USA	CC	146	0.75 (0.47 to 1.20)	-0.29 (0.24)
Jee *et al* [52]	1999	Korea	P	79	1.72 (0.93 to 3.18)	0.54 (0.31)
Jiang *et al* [53]	2010	China	CC	98	2.27 (1.13 to 4.53)	0.82 (0.35)
Johnson *et al* [54]	2001	Canada	CC	71	1.20 (0.62 to 2.30)	0.18 (0.33)
Kabat and Wynder [55]	1984	USA	CC	53	0.79 (0.25 to 2.45)	-0.24 (0.58)
Kabat *et al* [56]	1995	USA	CC	69	1.08 (0.60 to 1.94)	0.08 (0.30)
Kalandidi *et al* [57]	1990	Greece	CC	91	2.11 (1.09 to 4.08)	0.75 (0.34)
Kiyohara *et al* [58]	2011	Japan	CC	49	1.01 (0.47 to 2.17)	0.01 (0.39)
Koo *et al* [59]	1987	Hong Kong	CC	88	1.64 (0.87 to 3.09)	0.49 (0.32)
Kurahashi *et al* [60]	2008	Japan	P	109	1.26 (0.78 to 2.03)	0.23 (0.24)
Lagarde *et al* [61]	2001	Sweden	CC	242	1.15 (0.84 to 1.58)	0.14 (0.16)
Lam [62]	1985	Hong Kong	CC	75	2.01 (1.09 to 3.72)	0.70 (0.31)
Lam *et al* [63]	1987	Hong Kong	CC	202	1.65 (1.16 to 2.35)	0.50 (0.18)
Layard [64]	1994	USA	CC	39	0.58 (0.30 to 1.13)	-0.54 (0.34)
Lee *et al* [65]	1986	UK	CC	32	1.00 (0.37 to 2.71)	0.00 (0.51)
Lee *et al* [66]	2000	Taiwan	CC	268	1.87 (1.29 to 2.71)	0.63 (0.19)
Liang *et al* [67]	2009	China	CC	226	1.45 (1.01 to 2.07)	0.37 (0.18)
Lim *et al* [68]	2012	Chinese women in Singapore	CC	433	1.12 (0.90 to 1.40)	0.12 (0.11)
Lin *et al* [69]	2012	China	CC	226	2.50 (1.66 to 3.77)	0.92 (0.21)
Liu *et al* [70]	1991	China	CC	54	0.77 (0.30 to 1.96)	-0.26 (0.48)
Liu *et al* [71]	1993	China	CC	38	1.72 (0.77 to 3.87)	0.54 (0.41)
López-Cima *et al* [72]	2007	Spain	CC	4	0.99 (0.00 to 509.87)	-0.01 (3.18)
Masjedi *et al* [74]	2013	Iran	CC	55	1.50 (0.77 to 2.91)	0.41 (0.34)
Malats *et al* [73]	2000	Europe/Brazil	CC	105	2.01 (1.01 to 4.00)	0.70 (0.35)
McGhee *et al* [75]	2005	Hong Kong	CC	179	1.38 (0.94 to 2.04)	0.32 (0.20)

Nishino *et al* [76]	2001	Japan	P	24	1.80 (0.67 to 4.60)	0.59 (0.49)
Ohno *et al* [77]	2002	Japan	CC	191	1.00 (0.67 to 1.49)	0.00 (0.20)
Pershagen *et al* [78]	1987	Sweden	CC	83	1.20 (0.70 to 2.10)	0.18 (0.28)
Rapiti *et al* [79]	1999	India	CC	41	1.20 (0.50 to 2.90)	0.18 (0.45)
Ren *et al* [80]	2013	China	CC	764	1.20 (0.99 to 1.46)	0.18 (0.10)
Rylander and Axelsson [81]	2006	Sweden	CC	31	1.37 (0.57 to 3.30)	0.31 (0.45)
Schoenberg *et al* [82]	1989	USA	CC	116	1.07 (0.70 to 1.64)	0.07 (0.22)
Schwartz *et al* [83]	1996	USA	CC	185	1.10 (0.72 to 1.68)	0.10 (0.22)
Seki *et al* [84]	2013	Japan	CC	292	1.31 (0.99 to 1.72)	0.27 (0.14)
Shen *et al* [85]	1998	China	CC	70	0.75 (0.31 to 1.78)	-0.29 (0.45)
Shimizu *et al* [86]	1988	Japan	CC	90	1.08 (0.64 to 1.82)	0.08 (0.27)
Sobue [87]	1990	Japan	CC	144	1.13 (0.78 to 1.63)	0.12 (0.19)
Speizer *et al* [88]	1999	USA	P	35	1.50 (0.30 to 6.30)	0.41 (0.78)
Stockwell *et al* [89]	1992	USA	CC	210	1.60 (0.80 to 3.00)	0.47 (0.34)
Sun *et al* [90]	1996	China	CC	230	1.16 (0.80 to 1.69)	0.15 (0.19)
Svensson *et al* [91]	1989	Sweden	CC	38	1.36 (0.53 to 3.49)	0.31 (0.48)
Torres-Duran *et al* [92]	2014	Spain	CC	153	0.71 (0.46 to 1.10)	-0.34 (0.22)
Trichopoulos *et al* [93]	1983	Greece	CC	77	2.08 (1.20 to 3.59)	0.73 (0.28)
Wang *et al* [94]	1996	China	CC	82	2.53 (1.26 to 5.10)	0.93 (0.36)
Wang *et al* [95]	1996	China	CC	135	1.11 (0.67 to 1.84)	0.10 (0.26)
Wang *et al* [96]	2000	China	CC	200	1.03 (0.60 to 1.70)	0.03 (0.27)
Wen *et al* [97]	2006	China	P	106	1.09 (0.74 to 1.61)	0.09 (0.20)
WHI-OS [98]	2013	USA	P	200	0.88 (0.52 to 1.49)	-0.13 (0.27)
Wu *et al* [99]	1985	USA	CC	31	1.20 (0.50 to 3.30)	0.18 (0.48)
Wu-Williams *et al* [14]	1990	China	CC	417	0.70 (0.60 to 0.90)	-0.36 (0.10)
Yang *et al* [100]	2008	USA	CC	74	2.00 (1.10 to 3.63)	0.69 (0.30)
Yu *et al* [101]	2006	Hong Kong	CC	213	1.35 (0.70 to 2.63)	0.30 (0.34)
Zaridze *et al* [102]	1998	Russia	CC	189	1.53 (1.06 to 2.21)	0.43 (0.19)
Zatloukal *et al* [103]	2003	Czech Republic	CC	84	0.48 (0.21 to 1.09)	-0.73 (0.42)
Zheng *et al* [104]	1997	China	CC	69	2.52 (1.09 to 5.85)	0.92 (0.43)
Zhong *et al* [105]	1999	China	CC	504	1.10 (0.80 to 1.50)	0.10 (0.16)

[a] P = prospective; CC = case-control

[b] Number of lung cancer cases in female lifelong nonsmokers

[c] RR = Relative risk of lung cancer in nonsmoking females (baseline = husband nonsmoker); 95% CI = 95% confidence interval for RR

[d] β = Slope of relationship of log RR to dose, with dose set as 1 for exposed and 0 for unexposed; SE(β) = standard error of β

[e] Based on data for two control groups combined

[f] Relative risks were presented for sexes combined and assumed to apply to each sex separately, with confidence intervals weighted according to number of subjects by sex

[g] Based on data for hospital controls. Data for population controls not used as non-response rate very high

[h] Based on data for two pathological groups of lung cancer combined

Table 21 Effect of adjustment for confounding and correction for misclassification on the estimated risk of lung cancer in lifelong nonsmoking females in relation to smoking by the husband (or nearest equivalent) (random-effects models)

Studies	N	Unadjusted for confounding Uncorrected for misclassification RR (95% CI)	Adjusted for confounding[a] Uncorrected for misclassification RR (95% CI)	Adjusted for confounding[a] Corrected for misclassification[b] RR (95% CI)
All	93	**1.219 (1.138 to 1.305)**	**1.139 (1.062 to 1.221)**	**1.077 (0.999 to 1.162)**
North America	29	1.074 (0.937 to 1.232)	1.004 (0.873 to 1.154)	0.898 (0.775 to 1.039)
Europe and New Zealand	20	1.174 (1.007 to 1.369)	1.092 (0.934 to 1.277)	1.062 (0.899 to 1.254)
China (including Hong Kong and Lim[68])	27	1.321 (1.144 to 1.524)	1.239 (1.071 to 1.433)	1.175 (1.005 to 1.374)
Rest of Asia	17	1.284 (1.187 to 1.389)	1.194 (1.103 to 1.291)	1.164 (1.072 to 1.262)
North America, Europe and New Zealand	49	1.112 (1.004 to 1.231)	1.037 (0.935 to 1.150)	0.959 (0.858 to 1.072)
Asia	44	1.314 (1.199 to 1.439)	1.229 (1.121 to 1.348)	1.181 (1.070 to 1.304)
Published in 1980s	26	1.361 (1.216 to 1.522)	1.267 (1.132 to 1.417)	1.194 (1.059 to 1.347)
Published in 1990s	27	1.152 (1.016 to 1.305)	1.077 (0.948 to 1.225)	1.005 (0.871 to 1.160)
Published in 2000s	26	1.240 (1.105 to 1.392)	1.163 (1.034 to 1.308)	1.115 (0.987 to 1.260)
Published in 2010s	14	1.139 (0.945 to 1.372)	1.059 (0.877 to 1.277)	1.026 (0.844 to 1.247)
<100 cases	49	1.339 (1.178 to 1.521)	1.249 (1.098 to 1.422)	1.192 (1.038 to 1.370)
100-199 cases	22	1.117 (0.973 to 1.284)	1.042 (0.904 to 1.200)	0.978 (0.846 to 1.131)
200-399 cases	13	1.363 (1.190 to 1.561)	1.275 (1.114 to 1.460)	1.226 (1.051 to 1.429)
400+ cases	9	1.101 (0.973 to 1.247)	1.027 (0.905 to 1.166)	0.957 (0.826 to 1.108)
With dose-response data[c]	24	1.308 (1.181 to 1.449)	1.226 (1.105 to 1.359)	1.170 (1.052 to 1.302)
Without dose-response data	69	1.182 (1.088 to 1.286)	1.104 (1.014 to 1.201)	1.040 (0.948 to 1.141)
With age adjustment[d]	75	1.184 (1.100 to 1.274)	1.106 (1.027 to 1.191)	1.048 (0.966 to 1.136)
Without age adjustment	18	1.437 (1.194 to 1.728)	1.340 (1.110 to 1.618)	1.264 (1.026 to 1.556)
Case-control studies	77	1.226 (1.133 to 1.326)	1.144 (1.057 to 1.239)	1.080 (0.990 to 1.177)
Prospective studies	16	1.187 (1.043 to 1.350)	1.111 (0.977 to 1.264)	1.064 (0.928 to 1.220)

[a] Adjusted for confounding by fruit, vegetables and dietary fat consumption and by education
[b] Using the Lee and Forey method [4] with an additive model and assuming a concordance ratio of 3 and misclassification rates of 2.5% for studies in North America and Europe and 10% for studies in Asia
[c] Specifically for smoking by the husband
[d] Or matching (within nonsmokers)

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Appendix 1

Studies/analyses not included in Table 1

In preparing Table 1, which presents the data on lung cancer risk by husband smoking, certain papers which might be thought to cite relevant data have not been used. The studies (their year of publication, country of origin and reference) and the reasons for not referring to them are given in Appendix 2 of the main paper "Environmental tobacco smoke exposure and lung cancer – a systematic review."

Appendix 2

Fuller details of the analyses relating lung cancer risk to the number of cigarettes smoked by the husband – unadjusted for confounding and uncorrected for misclassification

APPENDIX 2
ETS and Lung Cancer - Meta-Analysis of exposed/unexposed Risks, 02-NOV-15
Female (Husband's smoking)

BASIC DATA USED IN META-ANALYSES

	Study title	RR	RRL	RRU	CA1	CA0	CO1	CO0
#422	Akiba |	1.3000 |	0.6200 |	2.5700 |	24.0772 |	16.6388 |	70.5504 |	63.3808 |
#423	Akiba |	1.5000 |	0.7100 |	3.1600 |	20.1415 |	16.6388 |	51.1490 |	63.3808 |
#424	Akiba |	2.1000 |	0.5700 |	8.0700 |	4.0691 |	16.6388 |	7.3810 |	63.3808 |
#1658	Al-Zoughool |	0.3900 |	0.1500 |	0.9800 |	5.8691 |	22.6601 |	112.8202 |	169.8787 |
#1302	Asomaning |	0.9300 |	0.3100 |	2.7800 |	15.4332 |	5.5313 |	59.1915 |	19.7294 |
#817	Boffetta 2 |	1.0000 |	0.5000 |	1.9000 |	25.7383 |	25.3652 |	53.4266 |	52.6522 |
#599	Boffetta |	1.0000 |	0.7700 |	1.3100 |	174.0952 |	159.8269 |	327.6660 |	300.8116 |
#600	Boffetta |	0.5700 |	0.3400 |	0.9300 |	23.1359 |	159.8269 |	76.3935 |	300.8116 |
#601	Boffetta |	1.3400 |	0.8300 |	2.1700 |	33.8814 |	159.8269 |	47.5884 |	300.8116 |
#1404	Brenner |	0.4000 |	0.2500 |	0.6300 |	54.6755 |	35.7517 |	516.7407 |	135.1564 |
#66	Brownson 1 |	1.6800 |	0.3900 |	6.9000 |	3.7600 |	12.7800 |	6.0900 |	34.8200 |
#68	Brownson 2 |	1.0000 |	0.8000 |	1.2000 |	262.8000 |	249.6100 |	710.9600 |	675.2900 |
#70	Buffler |	0.8000 |	0.3400 |	1.9000 |	33.0000 |	8.0000 |	164.0000 |	32.0000 |
#72	Butler |	2.0200 |	0.4800 |	8.5600 |	2.7700 |	5.5800 |	11040.8400 |	44931.4800 |
#540	Cardenas |	1.1000 |	0.5000 |	2.2000 |	9.0500 |	31.0400 |	11951.2100 |	45105.4100 |
#541	Cardenas |	1.2000 |	0.7000 |	2.2000 |	18.8500 |	31.0400 |	22823.4400 |	45105.4100 |
#542	Cardenas |	1.9000 |	1.0000 |	3.6000 |	13.4300 |	31.0400 |	10273.5100 |	45105.4100 |
#73	Chan |	0.7500 |	0.4300 |	1.3000 |	34.0000 |	50.0000 |	66.0000 |	73.0000 |
#169	Choi |	1.6300 |	0.9200 |	2.8700 |	49.0000 |	26.0000 |	88.0000 |	76.0000 |
#75	Correa |	2.0700 |	0.8100 |	5.2500 |	14.0000 |	8.0000 |	61.0000 |	72.0000 |
#253	De Waard |	2.5700 |	0.8400 |	7.8500 |	19.0000 |	4.0000 |	124.0000 |	67.0000 |
#445	Du |	0.6729 |	0.3256 |	1.3904 |	13.0000 |	28.0000 |	69.0000 |	100.0000 |
#446	Du |	1.4881 |	0.8187 |	2.7047 |	30.0000 |	28.0000 |	72.0000 |	100.0000 |
#1036	Enstrom |	0.9400 |	0.6600 |	1.3300 |	105.7649 |	44.8930 |	15783.0932 |	6297.3389 |
#1398	EPIC Adulthood |	0.8400 |	0.3300 |	2.1700 |	9.3664 |	8.0480 |	13863.3285 |	10006.0387 |
#1310	Fang |	1.7700 |	1.0700 |	2.9200 |	23.2928 |	104.9022 |	85.7355 |	683.4344 |
#78	Fontham |	1.2900 |	1.0400 |	1.6000 |	372.1100 |	183.3900 |	653.6300 |	415.5600 |
#1400	Franco-Marina |	1.8000 |	0.9500 |	3.4200 |	21.7539 |	36.9675 |	39.3017 |	120.2171 |
#1304	Gallegos |	8.0000 |	0.8500 |	75.3100 |	12.9595 |	0.8640 |	38.8786 |	20.7349 |
#90	Gao |	1.3041 |	0.8700 |	1.9400 |	191.5800 |	52.8600 |	274.2500 |	98.3700 |
#457	Garfinkel 1 |	1.2700 |	0.8600 |	1.8900 |	39.0000 |	65.0000 |	38624.0000 |	81859.0000 |
#458	Garfinkel 1 |	1.1000 |	0.7600 |	1.5900 |	49.0000 |	65.0000 |	56256.0000 |	81859.0000 |
#459	Garfinkel 2 |	0.8413 |	0.4008 |	1.7661 |	11.0000 |	43.0000 |	45.0000 |	148.0000 |
#460	Garfinkel 2 |	1.0798 |	0.6404 |	1.8208 |	32.0000 |	43.0000 |	102.0000 |	148.0000 |
#461	Garfinkel 2 |	1.9857 |	1.1306 |	3.4875 |	30.0000 |	43.0000 |	52.0000 |	148.0000 |
#1519	GELAC study |	1.3000 |	1.0900 |	1.5600 |	449.4704 |	533.2445 |	386.5457 |	596.1692 |
#462	Geng |	1.4000 |	0.4900 |	4.0200 |	7.0000 |	20.0000 |	13.0000 |	52.0000 |
#463	Geng |	1.9500 |	0.6000 |	6.3300 |	6.0000 |	20.0000 |	8.0000 |	52.0000 |
#464	Geng |	2.7300 |	1.2300 |	6.0800 |	21.0000 |	20.0000 |	20.0000 |	52.0000 |
#1087	Gorlova |	1.1500 |	0.6300 |	2.1000 |	66.8200 |	29.5300 |	67.3200 |	34.3100 |
#1453	He |	2.0700 |	0.2300 |	18.3400 |	5.0641 |	0.9426 |	340.3803 |	131.1465 |
#33	Hill (study 1) |	1.0000 |	0.4900 |	2.0100 |	10.1641 |	31.9638 |	93216.1758 |	293144.8122 |
#1096	Hill (study 2) |	1.3800 |	0.7800 |	2.4100 |	14.9666 |	62.4129 |	63410.9424 |	364916.1456 |
#502	Hirayama |	1.3500 |	0.9200 |	1.9900 |	105.0600 |	34.3100 |	46960.8600 |	20702.3900 |
#503	Hirayama |	1.5900 |	1.0300 |	2.4600 |	49.8100 |	34.3100 |	18904.6400 |	20702.3900 |
#468	Hole |	1.3000 |	0.1200 |	14.2700 |	2.0000 |	1.0000 |	754.0000 |	489.0000 |
#469	Hole |	2.7100 |	0.2800 |	25.9800 |	3.0000 |	1.0000 |	541.0000 |	489.0000 |
#485	Humble 1 |	1.8000 |	0.4900 |	6.9600 |	6.3787 |	7.3413 |	8.9724 |	18.5878 |
#486	Humble 1 |	1.2000 |	0.2300 |	6.8900 |	2.6218 |	7.3413 |	5.5318 |	18.5878 |
#1053	IARC: Kreuzer |	0.8000 |	0.5000 |	1.3000 |	52.5746 |	45.5399 |	132.5006 |	91.8170 |
#1651	ILCCO |	1.2000 |	1.0600 |	1.3600 |	700.2118 |	619.7408 |	1941.0050 |	2061.5249 |
#472	Inoue |	2.5800 |	0.3100 |	6.6300 |	6.6162 |	3.2295 |	11.9847 |	15.0927 |
#473	Inoue |	3.0900 |	0.8400 |	15.2700 |	9.6860 |	3.2295 |	14.6495 |	15.0927 |
#115	Janerich |	0.7500 |	0.4700 |	1.2000 |	76.0000 |	68.0000 |	86.0000 |	58.0000 |
#649	Jee |	2.0000 |	1.1000 |	3.9000 |	41.1000 |	12.5100 |	62793.9200 |	38219.7800 |
#651	Jee |	1.5000 |	0.7000 |	3.3000 |	13.0600 |	12.5100 |	26605.0600 |	38219.7800 |
#1407	Jiang |	2.2670 |	1.1340 |	4.5330 |	47.3649 |	21.7629 |	33.8586 |	35.2680 |
#925	Johnson |	1.2000 |	0.6200 |	2.3000 |	38.7236 |	12.9554 |	395.2353 |	158.6764 |
#124	Kabat 1 |	0.7900 |	0.2500 |	2.4500 |	13.0000 |	11.0000 |	15.0000 |	10.0000 |
#493	Kabat 2 |	0.8200 |	0.4200 |	1.6100 |	18.1168 |	31.0459 |	56.8626 |	79.9029 |
#494	Kabat 2 |	1.0600 |	0.4900 |	2.3000 |	12.7339 |	31.0459 |	30.9181 |	79.9029 |
#495	Kalandidi |	1.5424 |	0.7929 |	3.0004 |	34.0000 |	26.0000 |	39.0000 |	46.0000 |
#496	Kalandidi |	1.7692 |	0.8258 |	3.7903 |	22.0000 |	26.0000 |	22.0000 |	46.0000 |
#497	Kalandidi |	1.5726 |	0.5411 |	4.5707 |	8.0000 |	26.0000 |	9.0000 |	46.0000 |
#1449	Kiyohara |	1.0050 |	0.4660 |	2.1670 |	31.9057 |	17.4021 |	43.5062 |	23.8479 |
#507	Koo |	2.3300 |	0.9200 |	5.9200 |	12.7249 |	23.8522 |	11.6984 |	51.0922 |

#508	Koo	1.7400	0.8100	3.7500	19.8412	23.8522	24.4256	51.0922
#509	Koo	1.1900	0.4600	3.0300	9.1628	23.8522	16.4934	51.0922
#1134	Kurahashi	1.0200	0.5100	2.0400	12.3802	22.5585	46979.9869	87316.2487
#1138	Kurahashi	1.4700	0.8700	2.4900	41.3638	20.9185	123721.7530	91975.7479
#971	Lagarde	1.1500	0.8400	1.5800	84.1500	119.3890	282.1461	460.3436
#510	Lam T	2.1800	1.1400	4.1500	22.0000	84.0000	22.0000	183.0000
#511	Lam T	1.8500	1.1900	2.8700	56.0000	84.0000	66.0000	183.0000
#512	Lam T	2.0700	1.0700	4.0300	20.0000	84.0000	21.0000	183.0000
#134	Lam W	2.0100	1.0900	3.7200	37.0000	23.0000	64.0000	80.0000
#621	Layard	0.6008	0.2274	1.5873	5.0000	24.0000	336.0000	969.0000
#622	Layard	0.6260	0.2792	1.4033	8.0000	24.0000	516.0000	969.0000
#142	Lee	1.0000	0.3700	2.7100	18.0900	8.4400	37.3000	17.4100
#755	Lee C-H	1.8700	1.2900	2.7100	145.3012	58.9669	192.8351	146.3413
#1320	Liang	1.4473	1.0123	2.0692	141.0000	85.0000	149.0000	130.0000
#1454	Lim	1.1231	0.9029	1.3970	200.0000	226.0000	602.0000	764.0000
#1478	Lin	2.5030	1.6600	3.7730	100.5614	77.2974	72.4017	139.2977
#515	Liu Q	0.7000	0.2300	2.2000	5.6756	13.0941	20.4219	32.9805
#516	Liu Q	2.9000	1.2000	7.3000	20.3981	13.0941	17.7163	32.9805
#144	Liu Z	0.7700	0.3000	1.9600	35.8200	6.8700	139.1500	20.5600
#1655	Lopez-Cima	0.9930	0.0020	509.8740	4.4400	0.1300	17.8800	0.5100
#867	Malats	1.5000	0.7700	2.9100	36.1634	45.3493	23.4436	44.0978
#1361	Masjedi	2.0074	1.0074	3.9998	21.0000	34.0000	28.0000	91.0000
#1074	McGhee	1.3800	0.9400	2.0400	80.5883	75.9186	131.1497	170.4993
#973	Nishino	1.8000	0.6700	4.6000	9.3962	7.4053	21398.0642	30355.3445
#996	Ohno	1.0000	0.6700	1.4900	138.9793	52.3348	239.3942	90.1475
#147	Pershagen	1.2000	0.7000	2.1000	36.1800	27.7800	139.8100	128.8400
#657	Rapiti	1.2000	0.5000	2.9000	12.7016	23.1855	18.3812	40.2637
#1536	Ren	1.2000	0.9900	1.4600	655.3649	238.7315	800.4530	349.8997
#1099	Rylander	1.3700	0.5700	3.3000	7.9200	23.0900	40.4300	161.5700
#1461	Schoenberg	1.0710	0.6980	1.6420	68.5216	41.3858	287.0856	185.7055
#165	Schwartz	1.1000	0.7200	1.6800	125.0000	65.9500	115.6000	67.0900
#1556	Seki	1.3100	0.9900	1.7200	196.0403	81.8593	1113.5021	609.0952
#614	Shen	0.6500	0.2100	2.0700	10.0000	14.0000	12.0000	11.0000
#615	Shen	1.0500	0.3200	3.3800	12.0000	14.0000	9.0000	11.0000
#616	Shen	0.7000	0.2800	1.7600	34.0000	14.0000	38.0000	11.0000
#148	Shimizu	1.0800	0.6400	1.8200	52.0000	38.0000	91.0000	72.0000
#150	Sobue	1.1300	0.7800	1.6300	78.6600	59.2200	378.2100	321.7200
#688	Speize	1.5000	0.3000	6.3000	29.2793	1.7574	199924.6090	18000.0001
#152	Stockwell	1.6000	0.8000	3.0000	48.0800	19.6700	60.1000	39.3400
#160	Sun	1.1600	0.8000	1.6900	144.8200	86.2900	136.6600	94.4500
#356	Svensson	1.3600	0.5300	3.4900	18.2000	7.0400	84.6400	44.5500
#1649	Torres-Duran	0.7100	0.4600	1.1000	49.6338	85.0138	103.7945	126.2249
#523	Trichopoulos	0.5677	0.1223	2.6348	2.0000	24.0000	16.0000	109.0000
#524	Trichopoulos	2.4979	1.2622	4.9434	22.0000	24.0000	40.0000	109.0000
#525	Trichopoulos	3.9740	1.3143	12.0159	7.0000	24.0000	8.0000	109.0000
#526	Trichopoulos	1.8701	0.6984	5.0073	7.0000	24.0000	17.0000	109.0000
#904	Wang L	1.0300	0.6000	1.7000	125.1000	25.2300	253.2979	52.6138
#161	Wang S	2.5300	1.2600	5.1000	67.0000	15.0000	60.0000	34.0000
#534	Wang T	0.3500	0.1100	1.1600	4.0000	43.0000	13.0000	49.0000
#535	Wang T	1.3500	0.7400	2.4500	45.0000	43.0000	38.0000	49.0000
#536	Wang T	1.4000	0.7600	2.5700	43.0000	43.0000	35.0000	49.0000
#1103	Wen	1.0900	0.7400	1.6100	68.7718	40.2469	40928.3228	26107.9401
#1560	WHI-OS	0.8800	0.5200	1.4900	26.0505	29.6029	42114.6908	42114.6908
#156	Wu	1.2000	0.5000	3.3000	17.9700	9.9800	32.9400	21.9600
#158	Wu-Williams	0.7000	0.6000	0.9000	293.9500	343.8000	506.2200	414.4600
#1308	Yang	2.0000	1.1000	3.6300	68.7786	26.8357	55.6941	43.4609
#1120	Yu	1.3500	0.6950	2.6250	113.5206	15.7243	149.2588	27.9107
#576	Zaridze	1.6600	1.0900	2.5200	61.9147	78.6104	87.5660	184.5566
#577	Zaridze	1.3500	0.8400	2.1800	38.3678	78.6104	66.7241	184.5566
#1042	Zatloukal	0.4800	0.2100	1.0900	6.5824	64.9388	131.9736	624.9586
#793	Zheng	2.5200	1.0882	5.8521	62.0000	7.0000	179.0000	51.0000
#720	Zhong	1.4000	0.9000	2.2000	80.2700	64.2400	78.9700	88.4800
#722	Zhong	0.9000	0.6000	1.4000	83.2900	64.2400	127.4700	88.4800
#724	Zhong	1.4000	0.7000	2.6000	23.6700	64.2400	23.2900	88.4800

NOTES: RR,RL,RU   RELATIVE RISKS AND LOWER AND UPPER CONFIDENCE INTERVALS

CA1,CA0   NUMBERS (OR PSEUDO-NUMBERS) OF EXPOSED AND UNEXPOSED CASES

CO1,CO0   NUMBERS (OR PSEUDO-NUMBERS) OF EXPOSED AND UNEXPOSED CONTROLS

NCIGS   MIDPOINT OF NUMBER OF CIGARETTES SMOKED BY HUSBAND (IN UNITS OF 10)

REGRESSION ESTIMATES, WEIGHTS AND DETAILS OF RELEVANT FACTORS ADJUSTED FOR IN STUDIES

	Study title	Country	Beta	SE Beta	Z	Weight	FRU	VEG	FAT	EDU	AGE
#422	Akiba	Japan	0.1860	0.1406	1.3225	50.5750	0	0	0	0	1
#1658	Al-Zoughool	Canada	-0.5181	0.2634	-1.9665	14.4083	0	0	0	1	0
#1302	Asomaning	USA	-0.0313	0.2417	-0.1297	17.1235	0	0	0	0	0
#817	Boffetta 2	7 countries	0.0000	0.1874	0.0000	28.4801	0	0	0	0	1
#599	Boffetta	7 countries	0.0100	0.0516	0.1936	375.4503	0	0	0	0	1
#1404	Brenner	Canada	-0.5041	0.1297	-3.8861	59.4179	0	0	0	0	0
#66	Brownson 1	USA	0.2240	0.3165	0.7078	9.9818	0	0	0	1	1
#68	Brownson 2	USA	0.0000	0.0447	0.0000	501.2026	0	0	0	0	1
#70	Buffler	USA	-0.0964	0.1896	-0.5084	27.8310	0	0	0	0	0
#72	Butler	USA	0.3036	0.3174	0.9566	9.9269	0	0	0	0	1
#540	Cardenas	USA	0.1385	0.0727	1.9061	189.3056	0	1	1	2	1
#73	Chan	China	-0.1583	0.1553	-1.0193	41.4698	0	0	0	0	0
#169	Choi	Korea	0.2688	0.1597	1.6834	39.2151	0	0	0	0	0
#75	Correa	USA	0.3142	0.2059	1.5260	23.5899	0	0	0	0	0
#253	De Waard	Netherlands	0.5193	0.3137	1.6556	10.1625	0	0	0	0	0
#445	Du	China	0.1709	0.1166	1.4665	73.5915	0	0	0	0	1
#1036	Enstrom	USA	-0.0267	0.0772	-0.3462	167.8274	1	0	0	2	1
#1398	EPIC Adulthood	Western Europe	-0.0959	0.2644	-0.3629	14.3095	1	1	1	2	1
#1310	Fang	China	0.3142	0.1409	2.2294	50.3619	0	1	0	1	1
#78	Fontham	USA	0.1100	0.0475	2.3171	444.0208	1	1	0	2	1
#1400	Franco-Marina	Mexico	0.3234	0.1798	1.7988	30.9351	0	0	0	0	0
#1304	Gallegos	Mexico	1.1441	0.6294	1.8178	2.5243	0	0	0	0	0
#90	Gao	China	0.1461	0.1126	1.2977	78.9241	0	0	0	2	1
#457	Garfinkel 1	USA	0.0297	0.0683	0.4353	214.4683	0	0	0	0	1
#459	Garfinkel 2	USA	0.1515	0.0648	2.3393	238.3929	0	0	0	0	1
#1519	GELAC study	Taiwan	0.1444	0.0503	2.8687	394.9176	0	0	0	2	1
#462	Geng	China	0.3809	0.1536	2.4796	42.3845	0	0	0	0	0
#1087	Gorlova	USA	0.0604	0.1326	0.4550	56.8443	0	0	0	1	1
#1453	He	China	0.4003	0.6146	0.6513	2.6473	0	0	2	2	1
#33	Hill (study 1)	New Zealand	0.0000	0.1981	0.0000	25.4772	0	0	0	0	1
#1096	Hill (study 2)	New Zealand	0.1772	0.1583	1.1192	39.8858	0	0	0	3	1
#502	Hirayama	Japan	0.1488	0.0793	1.8765	158.9581	0	0	0	0	1
#468	Hole	Scotland	0.3652	0.3596	1.0156	7.7342	0	0	0	0	1
#485	Humble 1	USA	0.1074	0.2456	0.4371	16.5777	0	0	0	0	2
#1053	IARC: Kreuzer	Germany	-0.1228	0.1341	-0.9154	55.5946	0	0	0	0	1
#1651	ILCCO	International	0.1003	0.0350	2.8677	817.2471	0	0	0	0	1
#472	Inoue	Japan	0.3521	0.2660	1.3239	14.1375	0	0	0	0	1
#115	Janerich	USA	-0.1242	0.1033	-1.2031	93.7826	0	0	0	0	1
#649	Jee	Korea	0.0938	0.1491	0.6291	45.0125	0	1	0	3	1
#1407	Jiang	China	0.4503	0.1945	2.3154	26.4368	1	1	0	0	1
#925	Johnson	Canada	0.1003	0.1840	0.5452	29.5349	1	1	0	2	1
#124	Kabat 1	USA	-0.1018	0.2514	-0.4048	15.8177	0	0	0	0	1
#493	Kabat 2	USA	0.0013	0.1062	0.0118	88.5940	0	0	0	2	1
#495	Kalandidi	Greece	0.1124	0.0907	1.2390	121.4733	0	0	0	0	2
#1449	Kiyohara	Japan	0.0027	0.2157	0.0127	21.4885	0	0	0	0	0
#507	Koo	China	0.0858	0.1400	0.6129	51.0281	0	0	0	2	1
#1134	Kurahashi	Japan	0.1577	0.1003	1.5721	99.4355	0	0	0	0	1
#971	Lagarde	Sweden	0.0769	0.0887	0.8672	127.1672	0	0	0	3	1
#510	Lam T	China	0.2670	0.0900	2.9655	123.3411	0	0	0	0	0
#134	Lam W	China	0.3841	0.1723	2.2294	33.6844	0	0	0	0	0
#621	Layard	USA	-0.1814	0.1544	-1.1743	41.9297	0	0	0	0	2
#142	Lee	England	0.0000	0.2795	0.0000	12.8019	0	0	0	0	1
#755	Lee C-H	Taiwan	0.3444	0.1042	3.3054	92.1166	0	0	0	2	1
#1320	Liang	China	0.2034	0.1003	2.0271	99.3158	0	0	0	0	0
#1454	Lim	Singapore	0.0639	0.0613	1.0428	266.5072	0	0	0	0	0
#1478	Lin	China	0.5048	0.1152	4.3803	75.2943	0	0	0	2	0
#515	Liu Q	China	0.4354	0.1760	2.4736	32.2794	0	0	0	2	0
#144	Liu Z	China	-0.1438	0.2634	-0.5459	14.4083	0	0	0	0	1
#1655	Lopez-Cima	Spain	-0.0039	1.7473	-0.0022	0.3275	0	0	0	0	0
#867	Malats	7 Europe+Brazil	0.2231	0.1866	1.1955	28.7155	0	0	0	0	1
#1361	Masjedi	Iran	0.3834	0.1935	1.9810	26.6968	0	0	0	0	0
#1074	McGhee	China	0.1772	0.1088	1.6295	84.5468	0	0	0	2	1
#973	Nishino	Japan	0.3234	0.2704	1.1960	13.6758	1	1	1	0	1
#996	Ohno	Japan	0.0000	0.1122	0.0000	79.4576	0	0	0	0	1
#147	Pershagen	Sweden	0.1003	0.1542	0.6505	42.0548	0	0	0	0	1
#657	Rapiti	India	0.1003	0.2467	0.4066	16.4262	0	0	0	0	1
#1536	Ren	China	0.1003	0.0545	1.8397	336.3195	0	0	0	0	1
#1099	Rylander	Sweden	0.1732	0.2465	0.7027	16.4602	0	0	0	0	1
#1461	Schoenberg	USA	0.0296	0.0942	0.3143	112.5978	0	1	0	2	1
#165	Schwartz	USA	0.0412	0.0933	0.4409	114.7752	0	0	0	0	1

#1556	Seki	Japan	0.1486	0.0775	1.9162	166.3555	0	0	0	0	1
#614	Shen	China	-0.0917	0.1567	-0.5855	40.7451	0	0	0	0	1
#148	Shimizu	Japan	0.0423	0.1467	0.2887	46.4696	0	0	0	0	1
#150	Sobue	Japan	0.0672	0.1035	0.6500	93.4374	0	0	0	2	1
#688	Speize	USA	0.1751	0.3354	0.5221	8.8896	0	0	0	0	1
#152	Stockwell	USA	0.2030	0.1456	1.3939	47.1648	0	0	0	2	1
#160	Sun	China	0.0817	0.1050	0.7779	90.7507	0	0	0	2	1
#356	Svensson	Sweden	0.1692	0.2646	0.6395	14.2884	0	0	0	0	1
#1649	Torres-Duran	Spain	-0.1884	0.1224	-1.5399	66.7778	0	0	0	0	1
#523	Trichopoulos	Greece	0.2587	0.1066	2.4265	87.9547	0	0	0	0	0
#904	Wang L	China	0.0163	0.1462	0.1113	46.7977	0	0	0	1	1
#161	Wang S	China	0.5107	0.1962	2.6024	25.9663	0	0	0	0	0
#534	Wang T	China	0.1656	0.1181	1.4030	71.7417	0	0	0	0	1
#1103	Wen	China	0.0474	0.1091	0.4346	84.0008	1	1	0	2	1
#1560	WHI-OS	USA	-0.0552	0.1160	-0.4760	74.3548	0	0	0	0	0
#156	Wu	USA	0.0787	0.2079	0.3787	23.1390	0	0	0	0	1
#158	Wu-Williams	China	-0.1962	0.0569	-3.4482	308.7433	0	0	0	2	1
#1308	Yang	USA	0.2993	0.1315	2.2758	57.8053	0	0	0	0	1
#1120	Yu	China	0.1651	0.1865	0.8852	28.7411	1	1	0	2	1
#576	Zaridze	Russia	0.1315	0.1061	1.2393	88.8308	0	0	0	2	1
#1042	Zatloukal	Czech Republic	-0.4038	0.2312	-1.7471	18.7158	0	0	0	2	1
#793	Zheng	China	0.5085	0.2361	2.1536	17.9351	0	0	0	0	1
#720	Zhong	China	-0.0056	0.0896	-0.0621	124.4775	1	0	0	1	1

NOTES: BETA SLOPE OF LOG RR

SE BETA STANDARD ERROR OF BETA

Z RATIO OF BETA TO ITS STANDARD ERROR (APPROXIMATE NORMAL STATISTIC)

WEIGHT INVERSE OF THE VARIANCE OF BETA

FRU = 1 ANALYSIS ADJUSTED FOR FRUIT

VEG = 1 " " " VEGETABLES

FAT = 1 " " " FRUIT

EDU = 1 " " " INCOME

= 2 " " " EDUCATION

= 3 " " " SOCIO-ECONOMIC STATUS

AGE = 0 NO ADJUSTMENT (OR MATCHING) FOR AGE

= 1 ADJUSTMENT (OR MATCHING) FOR AGE

LISTING OF VARIOUS STUDY VARIABLES

Study title	Country	REG	PUBYR	NLC	DOSER	COAGE	STYPE
Akiba	Japan	RestAsia	1981-86	50-99	Yes	Yes	Case-control
Al-Zoughool	Canada	NAmerica	2010-15	1-49	No	Yes	Case-control
Asomaning	USA	NAmerica	2000-09	50-99	No	No	Case-control
Boffetta 2	7 countries	EuropeNZ	1995-99	50-99	No	Yes	Case-control
Boffetta	7 countries	EuropeNZ	1995-99	400+	Yes	Yes	Case-control
Brenner	Canada	NAmerica	2010-15	100-199	No	Yes	Case-control
Brownson 1	USA	NAmerica	1987-89	1-49	No	Yes	Case-control
Brownson 2	USA	NAmerica	1990-94	400+	No	Yes	Case-control
Buffler	USA	NAmerica	1981-86	1-49	No	No	Case-control
Butler	USA	NAmerica	1987-89	1-49	No	Yes	Prospective
Cardenas	USA	NAmerica	1995-99	200-399	Yes	Yes	Prospective
Chan	China	ChinaHK	1981-86	50-99	No	No	Case-control
Choi	Korea	RestAsia	1987-89	50-99	No	No	Case-control
Correa	USA	NAmerica	1981-86	1-49	No	No	Case-control
De Waard	Netherlands	EuropeNZ	1995-99	1-49	No	No	Case-control
Du	China	ChinaHK	1990-94	50-99	Yes	Yes	Case-control
Enstrom	USA	NAmerica	2000-09	100-199	No	Yes	Prospective
EPIC Adulthood	Western Europe	EuropeNZ	2000-09	1-49	No	Yes	Prospective
Fang	China	ChinaHK	2000-09	100-199	No	Yes	Case-control
Fontham	USA	NAmerica	1990-94	400+	No	Yes	Case-control
Franco-Marina	Mexico	NAmerica	2000-09	50-99	No	Yes	Case-control
Gallegos	Mexico	NAmerica	2000-09	1-49	No	No	Case-control
Gao	China	ChinaHK	1987-89	200-399	No	Yes	Case-control
Garfinkel 1	USA	NAmerica	1981-86	100-199	Yes	Yes	Prospective

Garfinkel 2	USA	NAmerica	1981-86	100-199	Yes	Yes	Case-control
GELAC study	Taiwan	RestAsia	2010-15	400+	No	Yes	Case-control
Geng	China	ChinaHK	1987-89	50-99	Yes	No	Case-control
Gorlova	USA	NAmerica	2000-09	100-199	No	Yes	Case-control
He	China	ChinaHK	2010-15	1-49	No	Yes	Prospective
Hill (study 1)	New Zealand	EuropeNZ	2000-09	50-99	No	Yes	Prospective
Hill (study 2)	New Zealand	EuropeNZ	2000-09	100-199	No	Yes	Prospective
Hirayama	Japan	RestAsia	1981-86	200-399	Yes	Yes	Prospective
Hole	Scotland	EuropeNZ	1987-89	1-49	Yes	Yes	Prospective
Humble 1	USA	NAmerica	1987-89	1-49	Yes	Yes	Case-control
IARC: Kreuzer	Germany	EuropeNZ	2000-09	100-199	No	Yes	Case-control
ILCCO	International	RestAsia	2010-15	400+	No	Yes	Case-control
Inoue	Japan	RestAsia	1987-89	1-49	Yes	Yes	Case-control
Janerich	USA	NAmerica	1990-94	100-199	No	Yes	Case-control
Jee	Korea	RestAsia	1995-99	50-99	Yes	Yes	Prospective
Jiang	China	ChinaHK	2010-15	50-99	No	Yes	Case-control
Johnson	Canada	NAmerica	2000-09	50-99	No	Yes	Case-control
Kabat 1	USA	NAmerica	1981-86	50-99	No	Yes	Case-control
Kabat 2	USA	NAmerica	1995-99	50-99	Yes	Yes	Case-control
Kalandidi	Greece	EuropeNZ	1990-94	50-99	Yes	Yes	Case-control
Kiyohara	Japan	RestAsia	2010-15	50-99	No	No	Case-control
Koo	China	ChinaHK	1987-89	50-99	Yes	Yes	Case-control
Kurahashi	Japan	RestAsia	2000-09	100-199	Yes	Yes	Prospective
Lagarde	Sweden	EuropeNZ	2000-09	200-399	No	Yes	Case-control
Lam T	China	ChinaHK	1987-89	100-199	Yes	No	Case-control
Lam W	China	ChinaHK	1981-86	50-99	No	No	Case-control
Layard	USA	NAmerica	1990-94	1-49	Yes	Yes	Case-control
Lee	England	EuropeNZ	1981-86	1-49	No	Yes	Case-control
Lee C-H	Taiwan	RestAsia	2000-09	200-399	No	Yes	Case-control
Liang	China	ChinaHK	2000-09	200-399	No	No	Case-control
Lim	Singapore	ChinaHK	2010-15	400+	No	No	Case-control
Lin	China	ChinaHK	2010-15	200-399	No	Yes	Case-control
Liu Q	China	ChinaHK	1990-94	1-49	Yes	No	Case-control
Liu Z	China	ChinaHK	1990-94	50-99	No	Yes	Case-control
Lopez-Cima	Spain	EuropeNZ	2000-09	1-49	No	No	Case-control
Malats	7 Europe+Brazil	EuropeNZ	2000-09	100-199	No	Yes	Case-control
Masjedi	Iran	RestAsia	2010-15	50-99	No	Yes	Case-control
McGhee	China	ChinaHK	2000-09	100-199	No	Yes	Case-control
Nishino	Japan	RestAsia	2000-09	1-49	No	Yes	Prospective
Ohno	Japan	RestAsia	2000-09	100-199	No	Yes	Case-control
Pershagen	Sweden	EuropeNZ	1987-89	50-99	No	Yes	Case-control
Rapiti	India	RestAsia	1995-99	1-49	No	Yes	Case-control
Ren	China	ChinaHK	2010-15	400+	No	Yes	Case-control
Rylander	Sweden	EuropeNZ	2000-09	1-49	No	Yes	Case-control
Schoenberg	USA	NAmerica	1987-89	100-199	No	Yes	Case-control
Schwartz	USA	NAmerica	1995-99	100-199	No	Yes	Case-control
Seki	Japan	RestAsia	2010-15	200-399	No	Yes	Case-control
Shen	China	ChinaHK	1995-99	50-99	Yes	Yes	Case-control
Shimizu	Japan	RestAsia	1987-89	50-99	No	Yes	Case-control
Sobue	Japan	RestAsia	1990-94	100-199	No	Yes	Case-control
Speize	USA	NAmerica	1995-99	1-49	No	Yes	Prospective
Stockwell	USA	NAmerica	1990-94	200-399	No	Yes	Case-control
Sun	China	ChinaHK	1995-99	200-399	No	Yes	Case-control
Svensson	Sweden	EuropeNZ	1987-89	1-49	No	Yes	Case-control
Torres-Duran	Spain	EuropeNZ	2010-15	100-199	No	Yes	Case-control
Trichopoulos	Greece	EuropeNZ	1981-86	50-99	Yes	No	Case-control
Wang L	China	ChinaHK	2000-09	200-399	No	Yes	Case-control
Wang S	China	ChinaHK	1995-99	50-99	No	No	Case-control
Wang T	China	ChinaHK	1995-99	100-199	Yes	Yes	Case-control
Wen	China	ChinaHK	2000-09	100-199	No	Yes	Prospective
WHI-OS	USA	NAmerica	2010-15	200-399	No	No	Prospective
Wu	USA	NAmerica	1981-86	1-49	No	Yes	Case-control
Wu-Williams	China	ChinaHK	1990-94	400+	No	Yes	Case-control
Yang	USA	NAmerica	2000-09	100-199	No	Yes	Case-control
Yu	China	ChinaHK	2000-09	200-399	No	Yes	Case-control
Zaridze	Russia	EuropeNZ	1995-99	100-199	Yes	Yes	Case-control
Zatloukal	Czech Republic	EuropeNZ	2000-09	50-99	No	Yes	Case-control
Zheng	China	ChinaHK	1995-99	50-99	No	Yes	Case-control
Zhong	China	ChinaHK	1995-99	400+	Yes	Yes	Case-control

NOTES: REG REGION

PUBYR	PUBLICATION YEAR
NLC	NUMBER OF LUNG CANCER CASES
DOSER	DOSE RESPONSE DATA AVAILABLE FOR GIGARETTES PER DAY
COAGE	ADJUSTMENT (OR MATCHING) FOR AGE IN DOSE-RESPONSE ANALYSES
STYPE	STUDY TYPE

DISTRIBUTIONS OF VARIOUS STUDY VARIABLES

Region						
	N	29	20	27	17	93
NAmerica		29	0	0	0	29
EuropeNZ		0	20	0	0	20
ChinaHK		0	0	27	0	27
RestAsia		0	0	0	17	17
Year of publication						
	N	29	20	27	17	93
1981-86		6	2	2	2	12
1987-89		4	3	4	3	14
1990-94		5	1	4	1	11
1995-99		4	4	6	2	16
2000-09		7	9	6	4	26
2010-15		3	1	5	5	14
Number of lung cancer cases						
	N	29	20	27	17	93
1-49		10	7	2	3	22
50-99		5	6	10	6	27
100-199		9	5	5	3	22
200-399		3	1	6	3	13
400+		2	1	4	2	9
Studies with DR data						
	N	29	20	27	17	93
Yes		6	5	8	5	24
No		23	15	19	12	69
Age as confounder						
	N	29	20	27	17	93
Yes		24	17	19	15	75
No		5	3	8	2	18
Study type						
	N	29	20	27	17	93
Case-control		23	16	25	13	77
Prospective		6	4	2	4	16

FIXED- AND RANDOM-EFFECTS META-ANALYSES OF DATA FROM ALL THE STUDIES

Log RR (Beta)
WEIGHTED on Beta Weight

	Deviance	**(DF)**				
Model 1	169.9299	(92)				
	Estimate	**S.E.**	**P**	**RR**	**95%Cll**	**95%Clu**
Constant	0.0846	0.0109	+++	1.0882	1.0652	1.1118

RANDOM EFFECTS MODEL
Log RR (Beta)
WEIGHTED on Beta Weight

	Deviance	**(DF)**				
Model 1	99.7906	(92)				
	Estimate	**S.E.**	**P**	**RR**	**95%Cll**	**95%Clu**
Constant	0.0970	0.0172	+++	1.1019	1.0653	1.1397

FIXED-EFFECTS HETEROGENEITY META-ANALYSES BY VARIOUS FACTORS

	Deviance	**(DF)**				
Model 1	169.9299	(92)				
	Estimate	**S.E.**	**P**	**RR**	**95%Cll**	**95%Clu**
Constant	0.0846	0.0109	+++	1.0882	1.0652	1.1118
	Deviance	**(DF)**	**Drop Dev**		**P**	
Model 2	158.4818	(89)	11.4480		**	
	Estimate	**S.E.**	**P**	**RR**	**95%Cll**	**95%Clu**
Constant	0.0438	0.0191	+	1.0447	1.0063	1.0847

Region							
NAmerica	29	Aliased			1.0447	1.0063	1.0847
EuropeNZ	20	0.0106	0.0348	N.S.	1.0559	0.9974	1.1178
ChinaHK	27	0.0596	0.0284	+	1.1089	1.0642	1.1554
RestAsia	17	0.0889	0.0287	++	1.1418	1.0948	1.1908
		Deviance	**(DF)**	**Drop Dev**		**P**	
Model 2		154.0507	(87)	15.8792		**	
		Estimate	**S.E.**	**P**	**RR**	**95%CIl**	**95%CIu**
Constant		0.1181	0.0328	+++	1.1253	1.0552	1.2001
Year of publication							
1981-86	12	Aliased			1.1253	1.0552	1.2001
1987-89	14	0.0500	0.0522	N.S.	1.1830	1.0927	1.2808
1990-94	11	-0.1050	0.0405	-	1.0131	0.9670	1.0614
1995-99	16	-0.0459	0.0427	N.S.	1.0748	1.0187	1.1339
2000-09	26	-0.0053	0.0425	N.S.	1.1194	1.0616	1.1803
2010-15	14	-0.0237	0.0388	N.S.	1.0989	1.0554	1.1443
		Deviance	**(DF)**	**Drop Dev**		**P**	
Model 2		154.4007	(88)	15.5292		**	
		Estimate	**S.E.**	**P**	**RR**	**95%CIl**	**95%CIu**
Constant		0.1231	0.0547	+	1.1310	1.0160	1.2590
Number of lung cancer cases							
1-49	22	Aliased			1.1310	1.0160	1.2590
50-99	27	0.0114	0.0624	N.S.	1.1440	1.0784	1.2135
100-199	22	-0.0594	0.0589	N.S.	1.0657	1.0209	1.1125
200-399	13	0.0371	0.0615	N.S.	1.1737	1.1110	1.2399
400+	9	-0.0724	0.0572	N.S.	1.0520	1.0181	1.0871
		Deviance	**(DF)**	**Drop Dev**		**P**	
Model 2		167.8023	(91)	2.1275		N.S.	
		Estimate	**S.E.**	**P**	**RR**	**95%CIl**	**95%CIu**
Constant		0.1097	0.0204	+++	1.1160	1.0722	1.1615
Studies with DR data							
Yes	24	Aliased			1.1160	1.0722	1.1615
No	69	-0.0353	0.0242	N.S.	1.0773	1.0503	1.1050
		Deviance	**(DF)**	**Drop Dev**		**P**	
Model 2		162.5352	(91)	7.3947		**	
		Estimate	**S.E.**	**P**	**RR**	**95%CIl**	**95%CIu**
Constant		0.0738	0.0116	+++	1.0766	1.0523	1.1014
Age as confounder							
Yes	75	Aliased			1.0766	1.0523	1.1014
No	18	0.0929	0.0342	++	1.1814	1.1093	1.2581
		Deviance	**(DF)**	**Drop Dev**		**P**	
Model 2		169.8714	(91)	0.0584		N.S.	
		Estimate	**S.E.**	**P**	**RR**	**95%CIl**	**95%CIu**
Constant		0.0856	0.0118	+++	1.0894	1.0645	1.1148
Study type							
Case-control	77	Aliased			1.0894	1.0645	1.1148
Prospective	16	-0.0077	0.0317	N.S.	1.0811	1.0205	1.1452

SEPARATE FIXED- AND RANDOM-EFFECTS META-ANALYSES BY REGION

NORTH AMERICA

Log RR (Beta)

WEIGHTED on Beta Weight

	Deviance	**(DF)**				
Model 1	50.8219	(28)				
	Estimate	**S.E.**	**P**	**RR**	**95%CIl**	**95%CIu**
Constant	0.0438	0.0191	+	1.0447	1.0063	1.0847

RANDOM EFFECTS MODEL

Log RR (Beta)
WEIGHTED on Beta Weight

	Deviance	(DF)
Model 1	32.9830	(28)

	Estimate	S.E.	P	RR	95%CIl	95%CIu
Constant	0.0363	0.0304	N.S.	1.0370	0.9770	1.1006

EUROPE AND NEW ZEALAND

Log RR (Beta)
WEIGHTED on Beta Weight

	Deviance	(DF)
Model 1	20.4209	(19)

	Estimate	S.E.	P	RR	95%CIl	95%CIu
Constant	0.0544	0.0291	(+)	1.0559	0.9974	1.1178

RANDOM EFFECTS MODEL

Log RR (Beta)
WEIGHTED on Beta Weight

	Deviance	(DF)
Model 1	18.9284	(19)

	Estimate	S.E.	P	RR	95%CIl	95%CIu
Constant	0.0578	0.0320	(+)	1.0595	0.9951	1.1281

CHINA AND HONG KONG

Log RR (Beta)
WEIGHTED on Beta Weight

	Deviance	(DF)
Model 1	75.7017	(26)

	Estimate	S.E.	P	RR	95%CIl	95%CIu
Constant	0.1033	0.0210	+++	1.1089	1.0642	1.1554

RANDOM EFFECTS MODEL

Log RR (Beta)
WEIGHTED on Beta Weight

	Deviance	(DF)
Model 1	24.1987	(26)

	Estimate	S.E.	P	RR	95%CIl	95%CIu
Constant	0.1564	0.0395	+++	1.1693	1.0822	1.2634

REST OF ASIA

Log RR (Beta)
WEIGHTED on Beta Weight

	Deviance	(DF)
Model 1	11.5372	(16)

	Estimate	S.E.	P	RR	95%CIl	95%CIu
Constant	0.1326	0.0214	+++	1.1418	1.0948	1.1908

RANDOM EFFECTS MODEL

Log RR (Beta)
WEIGHTED on Beta Weight

	Deviance	(DF)
Model 1	11.5372	(16)

	Estimate	S.E.	P	RR	95%CIl	95%CIu
Constant	0.1326	0.0214	+++	1.1418	1.0948	1.1908

NORTH AMERICA, EUROPE AND NEW ZEALAND

Log RR (Beta)
WEIGHTED on Beta Weight

	Deviance	(DF)
Model 1	71.3363	(48)

	Estimate	S.E.	P	RR	95%CIl	95%CIu
Constant	0.0470	0.0160	++	1.0481	1.0158	1.0815

RANDOM EFFECTS MODEL

Log RR (Beta)
WEIGHTED on Beta Weight

	Deviance	(DF)				
Model 1	52.2558	(48)				
	Estimate	**S.E.**	**P**	**RR**	**95%CIl**	**95%CIu**
Constant	0.0454	0.0226	+	1.0464	1.0012	1.0938

ASIA

Log RR (Beta)
WEIGHTED on Beta Weight

	Deviance	(DF)				
Model 1	88.1925	(43)				
	Estimate	**S.E.**	**P**	**RR**	**95%CIl**	**95%CIu**
Constant	0.1177	0.0150	+++	1.1249	1.0923	1.1584

RANDOM EFFECTS MODEL

Log RR (Beta)
WEIGHTED on Beta Weight

	Deviance	(DF)				
Model 1	42.1869	(43)				
	Estimate	**S.E.**	**P**	**RR**	**95%CIl**	**95%CIu**
Constant	0.1469	0.0247	+++	1.1582	1.1035	1.2156

SEPARATE FIXED- AND RANDOM-EFFECTS META-ANALYSES BY YEAR OF PUBLICATION

PUBLISHED IN 1980S

Log RR (Beta)
WEIGHTED on Beta Weight

	Deviance	(DF)				
Model 1	21.7503	(25)				
	Estimate	**S.E.**	**P**	**RR**	**95%CIl**	**95%CIu**
Constant	0.1379	0.0255	+++	1.1478	1.0918	1.2066

RANDOM EFFECTS MODEL

Log RR (Beta)
WEIGHTED on Beta Weight

	Deviance	(DF)				
Model 1	21.7503	(25)				
	Estimate	**S.E.**	**P**	**RR**	**95%CIl**	**95%CIu**
Constant	0.1379	0.0255	+++	1.1478	1.0918	1.2066

PUBLISHED IN 1990S

Log RR (Beta)
WEIGHTED on Beta Weight

	Deviance	(DF)				
Model 1	51.2683	(26)				
	Estimate	**S.E.**	**P**	**RR**	**95%CIl**	**95%CIu**
Constant	0.0384	0.0179	+	1.0392	1.0033	1.0764

RANDOM EFFECTS MODEL

Log RR (Beta)
WEIGHTED on Beta Weight

	Deviance	(DF)				
Model 1	27.1081	(26)				
	Estimate	**S.E.**	**P**	**RR**	**95%CIl**	**95%CIu**
Constant	0.0609	0.0290	+	1.0628	1.0041	1.1249

PUBLISHED IN 2000S

Log RR (Beta)
WEIGHTED on Beta Weight

	Deviance	(DF)				
Model 1	30.4638	(25)				
	Estimate	**S.E.**	**P**	**RR**	**95%CIl**	**95%CIu**
Constant	0.1128	0.0270	+++	1.1194	1.0616	1.1803

RANDOM EFFECTS MODEL

Log RR (Beta)
WEIGHTED on Beta Weight

	Deviance	(DF)
Model 1	24.6933	(25)

	Estimate	S.E.	P	RR	95%CIl	95%CIu
Constant	0.1157	0.0312	++	1.1227	1.0561	1.1935

PUBLISHED IN 2010S

Log RR (Beta)
WEIGHTED on Beta Weight

	Deviance	(DF)
Model 1	54.1498	(13)

	Estimate	S.E.	P	RR	95%CIl	95%CIu
Constant	0.0944	0.0206	+++	1.0989	1.0554	1.1443

RANDOM EFFECTS MODEL

Log RR (Beta)
WEIGHTED on Beta Weight

	Deviance	(DF)
Model 1	24.9995	(13)

	Estimate	S.E.	P	RR	95%CIl	95%CIu
Constant	0.0706	0.0518	N.S.	1.0731	0.9696	1.1877

SEPARATE FIXED- AND RANDOM-EFFECTS META-ANALYSES BY NUMBER OF LUNG CANCER CASES

<100 CASES

Log RR (Beta)
WEIGHTED on Beta Weight

	Deviance	(DF)
Model 1	58.5684	(48)

	Estimate	S.E.	P	RR	95%CIl	95%CIu
Constant	0.1318	0.0264	+++	1.1409	1.0834	1.2015

RANDOM EFFECTS MODEL

Log RR (Beta)
WEIGHTED on Beta Weight

	Deviance	(DF)
Model 1	48.5647	(48)

	Estimate	S.E.	P	RR	95%CIl	95%CIu
Constant	0.1333	0.0304	+++	1.1426	1.0765	1.2128

100-199 CASES

Log RR (Beta)
WEIGHTED on Beta Weight

	Deviance	(DF)
Model 1	48.4755	(21)

	Estimate	S.E.	P	RR	95%CIl	95%CIu
Constant	0.0636	0.0219	++	1.0657	1.0209	1.1125

RANDOM EFFECTS MODEL

Log RR (Beta)
WEIGHTED on Beta Weight

	Deviance	(DF)
Model 1	24.0431	(21)

	Estimate	S.E.	P	RR	95%CIl	95%CIu
Constant	0.0606	0.0345	(+)	1.0624	0.9930	1.1367

200-399 CASES

Log RR (Beta)
WEIGHTED on Beta Weight

	Deviance	(DF)
Model 1	18.3486	(12)

	Estimate	S.E.	P	RR	95%CIl	95%CIu
Constant	0.1601	0.0280	+++	1.1737	1.1110	1.2399

RANDOM EFFECTS MODEL

Log RR (Beta)
WEIGHTED on Beta Weight

	Deviance	(DF)
Model 1	12.7727	(12)

	Estimate	S.E.	P	RR	95%CIl	95%CIu

Constant	0.1623	0.0357	+++	1.1762	1.0968	1.2614

400+ CASES
Log RR (Beta)
WEIGHTED on Beta Weight

	Deviance	**(DF)**
Model 1	29.0416	(8)

	Estimate	**S.E.**	**P**	**RR**	**95%CIl**	**95%CIu**
Constant	0.0507	0.0167	+	1.0520	1.0181	1.0871

RANDOM EFFECTS MODEL
Log RR (Beta)
WEIGHTED on Beta Weight

	Deviance	**(DF)**
Model 1	8.5557	(8)

	Estimate	**S.E.**	**P**	**RR**	**95%CIl**	**95%CIu**
Constant	0.0406	0.0329	N.S.	1.0414	0.9764	1.1107

SEPARATE FIXED- AND RANDOM-EFFECTS META-ANALYSES BY DOSE-RESPONSE OR NOT

RESULTS FOR DOSE-RESPONSE
Log RR (Beta)
WEIGHTED on Beta Weight

	Deviance	**(DF)**
Model 1	27.8124	(23)

	Estimate	**S.E.**	**P**	**RR**	**95%CIl**	**95%CIu**
Constant	0.1097	0.0204	+++	1.1160	1.0722	1.1615

RANDOM EFFECTS MODEL
Log RR (Beta)
WEIGHTED on Beta Weight

	Deviance	**(DF)**
Model 1	22.8187	(23)

	Estimate	**S.E.**	**P**	**RR**	**95%CIl**	**95%CIu**
Constant	0.1160	0.0236	+++	1.1230	1.0723	1.1761

NO RESULTS FOR DOSE-RESPONSE
Log RR (Beta)
WEIGHTED on Beta Weight

	Deviance	**(DF)**
Model 1	139.9899	(68)

	Estimate	**S.E.**	**P**	**RR**	**95%CIl**	**95%CIu**
Constant	0.0745	0.0129	+++	1.0773	1.0503	1.1050

RANDOM EFFECTS MODEL
Log RR (Beta)
WEIGHTED on Beta Weight

	Deviance	**(DF)**
Model 1	75.5208	(68)

	Estimate	**S.E.**	**P**	**RR**	**95%CIl**	**95%CIu**
Constant	0.0869	0.0222	+++	1.0908	1.0444	1.1393

SEPARATE FIXED- AND RANDOM-EFFECTS META-ANALYSES BY AGE ADJUSTMENT OR NOT

ADJUSTED (OR MATCHED) FOR AGE
Log RR (Beta)
WEIGHTED on Beta Weight

	Deviance	**(DF)**
Model 1	132.8342	(74)

	Estimate	**S.E.**	**P**	**RR**	**95%CIl**	**95%CIu**
Constant	0.0738	0.0116	+++	1.0766	1.0523	1.1014

RANDOM EFFECTS MODEL
Log RR (Beta)
WEIGHTED on Beta Weight

	Deviance	**(DF)**
Model 1	78.3370	(74)

	Estimate	**S.E.**	**P**	**RR**	**95%CIl**	**95%CIu**
Constant	0.0802	0.0180	+++	1.0835	1.0459	1.1225

NOT ADJUSTED (OR MATCHED) FOR AGE

Log RR (Beta)
WEIGHTED on Beta Weight

	Deviance	(DF)				
Model 1	29.7010	(17)				
	Estimate	**S.E.**	**P**	**RR**	**95%ClI**	**95%Clu**
Constant	0.1667	0.0321	+++	1.1814	1.1093	1.2581

RANDOM EFFECTS MODEL

Log RR (Beta)
WEIGHTED on Beta Weight

	Deviance	(DF)				
Model 1	17.9738	(17)				
	Estimate	**S.E.**	**P**	**RR**	**95%ClI**	**95%Clu**
Constant	0.1910	0.0484	++	1.2105	1.1009	1.3309

SEPARATE FIXED- AND RANDOM-EFFECTS META-ANALYSES BY STUDY TYPE

CASE-CONTROL STUDIES

Log RR (Beta)
WEIGHTED on Beta Weight

	Deviance	(DF)				
Model 1	160.6937	(76)				
	Estimate	**S.E.**	**P**	**RR**	**95%ClI**	**95%Clu**
Constant	0.0856	0.0118	+++	1.0894	1.0645	1.1148

RANDOM EFFECTS MODEL

Log RR (Beta)
WEIGHTED on Beta Weight

	Deviance	(DF)				
Model 1	86.4952	(76)				
	Estimate	**S.E.**	**P**	**RR**	**95%ClI**	**95%Clu**
Constant	0.1007	0.0199	+++	1.1060	1.0636	1.1500

PROSPECTIVE STUDIES

Log RR (Beta)
WEIGHTED on Beta Weight

	Deviance	(DF)				
Model 1	9.1777	(15)				
	Estimate	**S.E.**	**P**	**RR**	**95%ClI**	**95%Clu**
Constant	0.0780	0.0294	+	1.0811	1.0205	1.1452

RANDOM EFFECTS MODEL

Log RR (Beta)
WEIGHTED on Beta Weight

	Deviance	(DF)				
Model 1	9.1777	(15)				
	Estimate	**S.E.**	**P**	**RR**	**95%ClI**	**95%Clu**
Constant	0.0780	0.0294	+	1.0811	1.0205	1.1452

Appendix 3

Review of papers since 2000 relating risk of lung cancer to potential confounding variables

INDEX

A. FRUIT, VEGETABLES AND DIETARY FAT CONSUMPTION

1. Balder [1]

This was a case-control study nested within a prospective study in the Netherlands. The prospective study was on males and females, but the paper reports on males only. Table 5 on page 488 gave the RR and 95% CI for lung cancer per increment in 1 SD in factor score for dietary patterns, stratified by smoking status and histologic type of cancer and adjusted for age and energy. For never smokers there were 52 cases of lung cancer in a person time of 2,452, giving for "Salad vegetables pattern" values an RR of 1.21 (0.94 – 1.56), for Cooked vegetables pattern 0.84 (0.63-1.12) and for Pork, process meat and potatoes pattern 0.51 (0.33 – 0.77). Note there was a negative RR for smokers and former smokers for "Salad vegetables pattern," with values of 0.77 (0.65 – 0.90) and 0.90 (0.80 – 1.01) respectively.

2. Brennan [2]

This was a multicenter case-control study involving centers in countries in Europe (3 from Germany and 1 each from Sweden, France, Spain, UK and Italy) concentrating at looking at the effect of diet on lung cancer in non-smokers. The results, given in Table 2 on page 52, were for fruits and vegetables, males and females combined, adjusted for age, sex and center, with results divided into thirds. Particular results of interest were:

	Tertile 1	2	3	Linear trend
Fruit	1.0 139/273	0.9 (0.6-1.3) 124/251	1.0 (0.6-1.5) 212/371	0.81
Fresh vegetables	1.0 46/83	0.9 (0.7-1.1) 180/362	0.7 (0.5-1.0) 110/237	0.09

[Here and subsequently summary tables show odds ratios or relative risks (95% CIs) and numbers of cases/controls (or at risk) by level of dietary exposure, with p-values for linear trend where available.]

In Table 3 on page 53 results are given for consumption of meat, fish and dairy products, with particular results:

	Tertile 1	2	3	Linear trend
Eggs	1.0 110/206	1.0 (0.6–1.6) 154/306	0.9 (0.8–1.1) 232/519	0.63
Cheese	1.0 113/222	0.9 (0.7–1.2) 164/331	0.7 (0.5–1.0) 219/477	0.01
Butter	1.0 65/194	1.2 (0.9–1.5) 21/49	1.3 (0.9–1.9) 88/207	0.24
Margarine	1.0 98/189	0.7 (0.4–1.1) 19/53	0.7 (0.6–0.8) 57/208	0.05

It can be noted that combinations of protective foods often produced extra protection – with eating vegetables and cheese having an OR of 0.6 (0.5 – 0.7).

Individual results for particular centers have been reported by Nyberg [3] and Jöckel [4]. The results from Nyberg were used in our previous work on estimating the effects of confounding.

For estimating odds ratios the authors made use of what they called a “sandwich estimator” with reference made to a paper by White [5].

3. Breslow [6]

This paper was based on analysis of a cohort created by linking the US NHIS data with the National Death Index. All results were based on models using all the data, adjusting for sex and smoking, so data were not available for non-smokers on their own. It is worth noting that 41.8% were men, 47% were never smokers, 21% were ex-smokers and that when checking for interactions between the variables and smoking, there was only a significant effect for alcohol. Although there was no interaction, taking the results as applicable to never-smokers would not agree with our previous work. Results for quartiles of consumption are given in Table 2 on pages 423 and 424. Particularly of interest were:

	Quartile 1	2	3	4	Linear trend
Fruit	1.0 35/39,880	1.2 (0.7–1.9) 46/41,087	0.8 (0.4–1.4) 31/39,865	0.9 (0.5–1.6) 42/39,893	0.489
Vegetables	1.0 36/40,478	1.0 (0.6–1.8) 38/41,474	1.3 (0.8–2.0) 49/41,078	0.9 (0.5–1.5) 35/41,088	0.786
Dairy produce	1.0 51/39,138	0.9 (0.5–1.4) 50/46,437	0.7 (0.4–1.2) 33/36,161	0.5 (0.3–0.8) 22/40,562	0.009
Added fats	1.0 31/40,763	1.1 (0.6–1.9) 38/39,894	1.0 (0.5–2.1) 36/39,447	1.2 (0.7–2.0) 52/42,152	0.603
Alcohol	1.0 52/47,779	0.7 (0.4–1.3) 23/31,894	1.0 (0.6–1.6) 32/41,061	1.3 (0.8–2.0) 50/41,026	0.101

4. Chan-Yeung [7]

This paper reports on a case-control study in Hong Kong. Unfortunately all the results are for smokers and non-smokers together, though there are values adjusted for smoking. These are given in Table 4 on page 137 and it is interesting to note that there seems to be an increase in OR for increasing consumption of vegetables and fruits and a decrease for increasing amounts of fatty food:

Women	ORs are adjusted for educational status and smoking		
	<15 p/wk*	15-30 p/wk	30+ p/wk
Fruit	1.0	0.58 (0.27–1.22)	1.25 (0.65–2.44)
	<45 p/wk	45-65 p/wk	65+ p/wk
Green vegetables	1.0	2.11 (0.91–4.86)	1.74 (0.86–3.52)
	<70 p/wk	70-100 p/wk	100+ p/wk
Fruit, tubers and green veg	1.0	1.60 (0.74–3.47)	1.86 (0.89–3.90)
	<1 p/wk	1-2 p/wk	>2 p/wk
Fatty food	1.0	0.94 (0.45–1.96)	0.45 (0.20–1.02)

*p/wk = portions/week

5. Darby [8]

This paper reported on diet in relation to smoking and lung cancer based on a very large case-control study in the UK. However, "there were only 26 subjects with lung cancer in the study who had never smoked, which was too few to provide useful data on diet and lung cancer among never smokers". It is also worth mentioning the footnote to Table 1 on page 729 which states "The number of males with lung cancer who were lifelong non-smokers is atypically low and should not be used to estimate relative risk. See Peto et al (2000) for further details." [9] Checking the Peto (2000) paper they seem to use the data from non-smokers in CPS II as the numbers of non-smokers is so small, but they don't seem to give a clue as to why the numbers are so small!

This paper shows no significant decreases in lung cancer risk for increasing consumption of vegetables or green vegetables. However, estimates of intake of carotene, carrots and tomatoes all showed some decreasing effects. Butter and milk showed some increase in risk with increasing dose while margarine showed decreasing risk with dose. The authors speculate about some extra confounder not being measured. They do also say "It is clear that the commonly observed association between carotene rich foods and lung cancer risk is partially confounded by smoking, since it is well established that smokers have a lower intake of carotene rich foods than non-smokers (Margetts and Jackson, 1993)." [10] and see also Margetts 1996 [11].

6. Feskanich [12]

This paper investigates fruit and vegetable consumption and risk of lung cancer by examining the women in the Nurses' Health Study (NHS) and the men in the Health Professionals' Follow-up Study. This gave sufficient numbers to be able to look at men, women, smokers and non-smokers separately. Table 4 gives RRs for total fruits, vegetables and fruits + vegetables for the various groups.

NHS Women Never Smokers	OR are adjusted for age, follow-up cycle, total energy intake and availability of diet data		
	Tertile 1	2	3
Total fruits	1.0	Not given	0.34 (0.16–0.72)
Total vegetables	1.0	Not given	0.94 (0.46–1.91)
Total fruit + veg	1.0	Not given	0.58 (0.28–1.18)

7. Hirvonen [13]

This paper was based on a large cohort study of men aged 50 – 69 years, the Alpha-Tocopherol, Beta-Carotene Cancer Prevention study (ATBC). Enrolment took place in southwestern Finland between 1985 and 1988 and was restricted to men who smoked at least 5 cigarettes a day at the time of the questionnaire. This report was looking at flavonol and flavine intake in relation to cancer in smokers. Table 5 on page 793 does give relative risks for vegetables, fruit, berries, tea and wine, all of which show reductions with increasing consumption. However as this is only in smokers it will not be included in our files.

8. Holick [14]

This is another report on the ATBC study in Finland. Table 3 gives results for Fruits, vegetables and fruits + vegetables, but this is still a study on smokers only and will not be added to the database.

9. Hu [15]

This is a report on a case-control study in non-smoking women in Canada, with the data collected between 1993 and 1997. Detailed tables for vegetables and fruit are given in Table 2 on page 132 and for beverages are given in Table 3 on page 133. In particular there are the following RRs, adjusted for 10 year age, province, education, social class and total energy:

	Quartile 1	2	3	4	Linear trend
Total fruit	1.0 46/119	0.8 (0.4–1.5) 34/122	0.9 (0.5–1.6) 39/120	1.1 (0.6–2.0) 38/118	0.83
Total vegetables	1.0 40/118	1.3 (0.7–2.4) 49/138	1.3 (0.6–2.6) 29/98	1.4 (0.7–3.0) 41/127	0.37
Total veg, fruit and juices	1.0 42/121	1.1 (0.6–2.1) 46/121	1.0 (0.5–1.9) 29/120	1.3 (0.6–2.6) 42/120	0.63
French fries or fried potatoes	1.0 59/184	0.8 (0.5–1.4) 45/165	1.7 (1.0–3.0) 53/120		0.05
Tea (cups per week)	0 1.0	1–7 0.6 (0.3–0.9)	>7 0.4 (0.2–0.7)		0.0008
Alcohol (servings per week)	0 1.0	1 0.8 (0.5–1.4)	>1 0.8 (0.5–1.2)		0.25

Data on occupational exposure to asbestos, oil, pesticides, herbicides, radiation sources and wood dust are given in Table 4 on page 134.

Note that this data set was also reported on by Johnson [16], though in that paper they only used those cases with a relatively complete history of residential passive smoke exposure.

10. Jansen [17]

This paper looks at some of the data from the Seven Countries study, a cohort study in men aged 40 – 59, initiated between 1958 and 1964. Dietary intake of the Finnish, Italian and Dutch survivors was assessed in 1970 and information on survival was available up to 1995. Table 1 gives some baseline figures for current and non smokers (never + ex), but the main results in Table II gives results only for smokers. Figures 2a and 2b give relative risks of lung cancer for nonsmokers, light and heavy smokers by consumption of (a) fruit and (b) vegetables, relative to heavy smokers with a low consumption of the dietary variable considered. This gives relative risks for nonsmokers of 0.07, 0.07 and 0.14 for fruit consumption and 0.1, 0.17 and 0.1 for vegetable consumption. No CIs are available for these figures, but there is an impression of a fall in risk for heavy smokers (1, 0.47, 0.4 for fruit, 1, 0.92 0.64 for vegetables) but not for nonsmokers. However, there were only 38 lung cancer deaths in nonsmokers, of which only 10 were in never smokers.

11. Kreuzer [18]

This paper is based on a case-control study in Germany conducted between 1991 and 1996, but looking specifically at the non-smoking women. Data for RRs for lung cancer in relation to the consumption of fruits, vegetables, meat, fish and dairy products are given in Table IV on page 710. These are adjusted for age and region. In particular:

	Nev/lm/lw/w[a]	Sw	Daily	Linear trend
Fruit	1.0 17/34	0.55(0.28–1.09) 36/98	0.66 (0.37–1.19) 177/403	0.94
Fresh vegetables	1.0 22/43	0.57 (0.33–0.99) 147/326	0.45 (0.25–0.82) 60/165	0.03

Meat	1.0 16/63	1.57(0.90–2.75) 142/311	1.61 (0.90–2.89) 72/157	0.44
Sausages	1.0 30/71	0.99 (0.60–1.62) 81/182	0.99 (0.61–1.62) 120/279	0.43

	Nev/lm/lw	W	Sw/Daily	Linear trend
Eggs	1.0 52/102	0.68 (0.44–1.05) 70/186	0.69 (0.46–1.05) 107/245	0.22

	Nev/lm	Lw/w/sw	Daily	Linear trend
Milk	1.0 78/159	0.98 (0.67–1.45) 81/160	0.65 (0.44–0.95) 72/215	0.16

[a] Nev, never; lm, less than monthly; lw, less than weekly; w, weekly; sw several times weekly

Note that Table V gives some odds ratios for various occupations.

12. Liu [19]

This study reported on data from two large cohort studies in Japan, the first for men and women aged 40-59, interviewed in 1990 and the second for men and women aged 40 – 69, interviewed in 1993. Follow-up was to the end of 1999. Table 3 on page 353 gives RRs for lung cancer by food consumption for never and ever smokers separately. The relevant data for never smokers (males and females combined) adjusted for age, gender, area, sports, frequency of alcohol intake, BMI, vitamin supplement use, salted fish and meat and pickled vegetables, were:

	Low	Middle	High	Linear trend
Fruit	1.0 25/110627	1.17 (0.25–5.48) 26/143425	2.09 (0.56–7.83) 55/189726	0.22
Vegetables	1.0 28/130452	0.96 (0.37–2.45) 31/150722	1.37 (0.79–2.37) 47/162604	0.20
Veg + fruit	1.0 24/121244	1.34 (0.52–3.42) 32/149661	1.95 (0.84–4.52) 50/172873	0.17

Note that the authors claim that references Mayne [20], Brennan [2], Nyberg [3] and Feskanich [12] have showed strong protective effect of diets high in fruit and vegetables for lung cancer.

13. Michaud [21]

This paper investigates specific carotenoids and risk of lung cancer by examining the women in the Nurses' Health Study and the men in the Health Professionals' Follow-up Study. These data have already been looked at for vegetable and fruit consumption in Feskanich [12] given above. In this study subjects who never smoked had a 63% lower incidence of lung cancer for the top compared to the bottom quintile of α-carotene, RR 0.37 (0.18 – 0.77).

14. Miller [22]

This study was a large prospective investigation of diet and cancer, the European Prospective Investigation Into Cancer and Nutrition (EPIC). It involved 478,021 individuals recruited from 10 European countries, who completed a dietary questionnaire during 1992 – 1998, with follow-up to December 1998 or 1999. Some centres had additional active follow-up to June 2002. Table V on page 274 gave RRs for lung cancer by quintiles of fruit and vegetable consumption for life-long nonsmokers. The relevant data for sexes combined, adjusted for weight, height, sex and centre are:

	Quintile 1	2	3	4	5	Linear trend
Total fruit	1.0 13 / -*	1.02 (0.48-2.16) 19 / -	0.64 (0.29-1.42) 14 / -	1.19 (0.59-2.39) 32 / -	0.33 (0.13-0.83) 10 / -	0.2429
Total vegetables	1.0 18 / -	0.56 (0.24-1.28) 10 / -	1.14 (0.56-2.33) 20 / -	0.98 (0.47-2.04) 21 / -	0.99 (0.45-2.21) 19 / -	0.6741

* Number of controls not given

15. Miller [23]

This was an earlier report than that given above in (14) and thus has been superseded.

16. Mulder [24]

This is another report on the Seven Countries Study already referred to above in Jansen [17]. This time an attempt was made to estimate dietary consumption for all of the cohorts involved. This involved making various assumptions for each of the countries, but it did increase numbers to a state where analyses involving non-smokers could be given. The following RRs for 25-Year lung cancer mortality in never smokers, adjusted for average age and energy intake are given in Table IV on Page 668:

	Unit of change = change of 10% of the average dietary intake over the 16 cohorts	RR (CI)
Fruit	13 g	0.99 (0.93–1.04)
Total vegetables	18 g	0.86 (0.67–1.08)
Total fat	12 g	0.96 (0.75–1.27)

17. Neuhouser [25]

This paper described an analysis of the data from the β-carotene and Retinol efficacy Trial (CARET) in the US run from 1989 to 1996. Follow-up had been continued to 2003 and the analysis examined the effects of fruits and vegetables in the subjects' diet as opposed to the supplements of β-carotene and retinol that the treatment arm of the trial had been given. The study was restricted to people thought to be of high risk of lung cancer, that is heavy smokers or asbestos exposed people. As such it has no information for non-smokers, though it is interesting to note that they did find a reduction in risk with increasing fruit and vegetables, but only in the arm of the trial not given the supplements.

18. Ozasa [26]

This paper was based on the Japan Collaborative Cohort (JACC) Study, a prospective trial established in 1988 – 1990 with follow-up for deaths continued until the end of 1997. It contained both males and females aged between 40 to 79 from 45 areas in Japan. Table V on Page 1266 gave details of hazard ratios for lung cancer deaths using Cox proportional hazard models for female, nonsmokers divided by various dietary factors. In particular we have the following RRs adjusted for age and parental history of lung cancer:

	≤1-2/w	3-4/w	Almost every day	Linear trend
Vegetables (Green-leafy)	1.0 23/130087	1.19(0.68–2.09) 27/118378	1.35 (0.79–2.30) 35/126081	0.26

	≤1-2/m	1-2/w	3-4/w+	Linear trend
Oranges	1.0 8/42090	0.95(0.38–2.34) 12/68271	1.18 (0.54–2.57) 53/223275	0.053
Fried foods	1.0 15/96003	1.47(0.79–2.70) 35/165130	1.91 (0.98–3.72) 24/83589	0.056

19. Rachtan [27]

This describes a case control study of lung cancer in Polish women in Cracow. Cases were women admitted to hospital between 1 March 1991 and 31 December 1997. From Table 1 on Page 390 we learn that 54 cases and 251 controls never smoked. There was also the impression of an effect of vodka drinking as well as of smoking. Thus in Table 3 on Page 392 ORs for lung cancer are given for non-smoking non-drinkers and for non-smoking vodka drinkers separately for extremes of consumption of vegetables, fruits and margarines. In particular:

Total cases/controls	Non-smoking non-drinkers 23/179	Non-smoking vodka drinkers 31/72
Carrots	5+ times/wk (vs rarely) 0.10 (0.03–0.36)	5+ times/wk (vs rarely) 0.05 (0.01–0.37)
Other vegetables	Every day (vs rarely) 0.10 (0.01–0.75)	Every day (vs rarely) 0.25 (0.05–1.19)
Fruits	0.38 (0.15–0.98)	0.30 (0.11–0.78)
Margarine	3+ times wk (vs rarely) 0.19 (0.07–0.54)	3+ times/wk vs rarely 0.23 (0.09–0.60)

20. Rylander [28]

This paper relates to a case control study of lung cancer in West Sweden undertaken from 1989 to 1994. Cases were 75 years and younger and of Scandinavian birth. Results for lung cancer risk for non-smoking men and women (combined) are given in Table III on Page 741 for quartiles of vegetable consumption, and in Table IV on Page 742 for fruit consumption. The quartiles for females were defined as 0–4, 4.1–8.9, 9.0–14.1 and >14.1 times/week for vegetables and 0–7.4, 7.5–11.9, 12.0–14.9 and >14.9 times a week for fruit. The results for vegetable/fruit consumption, adjusted for age, gender, ETS at home or work and fruit/vegetable consumption, were as follows:

	Quartile 1	2	3	4
Vegetables	1.0 15/75	0.92 (0.42–1.91) 17/95	0.51 (0.21–1.26) 9/100	0.37 (0.15–0.97) 8/114
Fruit	1.0 9/82	1.76 (0.71–4.36) 16/83	1.38 (0.55–3.74) 15/109	0.99 (0.36–2.74) 9/110

Note that in the paper the number of controls in Quartile 1 was given as 2 for fruit in Table IV. Checking the number of controls in Tables I and III the value 82 would allow the marginal tables to correctly add up to 384. This value also makes sense in terms of the relative risks and so that is the value that has been used.

21. Schabath [29]

This paper described a case-control study looking at the effect of photestrogens on lung cancer risk. These are plant-derived nonsteroidal compounds with weak estrogen-like activity. The cases and controls were US residents, with cases drawn from The University of Texas Cancer Center between July 1997 and October 2003. Table 3 on Page 1497 gives the top five food sources for each phytoestrogen examined, with 77% of phytosterol beta-sitosterol and 89% of ligan precursors matairesinol coming from tea (mainly black tea). Table 6 gave risk of lung cancer for non-smokers by quartiles of different phytoestrogens, adjusted for age, sex, ethnicity, education, income, body mass index and total energy:

	Quartile 1	2	3	4	Linear trend
Total phytosterols	1.0 87/72	0.63 (0.36–1.09) 55/73	0.57 (0.34–0.97) 63/73	0.63 (0.37–1.07) 61/72	0.06
Total isoflavones	1.0 75/72	0.72 (0.42–1.23) 61/73	0.81 (0.47–1.41) 68/73	0.53 (0.30–0.93) 62/72	0.25
Total ligans	1.0 71/72	0.89 (0.52–1.53) 69/73	0.73 (0.43–1.25) 65/73	0.66 (0.38–1.14) 61/72	0.06

As such these results are more indicative of some extra underlying substances that have yet to be examined fully than values to be added to the database.

22. Shen [30]

This paper described a case-control study looking at the effect of dietary folate intake and lung cancer risk in former smokers. The cases were taken from a sequential sample of confirmed lung cancer cases in The University Texas Cancer Center from July 1995 to July 2001. Significant reductions in lung cancer were seen for increasing levels of food folate, but as these findings were only given for ex-smokers they cannot be included in our database.

23. Shibata [31]

This study is of a cohort of men living in a retirement community in California in the US, followed up from June 1981 to December 1989 (the Leisure World Study). No results were given just for nonsmokers, though adjusted RRs showed small non-significant *increases* in risk of lung cancer with increasing fruit and vegetable consumption. No effect was seen with β-carotene.

24. Skuladottir [32]

This paper is based on men and women in the prospective cohort study "Diet, Cancer and Health" initiated by the Danish Cancer Society. Recruitment was between December 1993 and May 1997, with follow up with the Danish Cancer Registry obtained to the end of 2001. Table 2 on Page 5 suggests a lower intake of fruits and vegetables for current smokers than for never smokers – 109 vs 164.9 g/day for fruits and 138 vs 169.4 g/day for vegetables. When looking at the lung cancer risk by fruit/veg consumption there was a very large decrease in risk for increasing consumption when smoking was not allowed for, which was ameliorated by adjusted for various indices of smoking. However there was still indications of an effect when rates where fully adjusted for smoking. There were only nine non-smoking cases and so no separate data on nonsmokers were available.

25. Takezaki [33]

This paper concerned a 14 year population based prospective study in Japan with particular interest in fish consumption. The study started in April 1985 and follow-up was until December 1999 and was for all male residents aged 40 or more and female residents aged 30 or more in the Aichi Prefecture. Only 38 lung cancer cases were seen in the males and 13 in the females. There seemed to be a very large reduction in lung cancer risk with increasing levels of fish consumption. No data were available just for non-smokers.

26. Voorrips [34]

This paper relates to the Netherlands Cohort Study on diet and cancer, a prospective cohort study started in September 1986. The study was of men and women aged 55–69 originating from 204 municipalities with computerized population registries. After 6.3 years of follow-up over 1000 lung cancer cases were identified. Analyses were carried out using a case-cohort approach – finding a sub-cohort to match the cases of lung cancer. Table 7 on Page 113 gave RRs for lung cancer by quintiles of fruit or vegetable consumption for never smokers. The relevant data, adjusted for highest educational level, family history of lung cancer, age and sex, were:

	Quintile 1	2	3	4	5	Linear trend
All fruit 62 cases	1.0	0.9 (0.4–2.3)	0.7 (0.3–1.9)	0.7 (0.3–1.7)	1.4 (0.6–3.2)	0.44
All vegetables 57 cases	1.0	1.1 (0.4–3.1)	2.1 (0.8–5.6)	2.3 (0.9–5.8)	1.8 (0.7–4.7)	0.06

Note that the paper claims inverse associations with lung cancer, but for non-smokers the effects are, if anything, of an increasing risk with increasing consumption.

27. Voorrips 2 [35]

This is a second paper on the Netherlands Cohort Study mentioned above (26) [34]. This paper concentrated on antioxidants, such as α-carotene and β-carotene, and folate intake. Table 5 gave RRs for lung cancer for never smokers by tertiles of intake, adjusted for highest educational level, family history of lung cancer, age and sex:

Cases: n=35 Subcohort: n = 203	Tertile 1	2	3	Linear trend
α-carotene	1.0	1.32 (0.46–3.79)	1.61 (0.61–4.21)	0.27
β-carotene	1.0	2.35 (0.83–6.65)	1.98 (0.75–5.26)	0.14
Lutein,zeaxanthin	1.0	0.83 (0.29–2.35)	1.35 (0.56–3.26)	0.42
β-cryptoxantin	1.0	0.50 (0.18–1.41)	0.86 (0.36–2.06)	0.76
Lycopene	1.0	0.92 (0.32–2.65)	1.54 (0.61–3.90)	0.26
Vitamin C	1.0	0.72 (0.26–1.99)	0.67 (0.25–1.79)	0.39
Vitamin E	1.0	0.80 (0.32–2.02)	0.67 (0.26–1.67)	0.32
Folate	1.0	1.04 (0.39–2.77)	1.09 (0.44–2.72)	0.82

Though there seems to be little going on in non-smokers, risk did seem to reduce for current smokers, with β-cryptoxantin, Vitamin C and folate showing highly significant decreases in risk with increasing consumption.

28. Wright [36]

This paper looks at the effect of dietary carotenoids and vegetables on lung cancer risk in women, using the Missouri Women's Health Study. This was a case control study in the US of women with incident primary lung cancer, aged between 35 and 84, undertaken between 1 January 1993 and 31 January 1994. Table 4 on page 91 gave ORs separately for never and former smokers combined and for current smokers. It seems clear the effects are less strong in the never and former smokers than in the current smokers, but there are no data available for the never smokers to add to our database.

29. Zhong [37]

This paper relates to a population-based case-control study examining links between lung cancer and green tea consumption for women in Shanghai in China. The study used incident cases of lung cancer diagnosed between February 1992 and January 1994 with the controls randomly selected from the Shanghai residential registry, frequency matched to the expected age distribution of the cases. Table 2 on Page 698 gave RRs for lung cancer for non-smokers and smokers separately and by amount of tea consumed. The following results for non-smokers, adjusted for age, income, number of years of exposure to environmental tobacco smoke at work, high-risk occupation, family history of lung cancer, intake of dietary vitamin C, cooking food at high temperature, and respondent status, were given:

Cases: n=35 Subcohort: n = 203	Non-regular	1-500 (g/year)	501-1500 (g/year)	>1500 g/year
Green Tea	1.0 431/481	0.80 (0.45–1.42) 27/37	0.62 (0.36–1.08) 30/47	0.46 (0.22–0.96) 13/29
Other Tea	1.0 431/481	0.29 (0.05–1.52) 3/7		

Note that:

a) no effect was found in smokers

b) smokers drank less tea than non-smokers

c) no important associations were found with other dietary items such as fat and protein.

d) the authors mentioned nine other studies of tea and lung cancer, five of which showed no meaningful association [38-42], two significant increases, Tewes [43] and Kinlen [44], and two significant decreases with increasing consumption, Ohno [45] in Japan with an RR for women of 0.38 (0.12 – 1.18) and Mendilaharsu [46] in Uruguay with an RR for heavy drinkers of black tea of 0.34 (0.14 – 0.84). Note that the papers showing significant increases did not look at nonsmoking women only.

e) In Table 3 of their paper they produce a very interesting sensitivity analysis looking at the confounding effect of active smoking and green tea drinking. A high odds ratio of 1.69 for risk of lung cancer due to green tea drinking reduced to 1.23 when adjusted for number of cigarettes, to 1.09 when adjusted for pack years and to 0.94 when adjusting for pack years using techniques that allow for continuous variables.

30. Seow [47]

This extra paper was discovered by PNL checking papers on ETS and Lung Cancer. This paper is based on a hospital based case-control study of women in Singapore in China. The data were gathered between April 1996 and December 1998. Table II on page 368 gives RRs for smokers and for non-smokers by various dietary factors. In particular, we are given the following RRs for all lung cancer for lifelong non-smokers, adjusted for age, place of birth and first-degree relative with history of cancer (yes/no):

	Tertile 1	2	3	Linear trend
Total vegetables	1.0 62/208	0.93 (0.62–1.40) 63/232	0.78 (0.51–1.20) 51/223	0.3
Fruits	1.0 71/198	0.63 (0.41–0.97) 54/235	0.60 (0.39–0.93) 51/230	0.03
Soy foods	1.0 80/209	0.57 (0.38–0.86) 51/232	0.53 (0.34–0.81) 45/221	<0.01

B. AIR POLLUTION

1. Zhou [48]

This paper describes results of a small case-control study in Shenyang, China. It does not separate out results for non-smokers.

SUMMARY FOR AIR POLLUTION

There are no relevant data provided. Incorporating air pollution into the scheme of things would in any case be extremely difficult given the numerous indicators of air pollution.

C. ALCOHOL

1. Benedetti [49]

This paper reports on two population case-control studies in Montreal, one in men and the other in both sexes. Table 5 on p 475 gives results within strata of smoking, defined as light, moderate and heavy smokers. For men, the light category included smokers, but for women the light category was defined as never smokers. Only the results for women are relevant.

Women Study II	OR adjusted for age,respondent status,ethnicity,SES and schooling/n cases		
	Never	1-6	7+ drinks/wk
Total alcohol	1.0/25	0.2(0.0-0.6)/3	1.1(0.4-3.3)/5
Wine	1.0/27	0.2(0.1-0.6)/3	0.7(0.2-0.5)/3
	Never	1+ drinks/wk	
Beer	1.0/31	0.5(0.3-0.9)/2	
Spirits	1.0/29	0.8(0.5-1.5)/4	

2. Boffetta [50]

This paper compares the incidence of various cancers (including lung) in 182667 patients with a hospital discharge of alcoholism with that of the national population. The analyses do not relate to smoking or ETS at all, data on which would not have been available on the patients. ETS is not even mentioned in the paper.

3. DeStefani [51]

This paper describes a case-control study in Uruguay. Table 2 presents results relating ml ethanol per day to risk, with various adjustments for smoking, but no results are given for never smokers. Only 4 never smokers had lung cancer.

4. Djoussé [52]

This paper presents long-term follow-up results from the Framingham study. Results relating risk to alcohol intake are only presented for the whole population with adjustment for smoking, and not for never smokers alone.

5. Freudenheim [53]

This paper describes a case-control study in western New York. While Table 2 presents results adjusted for smoking, no results for never smokers alone are given.

6. Nishino [54]

This paper describes long-term follow-up (from 1988-1999) of men aged 40-79 living in Japan. Table 3 on p 53 presents some results for never smokers.

Drinking	Person-years	**No. of deaths**	HR*
Never	13368	5	1.00
Ever	36575	13	1.22 (0.43-3.45)
Current <25 g/day	21297	7	1.10 (0.35-5.31)
25-49.9 g/day	9607	1	0.37 (0.04-3.18)
≥50 g/day	3331	1	1.15 (0.13-9.98)
Ex-drinkers	2339	4	4.20 (1.12-15.72)

* Adjusted for age, family history of lung cancer, intake of green-leafy vegetables, oranges and fruits other than oranges

7. Zang [55]

This paper describes results from a case-control study conducted between 1969 and 1994 in hospitals in 8 US metropolitan areas. Controls excluded patients with smoking or alcohol related illnesses. Table 4 on p 365 presents odds ratios (adjusted for BMI, age and current cigs/day) for males only for <1 vs ≥5 whiskey-equivalent current daily alcohol intake of 1.1 (0.9-1.3) for current smokers only based on 874 cases and of 1.2 (1.0-1.4) for current and never smokers combined based on 911 cases. Whether it is possible to obtain valid estimates of the odds ratio for never smokers could be investigated. Table 7 on p 366 also presents results relating current alcohol use to lung cancer in non-smokers. The number of cases considered (53) seems far too low to include ex-smokers (judging by data in Table 1 implying there were over 1000 lung cancers in ex-smokers) and one can probably assume the data were for never smokers. These are:

Whiskey-equivalent ounces per day	Odds ratios adjusted for age and BMI*	Cases
0	1.0	23
1-5.9	1.2 (0.7-2.1)	26
6+	0.7 (0.2-2.0)	4

* Inferred from final paragraph of p 361

8. Rachtan [56]

This is the same case-control study of Polish women as considered under diet (study 19) but the paper is a different one. The controls were next-of-kin of patients without tobacco-related cancer. The relevant results for lifelong non-smokers are given in Tables 5, 6, 7 and 8 on pp 124 and 125.

	Cases	Controls	OR (95%)*
Average intake of vodka (g/wk)			
0	23	179	1.00
<100	25	69	2.26 (1.06-4.85)**
≥100	6	3	15.0 (2.34-96.00)**
Any	31	72	3.47 (1.88-6.39)
Amount of alcohol (g/wk)			
<1	23	198	1.00
≥1-4	15	37	3.89 (1.82-8.32)
≥4-8	7	9	8.76 (2.81-27.29)
≥8	9	7	12.06 (3.94-36.91)

Grams per wk	Mean for cases	Mean for controls	p
Vodka	11.7	1.9	0.0000
Wine	18.3	4.6	0.0219
Beer	25.9	5.5	0.4690
Total alcohol	6.7	1.3	0.0000

* Odds ratios are adjusted for age except where indicated by **

** Adjusted for age, passive smoking, consumption of milk, butter, margarine, cheese, meat, fruit, vegetables, carrots, spinach, siblings with cancer, tuberculosis, place of residence, occupational exposure to coal and other dusts, rubber, acid mist, solvents, metals and other chemicals

SUMMARY FOR ALCOHOL

Of the 8 papers provided, 4 are of no use for the project. The other 4 papers are all based on small numbers of cases in drinking never smokers (8 in study 1 – Benedetti[49], 13 in study 6 – Nishino[54], 30 in study 7 – Zang[55] and 31 in study 8 – Rachtan[56]), with the Rachtan study having results very different from those in the other studies. Given that the literature on lung cancer and alcohol generally shows little or no association once smoking is adjusted for[57] it seems a waste of effort to try to include alcohol as an additional factor in the analyses.

D. EDUCATION

1. Braaten [58]

This paper describes results from follow up to 2001 of Norwegian women responding to an extensive questionnaire in 1991/2 or 1996/7. The results given in Tables 2 and 3 on pp 2594 and 2595 only relate to the whole population and not to never smokers.

2. Chan-Yeung [7]

This study has already been considered under diet (study 4). No results relating education to lung cancer risk are given for never smokers.

3. Dreassi [59]

This is not an epidemiological study at all, but an ecological analysis fitting time trends in socioeconomic factors to time trends in lung cancer. No data on smoking are used.

4. Huisma [60]

This paper describes analyses based on national databases which linked vital registries to population censuses. Data on smoking were not collated or analyzed.

5. Louwma [61]

This paper describes results from a Dutch prospective study followed up from 1991 to 1998. Analyses relating education to lung cancer risk are not presented separately for never smokers.

6. Mackenbach [62]

As with Huisma (no 4), this paper describes analyses based on national databases for which smoking information was not available.

7. Martikainen [63]

This paper describes results of a follow-up study of Finnish male smokers that took part in a randomized trial of alpha-tocopherol and beta-carotene. There were no never smokers in this study.

8. Regidor [64]

This paper describes results based on a study in Spain involving mortality registry records and linked population census data. Smoking was not considered in the study, presumably as data were not available in the mortality records.

9. Ruano-Ravina [65]

This paper describes the results of a population-based case-control study conducted in Spain. Although there are some limited results for never smokers, they relate to occupation not education and will be considered elsewhere.

10. Steenland [66]

This paper describes detailed results relating education to mortality from a variety of causes based on the well known CPS-I and CPS-II studies. While results are presented adjusted for smoking, no results are given specifically for never smokers.

SUMMARY FOR EDUCATION

None of the references provided under the heading education add anything new to the data considered in the original analyses. However, there are data in references considered later (see income study 1 – Gorlova[67] and study 2 – Mao[68]).

E. INCOME

1. Gorlova [67]

This paper describes a hospital case-control study in Texas, USA involving 280 never smoking cases and 242 healthy controls who were also never smokers. The controls had never had cancer (except nonmelanoma skin cancer) and were matched on age, sex and ethnicity. Some unadjusted results for income and education are given in Table I on page 1799, but only for sexes combined.

	Cases	Controls	p	RR (95% CI)*
Education (years; mean ± SD)	14.6±3.5	14.1±2.9	0.11	
Income (per year)				
<$40,000	89	59	0.006	1.00
$40,000 to <$75,000	66	88	(trend)	0.50 (0.31-0.79)
$75,000+	101	79		0.85 (0.55-1.32)

*Estimated from numbers

No adjusted results are given. Neither income nor education was included in other analyses so no results adjusted even for age are available.

2. Mao [68]

This paper describes a case-control study in 8 Canadian provinces involving 3280 histologically confirmed lung cancer cases and 5073 population controls. Table 5 on page 814 gives odds ratios for never smokers for education, income and social class, adjusted for age, province, ETS exposure and consumption of vegetables, vegetable juices and meat. Table 2 on page 812 gives number of never smoking controls by sex and the 3 factors.

	Males		Females	
	Controls	OR (95% CI)	Controls	OR (95% CI)
Education (years)				
1-8	77	1.0	171	1.0
9-13	271	0.7 (0.3-2.0)	649	0.6 (0.4-0.9)
14+	319	0.9 (0.3-2.4)	430	0.6 (0.4-1.1)
Total	667		1250	
Family income				
High income	124	1.0	172	1.0
Upper middle	198	0.5 (0.2-1.4)	299	1.3 (0.7-2.3)
Low middle	104	1.2 (0.5-3.1)	222	0.8 (0.4-1.6)
Low	92	0.8 (0.3-2.5)	200	1.7 (0.9-3.3)
Total	518		893	
Social class				
I	69	1.0	43	1.0
II	165	1.2 (0.4-3.6)	356	0.9 (0.5-1.5)
IIIN	137	0.7 (0.2-2.2)	404	0.8 (0.5-1.3)
IIIM	155	0.6 (0.2-1.8)	100	0.7 (0.4-1.6)
IV	72	0.6 (0.2-2.4)*	126	1.0 (0.5-1.9)
V	28		42	1.2 (0.5-2.9)
Total	626		1071	

*Social class IV + V combined

According to Table 3, the total numbers of never smoking subjects are:

Males : 45 cases and 680 controls

Females : 161 cases and 1271 controls

but numbers of cases by factor level are not given.

3. Neuberger [69]

This paper describes a case-control study in Iowa women involving 413 lung cancer cases and 614 population controls aged 40-84. Some results of multivariate analyses are shown for the never smokers (56 cases and 414 controls based on Table 1). In the analyses of the total population (Table 2) only family history of kidney and bladder cancer and any lung disease emerged as significant factors. Table 3 presents additional analyses for living cases and controls only. Again only family history of cancer emerged as significant. However, in Table 4 (restricted to those reporting on first-degree relatives only) and Table 5 (further restricted to controls without cancer), asbestos exposure emerged as a factor.

		Cases*	Controls*	OR (95% CI)**
Asbestos exposure	- Table 4	37	413	4.38 (1.10-17.45)
	- Table 5	37	359	5.17 (1.20-22.36)

* Exposed + unexposed

** Adjusted for radon, education and age

The paper provides no relevant results for income.

4. Shaw [70]

This paper describes results of cohort studies in New Zealand based on linking census and mortality datasets. No data on smoking were recorded.

<u>SUMMARY FOR INCOME</u>

The available data on income, from only study 1 – Gorlova[67] and study 2 – Mao[68], the first of which provides only non age-adjusted results for sexes combined, seems too limited to be useful. Education and income are in any case likely to be strongly correlated and we had considerable data for education earlier. Note that the two studies that provide data for income also provide data for education.

F. OBESITY

1. Calle [71]

This paper describes results from 16 year follow up (1982-98) of about 1,000,000 men and women in CPS-II. Results for never smokers are available in Table 3 on page 1633.

	Body Mass Index				
	18.5-24.9	25.0-29.9	30.0-34.9	35.0*	Trend p
Males					
Lung cancer cases	156	179	30*		
Death rate	22.72	23.51	23.45		
RR (95% CI)**	1.00	1.00 (0.80-1.24)	0.93 (0.63-1.39)		0.78
Females					
Lung cancer cases	476	224	78	17	
Death rate	18.71	16.40	19.18	17.51	
RR (95% CI)**	1.00	0.85 (0.73-1.00)	0.99 (0.77-1.26)	0.81 (0.49-1.31)	0.21

* Results are for BMI 30.0+

** Age standardized

2. Eichholzer [72]

This paper describes 17 year follow up (1971/73-90) for cancer of 2974 working men in Basle. Of 87 lung cancers, 22 were in non-smokers. Figure 2 provides graphical Kaplan-Meier plots of survival from lung cancer jointly by smoking status and BMI quartiles. It would be impossible to derive suitable RR estimates from these 8 overlapping and not clearly distinguishable lines. It may well be in any case that their term “nonsmokers” includes former smokers.

3. Jeffreys [73]

This paper describes results of 50 year follow up of British children originally interviewed in 1937-39. No data were recorded on smoking habits and results for lung cancer were only shown for the whole population.

4. Kanashiki [74]

This paper describes results of a case-control study in Japan involving 363 lung cancer cases and 1089 controls selected from mass-screening subjects with no history of cancer and no abnormality on screening. Table 3 on page 1492 presents results for never smokers.

	Body Mass Index			
	<20.8	20.8-22.8	22.9-24.9	25+
Males				
Cases	1	4	3	4
Controls	33	48	36	42
OR (95% CI)*	0.6 (0.1-7.8)	1.1 (0.2-6.3)	1.0	1.8 (0.3-11.0)
Females				
Cases	25	20	35	36
Controls	81	106	87	109
OR (95% CI)*	0.8 (0.4-1.4)	0.5 (0.3-0.9)	1.0	0.9 (0.5-1.5)

* Age-adjusted (not entirely clear from the text, but the ORs and CIs are not the same in all analyses as would be obtained if these were crude ORs)

5. Olson [75]

This paper reports results of follow up (1986-98) of 41,836 Iowa women. 81 lung cancer cases occurred in never smokers. Table 4 on page 612 presents multivariate RRs and CIs for never smokers.

	Body Mass Index				
	≤22.89	22.90-25.04	25.05-27.43	30.69	30.70+
Lung cancer cases	18	19	13	10	16
Person years	50628	60129	61438	62269	63480
RR*	1.00	0.82	0.51	0.35	0.44
95% CI		(0.43-1.57)	(0.24-1.06)	(0.15-0.79)	(0.21-0.95)

* Adjusted for age, physical activity, educational level, beer consumption, height, waist circumference and BMI at age 18 years

Note that as the analysis is adjusted for earlier BMI it is really an analysis of change in BMI.

6. Rauscher [76]

This paper describes results from a case-control study conducted in New York involving subjects who had never smoked more than 100 cigarettes in their lifetime (never smokers). Data on height and weight were complete for 412 pairs of cases (confirmed histologically) and population controls matched on age, sex and district and usually the respondent (subject or surrogate). The results given in Tables 2 and 3 on pp 509-510 for never smokers (only presented for sexes combined) can be summarized as follows:

	Body Mass Index octile							
	1	2	3	4	5	6	7	8
Cases	23	28	25	19	24	20	21	28
Controls	35	31	21	26	17	19	22	17
Crude OR	1.0	1.4	1.8	1.1	2.1	1.6	1.5	2.5

	1	2-7	8
Matched OR (CI)	1.0	1.5 (0.9-2.7)	2.4 (1.1-6.0)
Education adjusted matched OR (CI)	1.0	1.2 (0.6-2.1)	1.8 (0.8-4.5)

<u>SUMMARY FOR OBESITY</u>

Of the 6 papers obtained, 4 include relevant data. The results are, however, extremely conflicting. Study 6 – Rauscher[76] suggests a positive association, as perhaps does study 4 – Kanashiki[74]. Study 5 – Olson[77] shows a negative association but with change in BMI rather than BMI itself, while the largest study, study 1 - Calle[71] shows no association. No reliable adjustment for obesity could be based on these data.

G. OCCUPATION

1. Armstrong [78]

This paper describes a review of 39 studies of risk of lung cancer after exposure to polycyclic aromatic hydrocarbons. The paper notes that only four studies conducted smoking adjustment and there is no mention of any results being available for never smokers.

2. Besso [79]

This paper describes a case-control study of subjects living in a municipality where a smelter was located (but not at the smelter). 316 decedent lung cancer cases were matched to 727 decedents from other causes, with information being obtained from next-of-kin and registry data. Table IV presents results for never smokers for residence in the area near the smelter.

		Never resident	**Ever resident**
Males	Cases	17	5
	Controls	211	31
	RR(95% CI)*	1.00	2.03 (0.68-6.09)
Females	Cases	43	12
	Controls	128	31
	RR(95% CI)*	1.00	1.03 (0.48-2.20)

* Adjusted for occupation, age and (for men only) period of recruitment

3. Boffetta [80]

This paper presents estimates of lung cancer rates among never smoking male Swedish construction workers, but provides no relative risk estimates in relation to working in this industry, i.e. there is no control group.

4. Durusoy [81]

This paper presents results from a large multicentric case-control study in Central and East Europe. Cases had histologically confirmed lung cancer and controls were mainly hospital patients with non-cancer diseases unrelated to smoking. The study included 48 male and 175 female never smoking cases and 534 male and 505 female never smoking controls. Tables II and III on pp 2545-6 present estimates by risk of two occupational exposures.

Exposure to	Exposed cases	Exposed controls	OR (95% CI)*
Meat aerosols	10	28	1.78 (0.79-4.02)
Live animals	22	89	1.11 (0.64-1.92)

* Adjusted for sex, age and centre

5. Ekberg-Aronsson [82]

This paper describes results from a long-term (1974-1992) prospective study in Malmo, Sweden. Table 3 on p 5 gives relative risks by SES among never smokers, and Table 2 on the same page gives numbers at risk.

	Low SES		High SES		
	At risk	RR	At risk	RR (CI)*	Total cases
Men	1496	1.0	1846	3.43 (1.59-7.41)	33
Women	1928	1.0	1928	0.70 (0.20-2.47)	11

* Adjusted for age and marital status

6. Fano [83]

This paper describes results of a case-control study in an industrialised area of Italy. No results are given for never smokers.

7. Guo [84]

This paper describes results of a very large follow-up study in Finland. Although standardized incidence ratios (SIRs) are presented for a large number of occupations, no results are presented for never smokers.

8. Gustavsson [85]

This paper describes the results of a population-based case-control study among men in Stockholm County, involving 1038 incident lung cancer cases and 2359 controls matched on age and year of inclusion in the study, and in part on vital status. Relevant data for never smokers for asbestos exposure are included in Table 2 (p 1018) and Tables 3 and 4 (p 1020).

Asbestos exposure (fibre-years)	Cases	Controls	RR (95%CI)*
None	26	620	1.0
<1 (mean 0.56)	4	51	1.8 (0.6-5.5)
1-2.49 (1.51)	3	26	2.7 (0.7-9.5)
2.5-4.49 (3.44)	1	4	
4.5+ (8.80)	2	4	
1.0+			4.2 (1.6-11.1)
2.5+			10.2 (2.5-41.2)

* Adjusted for age, year of inclusion, residential radon, environmental nitrogen dioxide, diesel exhaust and combustion products

9. Haldorsen [86]

This paper describes an ecological analysis relating lung cancer incidence data and smoking prevalence data by 53 occupational groups. It cannot contribute to our study.

10. Hart [87]

This paper describes 20 year mortality follow-up of 11073 men and 8354 women recruited in the 1970s. Table 2 on p 271 presents some results by social class (non-manual/manual) for never smokers.

	Non-manual			Manual			Ratio of rates**
	At risk	Deaths	Rate	At risk	Deaths	Rate	
Renfrew/Paisley men	457	3	3.9	709	6	4.8	1.23
Renfrew/Paisley women	1629	6	2.3	2030	13	3.3	1.43
Collaborative men	339	0	0.0	247	2	3.3	∞

* Age-adjusted ** Calculated from rates

11. Hart [88]

This paper describes a study linking data from the Scottish mental survey in 1932 and later, Midspan, studies of adults in the 1970s. Smoking was not considered.

12. Hemminki [89]

This paper presents SIRs for cancer in six socio-economic groups based on the Swedish Family-Cancer Database. This database does not contain data on smoking habits.

13. Kjaerheim [90]

This paper describes a case-control study involving 133 lung cancer cases among rock and slag wool (RSW) production workers and 513 matched controls. Although analyses are presented relating exposure to RSW to lung cancer risk adjusted for smoking, no such results are given for never smokers.

14. Li [91]

This paper describes a small case-control study in China involving workers in a rubber factory. Only 9 of the cases were never smokers and no results for never smokers relating to exposure to rubber are presented.

15. Mastrangelo [92]

This paper describes a small case-control study in Italy nested in a cohort study of dairy factors. Only one lung cancer occurred among never smokers (see Table 4 , p 1042).

16. Metcalfe [93]

This paper describes 25-year follow-up of 5577 men recruited from workplaces in the West of Scotland in 1970/73. No results are given for never smokers.

17. Pohlabeln [94]

This paper describes a multicentre case-control study conducted in seven West European countries involving 650 lung cancer cases and 1542 controls, a mixture of community-based controls and hospital-based controls (with diseases unrelated to smoking). All subjects were non-smokers defined as having smoked less than 400 cigarettes in their lifetime. Occupations and industries were classified as known (list A) or suspected (list B) to be associated with lung cancer. The main results are given in Table 4 on p 535.

Occupation	Sex	Cases	Controls	OR(95% CI)
Never A or B	Male	101	366	1.00
Ever A or B		40	165	1.20 (0.76-1.92)
- Ever B, never A		23	107	1.05 (0.60-1.83)
- Ever A		17	58	1.52 (0.78-2.99)
Never A or B	Female	463	942	1.00
Ever A or B		46	69	1.67 (1.10-2.52)
- Ever B, never A		41	59	1.69 (1.09-2.63)
- Ever A		5	10	1.50 (0.49-2.53)

The paper also presents, in Table 2 (p 534, List A) and Table 3 (p 535, List B) numbers of cases and controls and, for the more commonly worked in industries, estimates of OR and CI.

18. Pukkala [95]

This is another paper based on the large Finnish follow-up study; see also study 7 – Guo[84]. No results are presented for never smokers.

19. Richiardi[96]

This paper describes results from a case-control study conducted in two areas of Northern Italy. No results are given for non-smokers, it being noted that they were included in the multicentre study by Pohlabeln[94] – see study 17 above.

20. Ruano-Ravina [65]

This paper describes the results of a population-based case-control study conducted in Spain including 163 confirmed lung cancer cases and 241 controls without neoplasia or respiratory tract disease. Table IV on page 153 presents results for never smokers relating to number of years spent in a "risk profession" as defined by Ahrens and Merletti[97].

Years in risk profession	Cases	Controls	OR (95% CI)*
0	11	77	1.00
1-20	1	12	2.01 (0.19-21.36)
21+	1	18	2.03 (0.18-22.99)

* Adjusted for age and sex

21. Scelo [98]

This paper describes the results of a multicentre case-control study in 7 countries (UK, Central and East Europe), some subjects included in study 4 above[81]. The paper only considers 3 specific exposures (vinyl chloride, styrene and acrylonitrile) and no results are given for never smokers.

22. Sorahan [99]

This paper describes a follow-up study of chrome platers employed in the UK. No results relating employment to lung cancer risk in never smokers are given.

23. Sorahan [100]

This paper describes a follow-up study of nickel-cadmium battery workers employed in the UK. No data on smoking habits were considered.

24. Yiin [101]

This paper describes a follow-up study on UK naval shipyard workers. Smoking history data were not available.

SUMMARY FOR OCCUPATION

Of the 24 papers considered, 17 gave no results at all for never smokers and two[82,87] gave results only for SES – considered later. Three of the studies dealt only with specific occupations and involved small numbers of exposed cases:

Study 2 - Besso[79]	-	living near smelter (17 cases)
Study 4 - Durusoy[81]	-	meat aerosols (10 cases)
	-	live animals (22 cases)
Study 8 - Gustavsson[85]	-	asbestos (10 cases)

Only two studies dealt with more general indices of risky occupation. One, study 20 - Ruano-Ravina[65] included only two exposed cases. Only the large multicentre study, study 17 - Pohlabeln[94] involved moderate numbers – 22 working in List-A occupations and a further 64 working in List-B occupations. While it would be useful to be able to adjust for a general index of risky occupation (such as working in List-A occupations), the data seem too limited to be able to do so.

H. PHYSICAL ACTIVITY

1. Alfano [102]

This paper describes results from a sample of current and former smokers from the Beta-Carotene and Retinol Efficacy Trial and as such includes no results for never smokers.

2. Bak [103]

This paper describes results of follow up (1993/93-2002) of 57,053 persons in a Danish cohort study. As shown in Table 1 on page 441, only 13 lung cancer cases (2 in men, 11 in women) occurred in never smokers and no physical activity results are given specifically for never smokers.

3. Colbert [104]

This paper describes results from a sample of current smokers from the Alpha-Tocopherol Beta-Carotene Cancer Prevention Study and as such includes no results for never smokers.

4. Kubik [105]

This paper describes results from a case-control study in Prague women involving 419 lung cancer cases and 1593 controls who were spouses, relatives, or friends of other patients hospitalised at the same department as the cases. 111 of the cases and 933 of the controls were never smokers (less than 100 cigarettes in their lifetime). Results for physical activity for non-smokers are shown in Table 5 on page 140. However this includes those who had quit 20 or more years ago. The results, not shown in detail as they do not strictly relate to never smokers, show no significant trend (after adjustment for age, residence and education) with physical exercise (hours/week, including sport, walking) at any of the three times considered (last 10 years, 1 year before interview, 20 years interview) or with other non-occupational physical activities (e.g. in the garden or house).

It should be noted that Tables 3 and 4 on page 139 include results for non-smokers by other factors (residence, education, 9 food items, 4 beverage items, and 3 alcohol items). Significant associations were noted with urban residence (low risk: 0.41, 0.28-0.61), red meat consumption (high risk: 2.20, 1.07-4.51) and black tea consumption (low risk: 0.67, 0.46-0.99). Again the non-smokers include long-term exsmokers.

5. Mao [106]

This paper describes results from a case-control study of lung cancer in 8 Canadian provinces involving 2128 cases with histologically confirmed lung cancer and 3106 population controls. Table 5 on page 571 gives results for never smokers. Those adjusted for age, residence, education, BMI, caloric intake, vegetable intake, ETS, occupation and alcohol are shown below.

	Total recreational physical activity (metabolic equivalent hours/week)				
	<6.1	6.1 to <15.2	15.2 to <31.4	31.4+	Trend p
Men					
Cases	8	6	8	4	
Controls	88	114	100	118	
OR	1.00	0.53	0.87	0.31	
(95% CI)		(0.17-1.63)	(0.29-2.62)	(0.08-1.14)	
Women					
Cases	28	21	24	27	
Controls	174	198	160	179	
OR	1.00	0.70	0.82	0.80	
(95% CI)		(0.37-1.32)	(0.55-1.90)	(0.54-1.83)	

SUMMARY FOR PHYSICAL ACTIVITY

Of the five studies considered, three provide no useful information at all and two (study 4 – Kubik[105] and study 5 – Mao[106]) find no association, Kubik only in never smokers plus long-term exsmokers.

I. SOCIOECONOMIC FACTORS

1. Battersby [107]

This paper is to do with access to surgery for lung cancer and is irrelevant.

2. Dreassi [59]

As already noted under education, this is an ecological study with no data on smoking.

3. Ekberg-Aronsson [82]

See study 5 under occupation for results for never smokers.

4. Hart [87]

See study 10 under occupation for results for never smokers.

5. Hart [88]

For reasons described under study 11 in occupation, this is irrelevant.

6. Schwartz [108]

This paper describes a study relating stage of diagnosis of cancer to SES and is irrelevant.

7. Tammemagi [109]

This is a study of lung cancer patients only and is not relevant.

8. Tammemagi [110]

Again, this is a study of lung cancer patients only and is not relevant.

SUMMARY FOR SOCIOECONOMIC FACTORS

Of the 8 papers, 6 are irrelevant. Only study 3 – Ekberg-Aronsson[82] and study 4 – Hart[87] provide any relevant data at all, with the Hart study based on very few deaths.

J. CONCLUSIONS

It is clear from sections A and D that there are a number of studies providing information on the relationship of lung cancer risk in non-smokers to fruit, vegetables and dietary fat consumption and to education, additional to those considered earlier [111]. Are there any additional potential confounding variables for which there is sufficient evidence to derive a useful quantitative estimate of the relationship to risk? The relevant data presented in the remaining sections can be summarized as follows:

Section	Potential confounding variable	Summary of investigation
B.	Air pollution	No data at all.
C.	Alcohol	Only four relevant studies, with conflicting results.
E.	Income	Data very limited; income highly correlated with education.
F.	Obesity	Only four studies, conflicting results.
G.	Occupation	Only five studies, four very small and three of these presenting results only for specific occupation. Only one study is large and deals with risky occupation generally.
H.	Physical activity	Only two relevant studies, neither finding an association.
I.	Socioeconomic factors	Only two relevant studies, one very small.

For none of these seven potential confounding variables are there data which could be used to provide any sort of reliable quantitative estimate of their relationship to lung cancer risk in non-smokers.

As noted in section A (see sections 9 and 29), there are two studies [15,37] that present evidence of a markedly reduced risk of lung cancer in tea drinkers. Although two studies is too few to calculate a very reliable combined estimate, the results are used in some of the analyses in the main report.

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Appendix 4

Fuller details of the analyses relating lung cancer risk to fruit and vegetable consumption

APPENDIX 4

Fruit/Vegetable/Tea consumption and lung cancer - Meta-Analysis of Dose Response Exposure, 22-AUG-06

Scored by Standard Deviations

BASIC DATA USED IN META-ANALYSES - VEGETABLES

Study title	RR	RRL	RRU	CA1	CA0	CO1	CO0	REL SD
Agudo	0.6200	0.3000	1.2700	18.3600	28.6100	44.1700	42.7000	1.0908
Agudo	0.7700	0.3800	1.5600	21.2400	28.6100	41.1300	42.7000	2.1816
Alavanja	0.8300	0.5800	1.1800	77.7900	98.2700	199.4400	209.1000	0.8675
Alavanja	0.8600	0.6000	1.2200	78.8100	98.2700	195.0100	209.1000	1.3996
Alavanja	0.7700	0.5400	1.1100	72.3300	98.2700	199.8900	209.1000	1.9317
Alavanja	0.9900	0.7100	1.3800	106.3000	98.2700	228.5000	209.1000	2.7992
Candelora	0.4000	0.2000	0.7000	20.1600	51.0600	60.3200	61.1000	0.9464
Candelora	0.6000	0.4000	1.2000	35.2400	51.0600	70.3100	61.1000	1.5958
Candelora	0.2000	0.1000	0.5000	8.8000	51.0600	52.6700	61.1000	2.5422
Feskanich	0.9400	0.4600	1.9100					2.1816
Hirayama	0.7600	0.5600	1.0400	138.5400	56.6300	68164.3800	21176.9000	1.7072
Hu J	1.3000	0.7000	2.4000	40.1994	19.5239	113.7905	71.8448	0.9929
Hu J	1.3000	0.6000	2.6000	18.0938	19.5239	51.2173	71.8448	1.6294
Hu J	1.4000	0.7000	3.0000	18.9906	19.5239	49.9162	71.8448	2.5206
Kalandidi	0.7700	0.3700	1.6000	22.0000	27.0000	36.0000	34.0000	0.9464
Kalandidi	0.7800	0.3600	1.7000	18.0000	27.0000	29.0000	34.0000	1.5958
Kalandidi	1.4400	0.6600	3.1200	24.0000	27.0000	21.0000	34.0000	2.5422
Ko	0.4000	0.2000	0.8000	60.5700	31.3300	76.1000	15.7000	1.7909
Koo	0.4900	0.2000	1.1800	21.7400	16.4300	37.7100	14.0000	1.0727
Koo	0.4900	0.2200	1.1000	43.7100	16.4300	75.8300	14.0000	2.4024
Kreuzer	0.5700	0.3300	0.9900	110.1768	26.8645	254.1306	35.3200	1.5330
Kreuzer	0.4500	0.2500	0.8200	51.0583	26.8645	149.1747	35.3200	2.9955
Mayne	1.0000	0.5900	1.7000	60.7700	60.7500	50.0500	50.0000	0.9464
Mayne	0.8000	0.4700	1.3800	50.4800	60.7500	51.9700	50.0000	1.5958
Mayne	0.4800	0.2600	0.8600	27.9200	60.7500	47.9200	50.0000	2.5422
Ozasa	1.1900	0.6800	2.0900	25.1943	23.5993	109951.8109	122559.3174	1.0772
Ozasa	1.3500	0.7900	2.3000	31.2877	23.5993	120361.1961	122559.3174	2.1478
Rachtan	0.1000	0.0100	0.7500					1.6647
Seow	0.9300	0.6200	1.4000	60.8029	58.2345	222.1150	197.8410	1.1010
Seow	0.7800	0.5100	1.2000	48.3665	58.2345	210.6622	197.8410	2.2152
Shimizu	0.8900	0.4300	1.8300	76.0000	14.0000	140.0000	23.0000	1.8483
Steinmetz	0.5400	0.1300	2.3200	3.1800	4.5200	503.4700	387.1000	0.9464
Steinmetz	1.1500	0.3200	4.1300	5.0200	4.5200	373.2700	387.1000	1.5958
Steinmetz	1.0800	0.2700	4.3900	3.5900	4.5200	284.1400	387.1000	2.5422

NOTES: RR,RL,RU RELATIVE RISKS AND LOWER AND UPPER CONFIDENCE INTERVALS
CA1,CA0 NUMBERS (OR PSEUDO-NUMBERS) OF MORE EXPOSED AND LEAST EXPOSED CASES
CO1,CO0 NUMBERS (OR PSEUDO-NUMBERS) OF MORE EXPOSED AND LEAST EXPOSED CONTROLS
CA1,CA0,CO1,CO0 NOT SHOWN IF ORIGINAL RR PER STANDARD DEVIATION
REL SD NUMBER OF STANDARD DEVIATIONS FROM LEAST EXPOSED LEVEL

FEMALES
NEVER SMOKERS OR NEVER AND LONG TERM EX SMOKERS
NYBERG1998 REPLACED BY BRENNAN2000, GOODMAN1992 EXCLUDED

APPENDIX 4

Fruit/Vegetable/Tea consumption and lung cancer - Meta-Analysis of Dose Response Exposure, 22-AUG-06

Scored by Standard Deviations

BASIC DATA USED IN META-ANALYSES - FRUIT

Study title	RR	RRL	RRU	CA1	CA0	CO1	CO0	REL SD
Alavanja	1.0900	0.7700	1.5500	94.6900	84.7700	213.2100	208.1000	0.8675
Alavanja	1.0900	0.7700	1.5400	98.4800	84.7700	221.7400	208.1000	1.3996
Alavanja	0.8400	0.5800	1.2100	72.2100	84.7700	210.9900	208.1000	1.9317
Alavanja	1.1400	0.8000	1.6300	89.5000	84.7700	192.6900	208.1000	2.7992
Candelora	0.9000	0.5000	1.7000	31.6600	34.6000	54.5400	53.6000	0.9464
Candelora	0.4000	0.2000	0.9000	12.6200	34.6000	48.9100	53.6000	1.5958
Candelora	0.6000	0.3000	1.1000	22.2600	34.6000	57.5100	53.6000	2.5422
Feskanich	0.3400	0.1600	0.7200					2.1816
Hu J	0.8000	0.4000	1.5000	19.1851	28.4994	69.5307	82.6300	0.9521
Hu J	0.9000	0.5000	1.6000	32.0733	28.4994	103.3246	82.6300	1.6087
Hu J	1.1000	0.6000	2.0000	29.2583	28.4994	77.1184	82.6300	2.5547
Kalandidi	0.2700	0.1300	0.5800	19.0000	35.0000	44.0000	22.0000	0.9464
Kalandidi	0.3900	0.1700	0.9100	15.0000	35.0000	24.0000	22.0000	1.5958
Kalandidi	0.4600	0.2100	0.9900	22.0000	35.0000	30.0000	22.0000	2.5422
Ko	1.0000	0.5000	1.7000	76.9300	27.9800	76.9300	28.0000	1.6803
Koo	0.8100	0.3500	1.8600	20.3000	23.9500	22.6000	21.6000	0.8183
Koo	0.4200	0.2100	0.8300	42.0800	23.9500	90.3000	21.6000	2.0569
Kreuzer	0.5500	0.2800	1.0900	33.6807	20.6553	94.1401	31.7533	0.9180
Kreuzer	0.6600	0.3700	1.1900	160.4563	20.6553	373.7396	31.7533	2.3794
Mayne	0.6300	0.3700	1.0700	48.4200	75.1200	51.3200	50.2000	0.9464
Mayne	0.4500	0.2600	0.8000	34.1900	75.1200	50.7300	50.2000	1.5958
Mayne	0.5900	0.3400	1.0100	42.9100	75.1200	48.5700	50.2000	2.5422
Ozasa	0.9500	0.3800	2.3400	12.5414	7.3891	75198.3836	42089.9946	0.8833
Ozasa	1.1800	0.5400	2.5700	43.3078	7.3891	209059.9472	42089.9946	2.1838
Rachtan	0.3800	0.1500	0.9800					1.6647
Seow	0.6300	0.4100	0.9700	46.2995	62.8034	202.0805	172.6919	1.0992
Seow	0.6000	0.3900	0.9300	44.4010	62.8034	203.4837	172.6919	2.2261
Shimizu	1.1800	0.5500	2.5500	79.0000	11.0000	140.0000	23.0000	1.8483
Steinmetz	2.0100	0.5100	7.9400	6.1100	3.1100	370.2600	379.2000	0.9464
Steinmetz	0.7500	0.1400	3.8800	2.5500	3.1100	414.7600	379.2000	1.5958
Steinmetz	1.4500	0.3300	6.3000	4.1800	3.1100	351.3700	379.2000	2.5422

NOTES: RR,RL,RU RELATIVE RISKS AND LOWER AND UPPER CONFIDENCE INTERVALS
CA1,CA0 NUMBERS (OR PSEUDO-NUMBERS) OF EXPOSED AND UNEXPOSED CASES
CO1,CO0 NUMBERS (OR PSEUDO-NUMBERS) OF EXPOSED AND UNEXPOSED CONTROLS
CA1,CA0,CO1,CO0 NOT SHOWN IF ORIGINAL RR PER STANDARD DEVIATION
REL SD NUMBER OF STANDARD DEVIATIONS FROM LEAST EXPOSED LEVEL

FEMALES
NEVER SMOKERS OR NEVER AND LONG TERM EX SMOKERS
NYBERG1998 REPLACED BY BRENNAN2000, GOODMAN1992 EXCLUDED

APPENDIX 4

Fruit/Vegetable/Tea consumption and lung cancer - Meta-Analysis of Dose Response Exposure, 22-AUG-06

Scored by Standard Deviations

BASIC DATA USED IN META-ANALYSES - TEA

Study title	RR	RRL	RRU	CA1	CA0	CO1	CO0	REL SD
Hu J	0.6000	0.3000	0.9000	58.0761	27.8756	175.6951	50.5984	1.1994
Hu J	0.4000	0.2000	0.7000	26.2447	27.8756	119.0953	50.5984	2.5040
Zhong	0.8000	0.4500	1.4200	21.4046	356.8556	29.5149	393.6551	1.3364
Zhong	0.6200	0.3600	1.0800	21.3379	356.8556	37.9649	393.6551	1.7007
Zhong	0.4600	0.2200	0.9600	10.4252	356.8556	25.0005	393.6551	2.4080

NOTES: RR,RL,RU RELATIVE RISKS AND LOWER AND UPPER CONFIDENCE INTERVALS
CA1,CA0 NUMBERS (OR PSEUDO-NUMBERS) OF EXPOSED AND UNEXPOSED CASES
CO1,CO0 NUMBERS (OR PSEUDO-NUMBERS) OF EXPOSED AND UNEXPOSED CONTROLS
CA1,CA0,CO1,CO0 NOT SHOWN IF ORIGINAL RR PER STANDARD DEVIATION
REL SD NUMBER OF STANDARD DEVIATIONS FROM LEAST EXPOSED LEVEL

FEMALES
NEVER SMOKERS OR NEVER AND LONG TERM EX SMOKERS
NYBERG1998 REPLACED BY BRENNAN2000, GOODMAN1992 EXCLUDED

APPENDIX 4

Fruit/Vegetable/Tea consumption and lung cancer - Meta-Analysis of Dose Response Exposure, 22-AUG-06

Scored by Standard Deviations

REGRESSION ESTIMATES, WEIGHTS AND OTHER RELEVANT DETAILS

Study title	Country	Beta	St.Err. Beta	Z	Weight	Expos	RSEX	SMOKE
Agudo	Spain	-0.1293	0.1649	-0.7839	36.7763	veg	f	1
Alavanja	US	-0.0071	0.0574	-0.1232	303.8068	veg	f	2
Candelora	US	-0.4937	0.1361	-3.6284	54.0033	veg	f	1
Feskanich	US	-0.0284	0.1665	-0.1704	36.0850	veg	f	1
Hirayama	Japan	-0.1608	0.0925	-1.7378	116.8704	veg	f	1
Hu J	Canada	0.1235	0.1417	0.8715	49.8318	veg	f	1
Kalandidi	Greece	0.1166	0.1507	0.7738	44.0362	veg	f	1
Ko	Taiwan	-0.5116	0.1975	-2.5910	25.6451	veg	f	1
Koo	China	-0.2189	0.1565	-1.3982	40.8138	veg	f	1
Kreuzer	Germany	-0.2398	0.0957	-2.5065	109.2344	veg	f	1
Mayne	US	-0.2712	0.1142	-2.3748	76.6903	veg	f	2
Ozasa	Japan	0.1388	0.1265	1.0966	62.4446	veg	f	1
Rachtan	Poland	-1.3832	0.6616	-2.0906	2.2845	veg	f	1
Seow	Singapore	-0.1111	0.0985	-1.1287	103.1244	veg	f	1
Shimizu	Japan	-0.0630	0.1999	-0.3154	25.0270	veg	f	1
Steinmetz	US	0.0848	0.2694	0.3146	13.7756	veg	f	1
Alavanja	US	0.0124	0.0607	0.2049	271.4113	fruit	f	2
Candelora	US	-0.2512	0.1273	-1.9734	61.7102	fruit	f	1
Feskanich	US	-0.4945	0.1759	-2.8116	32.3282	fruit	f	1
Hu J	Canada	0.0406	0.1168	0.3473	73.3328	fruit	f	1
Kalandidi	Greece	-0.2598	0.1516	-1.7132	43.4873	fruit	f	1
Ko	Taiwan	0.0000	0.1858	0.0000	28.9696	fruit	f	1
Koo	China	-0.4413	0.1621	-2.7219	38.0450	fruit	f	1
Kreuzer	Germany	-0.0577	0.1028	-0.5616	94.6831	fruit	f	1
Mayne	US	-0.2381	0.1060	-2.2463	89.0097	fruit	f	2
Ozasa	Japan	0.1051	0.1585	0.6633	39.8093	fruit	f	1
Rachtan	Poland	-0.5812	0.2876	-2.0208	12.0880	fruit	f	1
Seow	Singapore	-0.2357	0.0994	-2.3706	101.1714	fruit	f	1
Shimizu	Japan	0.0895	0.2117	0.4230	22.3103	fruit	f	1
Steinmetz	US	0.0229	0.2821	0.0811	12.5621	fruit	f	1
Hu J	Canada	-0.3620	0.1271	-2.8490	61.9501	tea	f	1
Zhong	China	-0.2759	0.1058	-2.6079	89.3271	tea	f	1

NOTES:
- BETA — SLOPE OF LOG RR ON SD OF VARIABLE
- SE BETA — STANDARD ERROR OF BETA
- Z — RATIO OF BETA TO ITS STANDARD ERROR (APPROXIMATE NORMAL STATISTIC)
- WEIGHT — INVERSE OF THE VARIANCE OF BETA
- SMOKE — 1 = NEVER SMOKERS, 2 = NEVER OR LONG-TERM EX-SMOKERS
- RSEX — SEX FOR RR

FEMALES
NEVER SMOKERS OR NEVER AND LONG TERM EX SMOKERS
NYBERG1998 REPLACED BY BRENNAN2000, GOODMAN1992 EXCLUDED

APPENDIX 4

Fruit/Vegetable/Tea consumption and lung cancer - Meta-Analysis of Dose Response Exposure, 22-AUG-06

Scored by Standard Deviations

FIXED- AND RANDOM-EFFECTS META-ANALYSES OF DATA FOR VEGETABLES

ALL STUDIES
Dose Response (Beta)
WEIGHTED on Beta Weights

	Deviance	(DF)				
Model 1	33.2913	(15)				
	Estimate	S.E.	P	RR	95%CIl	95%CIu
Constant	-0.1068	0.0301	0.0030	0.8987	0.8472	0.9534

RANDOM EFFECTS MODEL
Dose Response (Beta)
WEIGHTED on Beta Weights

	Deviance	(DF)				
Model 1	17.3951	(15)				
	Estimate	S.E.	P	RR	95%CIl	95%CIu
Constant	-0.1264	0.0499	0.0230	0.8812	0.7991	0.9719

NORTH AMERICA AND EUROPE
Dose Response (Beta)
WEIGHTED on Beta Weights

	Deviance	(DF)				
Model 1	24.3813	(9)				
	Estimate	S.E.	P	RR	95%CIl	95%CIu
Constant	-0.0995	0.0371	0.0251	0.9053	0.8418	0.9736

RANDOM EFFECTS MODEL
Dose Response (Beta)
WEIGHTED on Beta Weights

	Deviance	(DF)				
Model 1	10.7784	(9)				
	Estimate	S.E.	P	RR	95%CIl	95%CIu
Constant	-0.1241	0.0714	0.1164	0.8833	0.7679	1.0160

ASIA
Dose Response (Beta)
WEIGHTED on Beta Weights

	Deviance	(DF)				
Model 1	8.7968	(5)				
	Estimate	S.E.	P	RR	95%CIl	95%CIu
Constant	-0.1209	0.0517	0.0665	0.8861	0.8007	0.9806

RANDOM EFFECTS MODEL
Dose Response (Beta)
WEIGHTED on Beta Weights

	Deviance	(DF)				
Model 1	5.6360	(5)				
	Estimate	S.E.	P	RR	95%CIl	95%CIu
Constant	-0.1289	0.0727	0.1365	0.8791	0.7624	1.0137

NEVER SMOKERS ONLY
Dose Response (Beta)
WEIGHTED on Beta Weights

	Deviance	(DF)				
Model 1	27.7640	(13)				
	Estimate	S.E.	P	RR	95%CIl	95%CIu
Constant	-0.1313	0.0373	0.0037	0.8769	0.8151	0.9434

RANDOM EFFECTS MODEL
Dose Response (Beta)
WEIGHTED on Beta Weights

	Deviance	(DF)				
Model 1	14.9956	(13)				
	Estimate	S.E.	P	RR	95%CIl	95%CIu
Constant	-0.1294	0.0583	0.0448	0.8786	0.7838	0.9849

FEMALES
NEVER SMOKERS OR NEVER AND LONG TERM EX SMOKERS
NYBERG1998 REPLACED BY BRENNAN2000, GOODMAN1992 EXCLUDED

APPENDIX 4

Fruit/Vegetable/Tea consumption and lung cancer - Meta-Analysis of Dose Response Exposure, 22-AUG-06

Scored by Standard Deviations

FIXED- AND RANDOM-EFFECTS META-ANALYSES OF DATA FOR FRUIT

ALL STUDIES
Dose Response (Beta)
WEIGHTED on Beta Weights

	Deviance	(DF)				
Model 1	26.1872	(13)				
	Estimate	S.E.	P	RR	95%CIl	95%CIu
Constant	-0.1132	0.0330	0.0044	0.8929	0.8371	0.9525

RANDOM EFFECTS MODEL
Dose Response (Beta)
WEIGHTED on Beta Weights

	Deviance	(DF)				
Model 1	13.5639	(13)				
	Estimate	S.E.	P	RR	95%CIl	95%CIu
Constant	-0.1452	0.0518	0.0149	0.8649	0.7814	0.9573

NORTH AMERICA AND EUROPE
Dose Response (Beta)
WEIGHTED on Beta Weights

	Deviance	(DF)				
Model 1	17.2874	(8)				
	Estimate	S.E.	P	RR	95%CIl	95%CIu
Constant	-0.1011	0.0381	0.0289	0.9038	0.8389	0.9738

RANDOM EFFECTS MODEL
Dose Response (Beta)
WEIGHTED on Beta Weights

	Deviance	(DF)				
Model 1	8.2665	(8)				
	Estimate	S.E.	P	RR	95%CIl	95%CIu
Constant	-0.1551	0.0635	0.0405	0.8564	0.7561	0.9699

ASIA
Dose Response (Beta)
WEIGHTED on Beta Weights

	Deviance	(DF)				
Model 1	8.4941	(4)				
	Estimate	S.E.	P	RR	95%CIl	95%CIu
Constant	-0.1496	0.0659	0.0857	0.8611	0.7567	0.9798

RANDOM EFFECTS MODEL
Dose Response (Beta)
WEIGHTED on Beta Weights

	Deviance	(DF)				
Model 1	4.1235	(4)				
	Estimate	S.E.	P	RR	95%CIl	95%CIu
Constant	-0.1198	0.1024	0.3069	0.8871	0.7258	1.0842

NEVER SMOKERS ONLY
Dose Response (Beta)
WEIGHTED on Beta Weights

	Deviance	(DF)				
Model 1	19.5696	(11)				
	Estimate	S.E.	P	RR	95%CIl	95%CIu
Constant	-0.1543	0.0422	0.0038	0.8570	0.7890	0.9310

RANDOM EFFECTS MODEL
Dose Response (Beta)
WEIGHTED on Beta Weights

	Deviance	(DF)				
Model 1	11.7977	(11)				
	Estimate	S.E.	P	RR	95%CIl	95%CIu
Constant	-0.1607	0.0595	0.0206	0.8516	0.7579	0.9568

FEMALES
NEVER SMOKERS OR NEVER AND LONG TERM EX SMOKERS
NYBERG1998 REPLACED BY BRENNAN2000, GOODMAN1992 EXCLUDED

APPENDIX 4

Fruit/Vegetable/Tea consumption and lung cancer - Meta-Analysis of Dose Response Exposure, 22-AUG-06

Scored by Standard Deviations

FIXED- AND RANDOM-EFFECTS META-ANALYSES OF DATA FOR TEA

ALL STUDIES
Dose Response (Beta)
WEIGHTED on Beta Weights

	Deviance	(DF)				
Model 1	0.2708	(1)				
	Estimate	S.E.	P	RR	95%CIl	95%CIu
Constant	-0.3112	0.0813	0.1627	0.7326	0.6247	0.8592

RANDOM EFFECTS MODEL
Dose Response (Beta)
WEIGHTED on Beta Weights

	Deviance	(DF)				
Model 1	0.2708	(1)				
	Estimate	S.E.	P	RR	95%CIl	95%CIu
Constant	-0.3112	0.0813	0.1627	0.7326	0.6247	0.8592

NORTH AMERICA AND EUROPE
Dose Response (Beta)
WEIGHTED on Beta Weights

	Deviance	(DF)				
Model 1	0.0000	(0)				
	Estimate	S.E.	P	RR	95%CIl	95%CIu
Constant	-0.3620	0.1271		0.6963	0.5428	0.8932

RANDOM EFFECTS MODEL
Dose Response (Beta)
WEIGHTED on Beta Weights

	Deviance	(DF)				
Model 1	0.0000	(0)				
	Estimate	S.E.	P	RR	95%CIl	95%CIu
Constant	-0.3620	0.1271		0.6963	0.5428	0.8932

ASIA
Dose Response (Beta)
WEIGHTED on Beta Weights

	Deviance	(DF)				
Model 1	0.0000	(0)				
	Estimate	S.E.	P	RR	95%CIl	95%CIu
Constant	-0.2759	0.1058		0.7589	0.6167	0.9337

RANDOM EFFECTS MODEL
Dose Response (Beta)
WEIGHTED on Beta Weights

	Deviance	(DF)				
Model 1	0.0000	(0)				
	Estimate	S.E.	P	RR	95%CIl	95%CIu
Constant	-0.2759	0.1058		0.7589	0.6167	0.9337

FEMALES
NEVER SMOKERS OR NEVER AND LONG TERM EX SMOKERS
NYBERG1998 REPLACED BY BRENNAN2000, GOODMAN1992 EXCLUDED

Appendix 5

Fuller details of the analyses relating lung cancer risk to dietary fat consumption

APPENDIX 5

Dietary fat consumption and lung cancer - Meta-Analysis of Dose Response Exposure, 07-AUG-06

Scored by Standard Deviations

BASIC DATA USED IN META-ANALYSES - DIETARY FAT

Study title	RR	RRL	RRU	CA1	CA0	CO1	CO0	REL SD
Alavanja	1.8600	1.0900	3.1800	57.0400	24.9400	131.2600	106.8000	0.8675
Alavanja	1.6300	0.9200	2.8900	38.5600	24.9400	101.2600	106.8000	1.3996
Alavanja	2.2400	1.3100	3.8500	58.2000	24.9400	111.2000	106.8000	1.9317
Alavanja	2.3800	1.3500	4.1700	46.7000	24.9400	83.9800	106.8000	2.7992
Hu J	0.8000	0.5000	1.4000	50.2200	39.8400	199.4900	94.8000	1.1577
Hu J	1.7000	1.0000	3.0000	44.5100	29.8400	83.2200	94.8000	2.2368
Kalandidi	1.1200	0.5300	2.3500	24.2400	24.5000	30.2400	34.2000	0.9464
Kalandidi	1.4000	0.6900	2.8300	33.5900	24.5000	33.5200	34.2000	1.5958
Kalandidi	0.5700	0.2300	1.4500	9.3500	24.5000	22.9200	34.2000	2.5422
Ozasa	1.4700	0.7900	2.7000	30.0400	15.3800	58492.9600	44012.1000	1.2538
Ozasa	1.9100	0.9800	3.7200	19.6800	15.3800	29494.8100	44012.1000	2.4948
Swanson	0.9000	0.3000	2.8000	8.5700	9.5100	19.4700	19.5000	2.7992
Wu	1.0000	0.4000	2.6000	9.0000	8.5800	5387.0200	5132.7000	0.9464
Wu	0.5000	0.2000	1.7000	5.5200	8.5800	6606.0600	5132.7000	1.5958
Wu	1.8000	0.7000	4.3000	10.2700	8.5800	3412.7700	5132.7000	2.5422

NOTES: RR,RL,RU RELATIVE RISKS AND LOWER AND UPPER CONFIDENCE INTERVALS
CA1,CA0 NUMBERS (OR PSEUDO-NUMBERS) OF MORE EXPOSED AND LEAST EXPOSED CASES
CO1,CO0 NUMBERS (OR PSEUDO-NUMBERS) OF MORE EXPOSED AND LEAST EXPOSED CONTROLS
CA1,CA0,CO1,CO0 NOT SHOWN IF ORIGINAL RR PER STANDARD DEVIATION
REL SD NUMBER OF STANDARD DEVIATIONS FROM LEAST EXPOSED LEVEL

FEMALES
NEVER SMOKERS OR NEVER AND LONG TERM EX SMOKERS
INCLUDING ONLY DATA FOR SELECTED FAT INDICES SHOWN IN TABLE 5

APPENDIX 5

Dietary fat consumption and lung cancer - Meta-Analysis of Dose Response Exposure, 07-AUG-06

Scored by Standard Deviations

REGRESSION ESTIMATES, WEIGHTS AND OTHER RELEVANT DETAILS

Study title	Country	Beta	St.Err. Beta	Z	Weight	RSEX	SMOKE
Alavanja	US	0.2666	0.0915	2.9136	119.4085	f	2
Hu J	Canada	0.2543	0.1251	2.0330	63.9103	f	1
Kalandidi	Greece	-0.0796	0.1678	-0.4742	35.5293	f	1
Ozasa	Japan	0.2567	0.1360	1.8884	54.0956	f	1
Swanson	US	-0.0376	0.2036	-0.1849	24.1332	f	2
Wu	US	0.1989	0.1771	1.1231	31.8743	f	1

NOTES: BETA SLOPE OF LOG RR ON SD OF VARIABLE
SE BETA STANDARD ERROR OF BETA
Z RATIO OF BETA TO ITS STANDARD ERROR (APPROXIMATE NORMAL STATISTIC)
WEIGHT INVERSE OF THE VARIANCE OF BETA
SMOKE 1 = NEVER SMOKERS, 2 = NEVER OR LONG-TERM EX-SMOKERS
RSEX SEX FOR RR

FEMALES
NEVER SMOKERS OR NEVER AND LONG TERM EX SMOKERS
INCLUDING ONLY DATA FOR SELECTED FAT INDICES SHOWN IN TABLE 5

APPENDIX 5

Dietary fat consumption and lung cancer - Meta-Analysis of Dose Response Exposure, 07-AUG-06

Scored by Standard Deviations

FIXED- AND RANDOM-EFFECTS META-ANALYSES OF DATA FOR DIETARY FAT

WEIGHTED on Beta Weights

	Deviance	(DF)				
Dose Response (Beta)						
Model 1	5.0281	(5)				
	Estimate	S.E.	P	RR	95%CIl	95%CIu
Constant	0.1963	0.0551	0.0162	1.2169	1.0923	1.3558

RANDOM EFFECTS MODEL
Dose Response (Beta)
WEIGHTED on Beta Weights

	Deviance	(DF)				
Model 1	5.0037	(5)				
	Estimate	S.E.	P	RR	95%CIl	95%CIu
Constant	0.1960	0.0554	0.0165	1.2166	1.0915	1.3560

USA AND CANADA
Dose Response (Beta)
WEIGHTED on Beta Weights

	Deviance	(DF)				
Model 1	1.9478	(3)				
	Estimate	S.E.	P	RR	95%CIl	95%CIu
Constant	0.2236	0.0646	0.0406	1.2506	1.1018	1.4195

RANDOM EFFECTS MODEL
Dose Response (Beta)
WEIGHTED on Beta Weights

	Deviance	(DF)				
Model 1	1.9478	(3)				
	Estimate	S.E.	P	RR	95%CIl	95%CIu
Constant	0.2236	0.0646	0.0406	1.2506	1.1018	1.4195

OTHER
Dose Response (Beta)
WEIGHTED on Beta Weights

	Deviance	(DF)				
Model 1	2.4255	(1)				
	Estimate	S.E.	P	RR	95%CIl	95%CIu
Constant	0.1234	0.1056	0.4506	1.1314	0.9198	1.3916

RANDOM EFFECTS MODEL
Dose Response (Beta)
WEIGHTED on Beta Weights

	Deviance	(DF)				
Model 1	1.0000	(1)				
	Estimate	S.E.	P	RR	95%CIl	95%CIu
Constant	0.1030	0.1675	0.6492	1.1084	0.7982	1.5393

NEVER SMOKERS ONLY
Dose Response (Beta)
WEIGHTED on Beta Weights

	Deviance	(DF)				
Model 1	3.0762	(3)				
	Estimate	S.E.	P	RR	95%CIl	95%CIu
Constant	0.1815	0.0734	0.0899	1.1990	1.0383	1.3847

RANDOM EFFECTS MODEL
Dose Response (Beta)
WEIGHTED on Beta Weights

	Deviance	(DF)				
Model 1	3.0076	(3)				
	Estimate	S.E.	P	RR	95%CIl	95%CIu
Constant	0.1809	0.0745	0.0934	1.1983	1.0356	1.3866

FEMALES
NEVER SMOKERS OR NEVER AND LONG TERM EX SMOKERS
INCLUDING ONLY DATA FOR SELECTED FAT INDICES SHOWN IN TABLE 5

Appendix 6

Fuller details of the analyses relating lung cancer risk to education

APPENDIX 6

Education and lung cancer - Meta-Analysis of Dose Response Exposure, 07-AUG-06

Scored by Years of Education (or equivalent)

BASIC DATA USED IN META-ANALYSES - EDUCATION

Study title	RR	RRL	RRU	CA1	CA0	CO1	CO0	Years
Boffetta	1.3300	0.8600	2.0500	80.0000	39.0000	226.0000	146.0000	-2.0000
Boffetta	2.3100	1.5700	3.4000	257.0000	39.0000	416.0000	146.0000	-4.0000
Fontham	1.0200	0.6500	1.5900	62.0000	46.0000	154.0000	116.0000	-2.0000
Fontham	0.7900	0.5300	1.1900	99.0000	46.0000	315.0000	116.0000	-3.0000
Fontham	1.3900	0.9500	2.0400	217.0000	46.0000	393.0000	116.0000	-5.0000
Fontham	2.0500	1.3900	3.0100	216.0000	46.0000	266.0000	116.0000	-7.0000
Kabat 1	0.8800	0.3200	2.4100	14.0000	16.0000	15.0000	15.0000	-3.0000
Kabat 1	0.6300	0.2700	1.5100	25.0000	16.0000	37.0000	15.0000	-5.0000
Kabat 1	1.2300	0.5200	2.8900	38.0000	16.0000	29.0000	15.0000	-7.0000
Kabat 2	0.6600	0.2800	1.5800	12.0000	15.0000	147.0000	39.0000	-3.0000
Kabat 2	1.0900	0.5200	2.2800	29.0000	15.0000	69.0000	39.0000	-5.0000
Kabat 2	1.0600	0.4400	2.5400	13.0000	15.0000	32.0000	39.0000	-7.0000
Kalandidi	0.8000	0.4000	1.6200	55.0000	20.0000	72.0000	21.0000	-4.5000
Kalandidi	0.7000	0.3000	1.6500	18.0000	20.0000	27.0000	21.0000	-7.5000
Ko	1.8700	0.6800	5.1100	8.0000	8.0000	29.0000	14.0000	-6.0000
Ko	1.8600	0.7300	4.7500	66.0000	8.0000	62.0000	14.0000	-11.0000
Mao	1.0000	0.6600	1.5100	107.0000	33.0000	909.0000	277.0000	-4.0000
Mao	1.6700	1.0100	2.7600	37.0000	33.0000	188.0000	277.0000	-8.0000
Sobue	2.0200	1.4000	2.9000	69.0000	75.0000	229.0000	502.0000	-6.0000
Stockwell	1.4900	0.4900	2.4500	36.0000	135.0000	40.0000	223.0000	-3.0000
Stockwell	1.7000	1.0300	2.8000	38.0000	135.0000	37.0000	223.0000	-6.0000
Wichmann BIPS	0.1400	0.0500	0.3900	15.0000	3.0000	24.0000	8.0000	-3.0000
Wichmann BIPS	1.4800	0.3700	5.9500	35.0000	3.0000	63.0000	8.0000	-4.5000
Wichmann GSF	0.7100	0.3700	1.3700	25.0000	21.0000	104.0000	62.0000	-3.0000
Wichmann GSF	1.4600	0.8700	2.4700	191.0000	21.0000	385.0000	62.0000	-4.5000
Wichmann GSF	2.5300	0.7600	8.3800	6.0000	21.0000	7.0000	62.0000	-7.0000
Zaridze	2.2900	1.4900	3.5200	94.0000	44.0000	129.0000	138.0000	-2.0000
Zaridze	1.7600	1.0900	2.8500	51.0000	44.0000	91.0000	138.0000	-4.0000

NOTES: RR,RL,RU RELATIVE RISKS AND LOWER AND UPPER CONFIDENCE INTERVALS
CA1,CA0 NUMBERS (OR PSEUDO-NUMBERS) OF MORE EXPOSED AND LEAST EXPOSED CASES
CO1,CO0 NUMBERS (OR PSEUDO-NUMBERS) OF MORE EXPOSED AND LEAST EXPOSED CONTROLS
CA1,CA0,CO1,CO0 NOT SHOWN IF ORIGINAL RR PER STANDARD DEVIATION
YEARS DIFFERENCE IN YEARS OF EDUCATION FROM LEAST EXPOSED LEVEL

FEMALES
NEVER SMOKERS OR NEVER PLUS OCCASIONAL SMOKERS

APPENDIX 6

Education and lung cancer - Meta-Analysis of Dose Response Exposure, 07-AUG-06

Scored by Years of Education (or equivalent)

REGRESSION ESTIMATES, WEIGHTS AND OTHER RELEVANT DETAILS

Study title	Country	Beta	St.Err. Beta	Z	Weight	RSEX	SMOKE
Boffetta	Western Europe	-0.2257	0.0450	-5.0111	492.8352	f	1
Fontham	US	-0.1390	0.0231	-6.0108	1870.6488	f	1
Kabat 1	US	-0.0227	0.0600	-0.3781	277.5818	f	1
Kabat 2	US	-0.0274	0.0588	-0.4661	288.9878	f	1
Kalandidi	Greece	0.0478	0.0574	0.8327	303.2483	f	1
Ko	Taiwan	-0.0484	0.0421	-1.1503	564.1308	f	1
Mao	Canada	-0.0653	0.0320	-2.0365	973.6386	f	1
Sobue	Japan	-0.1172	0.0310	-3.7846	1043.0639	f	1
Stockwell	US	-0.0902	0.0422	-2.1399	562.4202	f	1
Wichmann BIPS	Germany	0.0212	0.1569	0.1352	40.6113	f	w
Wichmann GSF	Germany	-0.1280	0.0547	-2.3385	333.6087	f	w
Zaridze	Russia	-0.1425	0.0613	-2.3243	266.1449	f	1

NOTES: BETA SLOPE OF LOG RR ON YEARS OF EDUCATION
SE BETA STANDARD ERROR OF BETA
Z RATIO OF BETA TO ITS STANDARD ERROR (APPROXIMATE NORMAL STATISTIC)
WEIGHT INVERSE OF THE VARIANCE OF BETA
SMOKE 1 = NEVER SMOKERS, W = NEVER PLUS OCCASIONAL SMOKERS
RSEX SEX FOR RR

FEMALES
NEVER SMOKERS OR NEVER PLUS OCCASIONAL SMOKERS

APPENDIX 6

Education and lung cancer - Meta-Analysis of Dose Response Exposure, 07-AUG-06

Scored by Years of Education (or equivalent)

FIXED- AND RANDOM-EFFECTS META-ANALYSES OF DATA FOR EDUCATION

WEIGHTED on Beta Weight

	Deviance	(DF)				
Dose Response (Beta)						
Model 1	24.7912	(11)				
	Estimate	S.E.	P	RR	95%CIl	95%CIu
Constant	-0.1018	0.0119	0.0000	0.9032	0.8823	0.9246

RANDOM EFFECTS MODEL
Dose Response (Beta)
WEIGHTED on Beta Weight

	Deviance	(DF)				
Model 1	11.9997	(11)				
	Estimate	S.E.	P	RR	95%CIl	95%CIu
Constant	-0.0917	0.0196	0.0007	0.9124	0.8781	0.9481

USA AND CANADA
Dose Response (Beta)
WEIGHTED on Beta Weight

	Deviance	(DF)				
Model 1	7.2317	(4)				
	Estimate	S.E.	P	RR	95%CIl	95%CIu
Constant	-0.0978	0.0159	0.0035	0.9069	0.8791	0.9355

RANDOM EFFECTS MODEL
Dose Response (Beta)
WEIGHTED on Beta Weight

	Deviance	(DF)				
Model 1	3.4075	(4)				
	Estimate	S.E.	P	RR	95%CIl	95%CIu
Constant	-0.0844	0.0236	0.0232	0.9191	0.8776	0.9626

EUROPE
Dose Response (Beta)
WEIGHTED on Beta Weight

	Deviance	(DF)				
Model 1	15.0030	(4)				
	Estimate	S.E.	P	RR	95%CIl	95%CIu
Constant	-0.1229	0.0264	0.0096	0.8844	0.8398	0.9313

RANDOM EFFECTS MODEL
Dose Response (Beta)
WEIGHTED on Beta Weight

	Deviance	(DF)				
Model 1	3.5111	(4)				
	Estimate	S.E.	P	RR	95%CIl	95%CIu
Constant	-0.1030	0.0549	0.1340	0.9021	0.8100	1.0047

ASIA
Dose Response (Beta)
WEIGHTED on Beta Weight

	Deviance	(DF)				
Model 1	1.7306	(1)				
	Estimate	S.E.	P	RR	95%CIl	95%CIu
Constant	-0.0931	0.0249	0.1667	0.9111	0.8677	0.9568

RANDOM EFFECTS MODEL
Dose Response (Beta)
WEIGHTED on Beta Weight

	Deviance	(DF)				
Model 1	1.0000	(1)				
	Estimate	S.E.	P	RR	95%CIl	95%CIu
Constant	-0.0887	0.0339	0.2321	0.9151	0.8563	0.9779

NEVER SMOKERS ONLY

FEMALES
NEVER SMOKERS OR NEVER PLUS OCCASIONAL SMOKERS

APPENDIX 6

Education and lung cancer - Meta-Analysis of Dose Response Exposure, 07-AUG-06

Scored by Years of Education (or equivalent)

FIXED- AND RANDOM-EFFECTS META-ANALYSES OF DATA FOR EDUCATION

Dose Response (Beta)
WEIGHTED on Beta Weight

	Deviance	(DF)				
Model 1	23.9452	(9)				
	Estimate	S.E.	P	RR	95%CIl	95%CIu
Constant	-0.1013	0.0123	0.0000	0.9037	0.8822	0.9257

RANDOM EFFECTS MODEL
Dose Response (Beta)
WEIGHTED on Beta Weight

	Deviance	(DF)				
Model 1	10.4299	(9)				
	Estimate	S.E.	P	RR	95%CIl	95%CIu
Constant	-0.0899	0.0214	0.0023	0.9140	0.8764	0.9532

FEMALES
NEVER SMOKERS OR NEVER PLUS OCCASIONAL SMOKERS

Appendix 7

Review of papers since 2000 relating ETS exposure at home to the potential confounding variables

1. Introduction

The objective is to obtain data relating ETS exposure to fruit, vegetable and dietary fat consumption and to education to add to the information presented in Tables 4, 5 and 6 of our 2001 paper [1]. Eleven papers were identified as potentially relevant. Not considered here is information directly available from accessible databases.

2. The studies

2.1 Curtin *et al* 1999 [2]

This is a population survey in Geneva, Switzerland involving 914 female never smokers aged 35-74. Data relating to education (from Table 1), and to diet (from Tables 2 and 3) are summarized below.

	Unexposed to ETS	Exposed to ETS			
		At home	At work	During leisure	
	(n=698)	(n=81)	(n=83)	(n=52)	p
Education (%)					
Tertiary	33.1	33.3	34.9	28.9	
Secondary	54.6	49.4	51.8	69.2	
Primary	12.3	17.3	13.3	1.9	0.16
% of total energy from					
Vegetable proteins	4.7	4.8	4.6	4.8	0.69
Animal proteins	10.2	10.5	10.5	10.7	0.76
Total fat	35.1	34.5	35.3	35.7	0.82
Saturated fat	12.9	12.2	13.0	13.2	0.46
Daily intake (g)					
Fried food	14.1	13.8	16.1	15.4	0.72
Fruits	182	171	184	188	0.95
Vegetables	225	221	186	236	0.04
Fat meat	17.5	16.7	15.8	17.2	0.76

Note that ETS exposure is defined "as an exposure of at least 1 hr per day for at least 1 year exclusively either at home, at work or during leisure time that was still on-going during the year preceding the interview." The "at home," "at work" and "during leisure" groups are mutually independent, 14 women who would have qualified under more than one exposure heading being excluded from the analysis. p values are based on an unadjusted 3x4 chisquared analysis for education and on an analysis of covariance adjusted for BMI, age and social class for diet.

Unfortunately, the data on diet included no information from which we could estimate standard errors of the means, and thus that data could not be included in our database. For education we took the following numeric values for the education categories – Tertiary =15 years; Secondary = 11 years and Primary = 7 years.

2.2 Dietrich *et al* [3]

This paper describes an experimental study of the effects of Vitamin C supplementation on biomarkers of oxidative stress in the plasma of ETS exposed non-smokers and is not relevant.

2.3 Enstrom and Kabat 2003 [4]

This paper describes follow-up from 1959 to 1998 of those 35561 never smokers in the California part of the well known CPS I study who had a spouse in the study with known smoking habits. Table 2 (males) and Table 3 (females) give unadjusted data relating education and diet to the smoking status of the spouse.

	Smoking status of wife, 1959						
				Current cigarettes/day			
	Never	Former		1-19	20-39	40+	Total
Males							
Participants in 1959	7458	624		905	587	45	9619
Education 12+ years (%)	67.3	80.6		71.3	74.2	84.5	69.0
(number)	(5017)	(403)		(645)	(436)	(38)	(6639)
Eat green salads	4.8	4.9		5.0	5.0	4.9	4.8
(mean days/wk)	(7201)	(617)		(887)	5(73)	(45)	(9323)
Eat fruits or drink fruit	6.0	6.0		5.9	5.5	5.3	5.9
juice (mean days/wk)	(7226)	(614)		(886)	(574)	(43)	(9343)
	Smoking status of husband, 1959						
				Current cigarettes/day			
	Never	Former	**Pipe/cigs**	1-19	20-39	40+	Total
Females							
Participants in 1959	7339	6858	2691	3219	4934	841	25942
Education 12+ years (%)	73.7	68.2	68.9	65.6	70.4	77.2	70.2
(number)	(5452)	(4685)	(1853)	(2109)	(3476)	(650)	(18225)
Eat green salads	5.1	5.0	5.1	4.9	5.1	5.1	5.0
(mean days/wk)	(7219)	(6701)	(2618)	(3122)	(4835)	(825)	(25320)
Eat fruits or drink fruit	6.4	6.3	6.3	6.1	6.0	6.0	6.2
juice (mean days/wk)	(7227)	(6727)	(2621)	(3132)	(4846)	(826)	(25379)

Unfortunately, the data on diet included no information from which we could estimate standard errors of the means, and thus that data could not be included in our database.

2.4 Farchi *et al* 2001 [5]

This paper gives further results from the study by Forastiere *et al* [6] relating to antioxidant vitamins. It provides no additional data of use to us.

2.5 Forastiere *et al* [6]

This cross-sectional study in four areas of Italy involved 1938 married women aged 25-74 who had reported never being cigarette smokers and who provided data on husband's smoking. Table 1 of the paper provides data relating ever exposure to husband's smoking with the education of the women.

	Husbands' smoking			
	Unexposed	Exposed		
Variable	n	n	OR[a]	95% CI
Womens' education (years)				
>13	92	120	1.00	-
9-13	252	362	1.24	(0.89-1.71)
6-8	187	314	1.44	(1.02-2.04)
<6	193	413	1.54	(1.04-2.28)
Total	724	1209		

[a]Odds ratios adjusted for center, age, and center x age.

Table 1 also includes data showing husband's smoking is similarly associated with husband's education. We took the following numeric values for the education categories – >13 =15 years; 9-13 = 11 years, 6-8 = 7 years and <6 = 5 years.

Table 4 includes data relating husband's smoking to various foods. Results for meat in general, cooked and fresh vegetables and fruit in general are given below.

Variable	Husbands' smoking Unexposed n	 Exposed n	OR[a]	OR[b]	95% CI
Meat in general					
Never	13	25			
<1/day	387	688	1.00	1.00	-
1/day	263	406	0.89	0.87	(0.71-1.07)
>1/day	58	81	0.85	0.80	(0.56-1.15)
Total	721	1200			
Cooked vegetables					
<1/day	311	557	1.00	1.00	-
1/day	248	450	1.01	1.03	(0.83-1.28)
>1/day	163	194	0.72	0.72	(0.55-0.93)
Total	722	1201			
Fresh vegetables					
<1/day	163	346	1.00	1.00	-
1/day	306	543	0.86	0.86	(0.67-1.09)
>1/day	256	319	0.64	0.63	(0.49-0.82)
Total	725	1208			
Fruit in general					
<1/day	122	174	1.00	1.00	-
1-2/day	330	545	1.11	1.12	(0.85-1.48)
>2/day	270	490	1.08	1.09	(0.82-1.45)
Total	722	1229			

Totals may vary because of missing values.
[a]Odds ratios adjusted for center, age, and center x age.
[b]Odds ratios adjusted for center, age, center x age, and woman's education

2.6 Iribarren *et al* 2001 [7]

This paper describes a cross sectional study in Northern California, USA using data from multiphasic health checkups between 1979 and 1985. 16524 men aged 15-89 and 26197 women aged 15-105 had never smoked. There are no data on diet. The data on education (in Table 3) are only in relation to hours/wk total exposure (home, small spaces other than home and large indoor areas) and not to spouse or household exposure which we insisted upon in our original work [1]. The authors note (p724) that "among those with the heaviest ETS exposure (≥40 weeks), and regardless of gender, there was a larger proportion of participants who were black, with no college or partial college education …". The study is not useful for our purposes.

2.7 Moussa *et al* [8]

The paper describes a study of a Swedish working population sample of 8270 individuals conducted in 2000. The study is not useful for various reasons – it only considers studies ETS at work, does not provide results for non-smokers, and gives no data on diet or education.

2.8 Reynolds *et al* [9]

This paper was based on 128,174 women aged 21+ in the California Teachers Study, for whom the data collected in 1995 included complete and usable information on tobacco. There were 85,114 never smokers, 60,343 of whom had passive smoking exposure, defined as ever living with a smoker during either childhood or adulthood, and 24,771 of which had none. The dietary analyses are restricted to 122,544 women with a daily intake of 600 to 5000 calories.

No results are given for education.

As shown in Table 5, after adjustment for age, race and caloric intake, results for fruit, vegetables and fat were as follows:

		Exposed vs not exposed to ETS	
		OR (95% CI)	Trend p
Fruit	3+ servings/day	0.84 (0.80-0.88)	n/a
	≤2 servings/day	1.00	
Vegetables	3+ servings/day	0.89 (0.84-0.93)	n/a
	≤2 servings/day	1.00	
Fat intake	Quartile 1	1.00	
	Quartile 2	1.03 (0.98-1.08)	
	Quartile 3	1.04 (0.99-1.10)	
	Quartile 4	1.07 (1.00-1.13)	
	Quartile 5	1.14 (1.06-1.24)	0.003

It is unclear why there are five quartiles! Numbers of cases exposed and unexposed to ETS were estimated by the RRest procedure and these values were entered into the database to use in the weighted regression analyses.

2.9 Scarinci *et al* 2000 [10]

This study, presumably (from the authors' affiliations) conducted in Memphis, USA involved 404 never smoking females aged 18-39 recruited in the community. The study related number of days per week exposed to ETS in the past year to various indicators of SES. Although there was a significant ($p<0.02$) tendency for post-college education to be associated with reduced ETS exposure, the results do not relate to spousal or household exposure so do not qualify for inclusion.

2.10 Stamatakis *et al* 2002 [11]

This study involved a nationally representative sample of 2326 nonsmoking US women aged 40 and older. Nonsmoking was defined as including former smokers as well as never smokers. As shown in Table 2, low education and low fruit/vegetable consumption was associated with an increased probability of ETS exposure at home.

		Odds ratio (95% CI)	
	%	Unadjusted	Adjusted*
Education			
≤8th grade	22.4	1.8 (1.2-2.8)	2.1 (1.3-3.6)
Some high school	18.6	1.4 (0.9-2.2)	1.3 (0.8-2.2)
High school graduate	24.7	2.0 (1.4-2.9)	2.2 (1.4-3.3)
Some college	14.3	1.0 (0.7-1.6)	1.1 (0.7-1.7)
College graduate +	13.9	1.0	1.0
Fruit/vegetables			
<5/day	20.5	1.6 (1.2-2.2)	1.5 (1.0-2.1)
≥5/day	13.8	1.0	1.0

*Adjusted for race, age, location and having children in the home.

2.11 Trobs *et al* 2002 [12]

This paper describes a study in Nuremberg, Germany involving 817 adults aged 27-66. The study involved 545 non-smokers, 149 living with a smoker, and 272 smokers. Nonsmoking status was confirmed by plasma cotinine, 21 self-reported non-smokers with a level ≥15 ng/ml being excluded from the evaluation. The definition of non-smokers does not exclude exsmokers (Dr W-D. Heller, personal communication).

The level of education was assessed by a standardized questionnaire taking into account the quality of school and degree of qualification. The scores ranged from 1 (no qualifications) to 5 (university degree). As shown in Table 3, level of education in non-smokers was lower in those living with a smoker.

	Score (SDev)	
Not living with a smoker	5.5 $\pm$ 2.7	
Living with a smoker	4.5 $\pm$ 2.6	$p<0.05$

Although 557 of the participants provided 7 day dietary data, no results for fruits, vegetables or dietary fat are given.

3. Summary

Of the 11 papers considered, one [3] was not an epidemiological study at all, and two gave no data on diet or education [5,8]. Two further studies [7,10] gave data on education, but only for total ETS exposure, not for spousal or household exposure. One study [11] gave results for education and for a combined index of fruit and vegetable consumption, but only for never plus former smokers combined. Another study [12] gave results for education, but apparently their definition of non-smokers also included former smokers.

This leaves four studies. Two [2,6] give some results for all four risk factors of interest, though the results for diet could not be used as noted above. One [4] gives results for all except dietary fat and one [9] gives results for all except education.

References

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Appendix 8

Fuller details of the analyses relating ETS exposure at home to fruit and vegetable consumption

APPENDIX 8

Fruit/Vegetable/Tea consumption in SDs between lifelong nonsmokers exposed or unexposed to ETS at home
Meta-Analysis of Differences, 08-SEP-06

BASIC DATA USED IN META-ANALYSES - VEGETABLES

Study Title	Continent	DELTA	St.Err. DELTA	WGT	WGTNS	WGTETS
Cardenas	US	-0.0852	0.0048	176320.0	71634.0	104686.0
Forastiere 2000	Europe	-0.2022	0.0470	1933.0	725.0	1208.0
Hamling (HALS2)	Europe	0.0447	0.0668	1265.0	974.0	291.0
Hamling (HSE93)	Europe	-0.0851	0.0431	3664.0	3007.0	657.0
Hamling (HULS)	Europe	-0.0718	0.0695	948.0	643.0	305.0
Hamling (HALS)	Europe	0.0527	0.0455	2351.0	1673.0	678.0
Hirayama 2	Asia	-0.0240	0.0534	1970.0	456.0	1512.0
Hirayama	Asia	0.0245	0.0077	91450.0	21895.0	69645.0
Koo (Hong Kong)	Asia	0.3532	0.1068	530.0	419.0	111.0
Koo (Japan)	Asia	-0.0863	0.0181	13047.0	8146.0	4901.0
Koo (Sweden)	Europe	-0.9022	0.2647	87.0	69.0	18.0
Koo (USA)	US	0.2859	0.1690	144.0	60.0	84.0
Matanoski	US	-0.0449	0.0360	3338.0	1214.0	2124.0
NHANES III	US	-0.2238	0.0449	3171.0	2555.0	616.0
NHIS 2000	US	-0.1170	0.0458	5096.0	4564.0	532.0
Reynolds 2004	US	-0.0582	0.0130	28801.0	8387.7	20412.9

NOTES: DELTA SD DIFFERENCE IN FRUIT, VEG OR TEA CONSUMPTION ASSOCIATED WITH ETS EXPOSURE AT HOME
SE DELTA STANDARD ERROR OF DELTA
WGT TOTAL NUMBER OF FEMALES
WGTNS NUMBER OF FEMALES WITH NO ETS EXPOSURE
WGTETS NUMBER OF FEMALES WITH ETS EXPOSURE

FEMALES
NEVER SMOKERS OR NEVER AND LONG TERM EX SMOKERS
EXCLUDING THORNTON AS INCLUDED WITHIN HAMLING RESULTS

APPENDIX 8

Fruit/Vegetable/Tea consumption in SDs between lifelong nonsmokers exposed or unexposed to ETS at home
Meta-Analysis of Differences, 08-SEP-06

BASIC DATA USED IN META-ANALYSES - FRUIT

Study Title	Continent	DELTA	St.Err. DELTA	WGT	WGTNS	WGTETS
Forastiere 2000	Europe	0.1043	0.0469	1931.0	722.0	1229.0
Hamling (HALS2)	Europe	-0.1256	0.0668	1265.0	974.0	291.0
Hamling (HSE93)	Europe	-0.0887	0.0431	3664.0	3007.0	657.0
Hamling (HULS)	Europe	-0.0446	0.0695	948.0	643.0	305.0
Hamling (HALS)	Europe	-0.0561	0.0455	2351.0	1673.0	678.0
Koo (Hong Kong)	Asia	-0.3009	0.1068	530.0	419.0	111.0
Koo (Japan)	Asia	-0.0818	0.0181	13047.0	8146.0	4901.0
Koo (Sweden)	Europe	-0.6795	0.2647	87.0	69.0	18.0
NHANES III	US	-0.0760	0.0449	3171.0	2555.0	616.0
NHIS 2000	US	-0.0846	0.0458	5100.0	4567.0	533.0
Reynolds 2004	US	-0.0871	0.0121	32513.0	9665.4	22847.8

NOTES: DELTA SD DIFFERENCE IN FRUIT, VEG OR TEA CONSUMPTION ASSOCIATED WITH ETS EXPOSURE AT HOME
SE DELTA STANDARD ERROR OF DELTA
WGT TOTAL NUMBER OF FEMALES
WGTNS NUMBER OF FEMALES WITH NO ETS EXPOSURE
WGTETS NUMBER OF FEMALES WITH ETS EXPOSURE

FEMALES
NEVER SMOKERS OR NEVER AND LONG TERM EX SMOKERS
EXCLUDING THORNTON AS INCLUDED WITHIN HAMLING RESULTS

APPENDIX 8

Fruit/Vegetable/Tea consumption in SDs between lifelong nonsmokers exposed or unexposed to ETS at home
Meta-Analysis of Differences, 08-SEP-06

BASIC DATA USED IN META-ANALYSES - TEA

Study Title	Continent	DELTA	St.Err. DELTA	WGT	WGTNS	WGTETS
Hamling (HALS)	Europe	-0.0341	0.0455	2349.0	1671.0	678.0
Hamling (HALS2)	Europe	-0.1263	0.0668	1265.0	974.0	291.0
Hamling (HSE93)	Europe	-0.1069	0.0431	3664.0	3007.0	657.0
Hamling (HULS)	Europe	-0.0753	0.0695	948.0	643.0	305.0
NHANES III	US	-0.0194	0.0449	3171.0	2555.0	616.0

NOTES: DELTA SD DIFFERENCE IN FRUIT, VEG OR TEA CONSUMPTION ASSOCIATED WITH ETS EXPOSURE AT HOME
SE DELTA STANDARD ERROR OF DELTA
WGT TOTAL NUMBER OF FEMALES
WGTNS NUMBER OF FEMALES WITH NO ETS EXPOSURE
WGTETS NUMBER OF FEMALES WITH ETS EXPOSURE

FEMALES
NEVER SMOKERS OR NEVER AND LONG TERM EX SMOKERS
EXCLUDING THORNTON AS INCLUDED WITHIN HAMLING RESULTS

APPENDIX 8

Fruit/Vegetable/Tea consumption in SDs between lifelong nonsmokers exposed or unexposed to ETS at home
Meta-Analysis of Differences, 08-SEP-06

REGRESSION ESTIMATES, WEIGHTS AND OTHER RELEVANT DETAILS

Study Title	Country	DELTA	St.Err. DELTA	Z	WGT	RWGT	Expos	SMOKE
Cardenas	US	-0.0852	0.0048	-17.5708	176320.0	42531.0624	Vegetables	1
Forastiere 2000	Italy	0.1043	0.0469	2.2243	1931.0	454.8119	Fruit	1
Forastiere 2000	Italy	-0.2022	0.0470	-4.3040	1933.0	453.0781	Fresh veg	1
Hamling (HALS)	UK	-0.0341	0.0455	-0.7489	2349.0	482.3065	Tea	1
Hamling (HALS2)	UK	-0.1263	0.0668	-1.8905	1265.0	224.0585	Tea	1
Hamling (HALS2)	UK	0.0447	0.0668	0.6691	1265.0	224.0585	Vegetables	1
Hamling (HALS2)	UK	-0.1256	0.0668	-1.8801	1265.0	224.0585	Fruit	1
Hamling (HSE93)	UK	-0.0851	0.0431	-1.9761	3664.0	539.1919	Vegetables	1
Hamling (HSE93)	UK	-0.0887	0.0431	-2.0597	3664.0	539.1919	Fruit	1
Hamling (HULS)	Hungary	-0.0718	0.0695	-1.0327	948.0	206.8724	Vegetables	1
Hamling (HULS)	Hungary	-0.0446	0.0695	-0.6415	948.0	206.8724	Fruit	1
Hamling (HALS)	UK	0.0527	0.0455	1.1576	2351.0	482.4730	Vegetables	1
Hamling (HALS)	UK	-0.0561	0.0455	-1.2323	2351.0	482.4730	Fruit	1
Hirayama 2	Japan	-0.0240	0.0534	-0.4492	1970.0	350.3415	Vegetables	1
Hirayama	Japan	0.0245	0.0077	3.1621	91450.0	16658.0432	Vegetables	1
Hamling (HSE93)	UK	-0.1069	0.0431	-2.4823	3664.0	539.1919	Tea	1
Hamling (HULS)	Hungary	-0.0753	0.0695	-1.0830	948.0	206.8724	Tea	1
Koo (Hong Kong)	Hong Kong	0.3532	0.1068	3.3087	530.0	87.7528	Vegetables	1
Koo (Hong Kong)	Hong Kong	-0.3009	0.1068	-2.8187	530.0	87.7528	Fruit	1
Koo (Japan)	Japan	-0.0863	0.0181	-4.7739	13047.0	3059.9790	Vegetables	1
Koo (Japan)	Japan	-0.0818	0.0181	-4.5249	13047.0	3059.9790	Fruit	1
Koo (Sweden)	Sweden	-0.9022	0.2647	-3.4088	87.0	14.2759	Vegetables	1
Koo (Sweden)	Sweden	-0.6795	0.2647	-2.5674	87.0	14.2759	Fruit	1
Koo (USA)	US	0.2859	0.1690	1.6914	144.0	35.0000	Vegetables	1
Matanoski	US	-0.0449	0.0360	-1.2479	3338.0	772.4793	Vegetables	1
NHANES III	US	-0.2238	0.0449	-4.9859	3171.0	496.3355	Vegetables	1
NHANES III	US	-0.0760	0.0449	-1.6932	3171.0	496.3355	Fruit	1
NHANES III	US	-0.0194	0.0449	-0.4322	3171.0	496.3355	Tea	1
NHIS 2000	US	-0.1170	0.0458	-2.5539	5096.0	476.4615	Vegetables	1
NHIS 2000	US	-0.0846	0.0458	-1.8483	5100.0	477.2963	Fruit	1
Reynolds 2004	US	-0.0582	0.0130	-4.4874	28801.0	5944.9206	Vegetables	1
Reynolds 2004	US	-0.0871	0.0121	-7.1783	32513.0	6792.1068	Fruit	1

NOTES: DELTA SD DIFFERENCE IN FRUIT, VEG OR TEA CONSUMPTION ASSOCIATED WITH ETS EXPOSURE AT HOME
SE DELTA STANDARD ERROR OF DELTA
Z RATIO OF DELTA TO ITS STANDARD ERROR (APPROXIMATE NORMAL STATISTIC)
WGT TOTAL NUMBER OF FEMALES FOR FIXED EFFECT MODELS
RWGT INVERSE OF THE VARIANCE OF DELTA FOR RANDOM EFFECTS MODELS
SMOKE 1 = NEVER SMOKERS, 2 = NEVER OR LONG-TERM EX-SMOKERS

FEMALES
NEVER SMOKERS OR NEVER AND LONG TERM EX SMOKERS
EXCLUDING THORNTON AS INCLUDED WITHIN HAMLING RESULTS

APPENDIX 8

Fruit/Vegetable/Tea consumption in SDs between lifelong nonsmokers exposed or unexposed to ETS at home
Meta-Analysis of Differences, 08-SEP-06

FIXED- AND RANDOM-EFFECTS META-ANALYSES OF DATA FOR VEGETABLES

ALL STUDIES

Difference in SDs (DELTA)

	Deviance	(DF)	
Model 1	1.0824	(15)	
	Estimate	S.E.	P
Constant	-0.0712	0.0672	0.3056

WEIGHTED on DELTA Weights

	Deviance	(DF)	
Model 1	1114.7005	(15)	
	Estimate	S.E.	P
Constant	-0.0525	0.0149	0.0031

RANDOM EFFECTS MODEL
WEIGHTED on Random Weights

	Deviance	(DF)	
Model 1	36.6213	(15)	
	Estimate	S.E.	P
Constant	-0.0559	0.0211	0.0185

NORTH AMERICA

	Deviance	(DF)	
Model 1	0.1483	(5)	
	Estimate	S.E.	P
Constant	-0.0405	0.0703	0.5893

WEIGHTED on DELTA Weights

	Deviance	(DF)	
Model 1	111.7051	(5)	
	Estimate	S.E.	P
Constant	-0.0835	0.0101	0.0004

RANDOM EFFECTS MODEL
WEIGHTED on Random Weights

	Deviance	(DF)	
Model 1	12.3193	(5)	
	Estimate	S.E.	P
Constant	-0.0866	0.0191	0.0062

EUROPE

	Deviance	(DF)	
Model 1	0.6462	(5)	
	Estimate	S.E.	P
Constant	-0.1940	0.1468	0.2435

FEMALES
NEVER SMOKERS OR NEVER AND LONG TERM EX SMOKERS
EXCLUDING THORNTON AS INCLUDED WITHIN HAMLING RESULTS

Fruit/Vegetable/Tea consumption in SDs between lifelong nonsmokers exposed or unexposed to ETS at home
Meta-Analysis of Differences, 08-SEP-06

FIXED- AND RANDOM-EFFECTS META-ANALYSES OF DATA FOR VEGETABLES

EUROPE

Difference in SDs (DELTA)
WEIGHTED on DELTA Weights

	Deviance	(DF)	
Model 1	146.6808	(5)	
	Estimate	S.E.	P
Constant	-0.0653	0.0535	0.2770

RANDOM EFFECTS MODEL
WEIGHTED on Random Weights

	Deviance	(DF)	
Model 1	10.5062	(5)	
	Estimate	S.E.	P
Constant	-0.0892	0.0596	0.1943

NORTH AMERICA AND EUROPE

	Deviance	(DF)	
Model 1	0.8652	(11)	
	Estimate	S.E.	P
Constant	-0.1173	0.0810	0.1754

WEIGHTED on DELTA Weights

	Deviance	(DF)	
Model 1	261.6496	(11)	
	Estimate	S.E.	P
Constant	-0.0827	0.0102	0.0000

RANDOM EFFECTS MODEL
WEIGHTED on Random Weights

	Deviance	(DF)	
Model 1	29.1865	(11)	
	Estimate	S.E.	P
Constant	-0.0813	0.0195	0.0015

ASIA

	Deviance	(DF)	
Model 1	0.1155	(3)	
	Estimate	S.E.	P
Constant	0.0669	0.0981	0.5445

WEIGHTED on DELTA Weights

	Deviance	(DF)	
Model 1	204.6070	(3)	
	Estimate	S.E.	P
Constant	0.0117	0.0252	0.6740

FEMALES
NEVER SMOKERS OR NEVER AND LONG TERM EX SMOKERS
EXCLUDING THORNTON AS INCLUDED WITHIN HAMLING RESULTS

APPENDIX 8

Fruit/Vegetable/Tea consumption in SDs between lifelong nonsmokers exposed or unexposed to ETS at home
Meta-Analysis of Differences, 08-SEP-06

FIXED- AND RANDOM-EFFECTS META-ANALYSES OF DATA FOR VEGETABLES

ASIA
RANDOM EFFECTS MODEL

Difference in SDs (DELTA)
WEIGHTED on Random Weights

	Deviance	(DF)	
Model 1	7.9570	(3)	
	Estimate	S.E.	P
Constant	0.0185	0.0471	0.7207

FEMALES
NEVER SMOKERS OR NEVER AND LONG TERM EX SMOKERS
EXCLUDING THORNTON AS INCLUDED WITHIN HAMLING RESULTS

APPENDIX 8

Fruit/Vegetable/Tea consumption in SDs between lifelong nonsmokers exposed or unexposed to ETS at home
Meta-Analysis of Differences, 08-SEP-06

FIXED- AND RANDOM-EFFECTS META-ANALYSES OF DATA FOR FRUIT

ALL STUDIES

Difference in SDs (DELTA)

	Deviance	(DF)	
Model 1	0.4089	(10)	
	Estimate	S.E.	P
Constant	-0.1382	0.0610	0.0468

WEIGHTED on DELTA Weights

	Deviance	(DF)	
Model 1	129.9031	(10)	
	Estimate	S.E.	P
Constant	-0.0812	0.0142	0.0002

RANDOM EFFECTS MODEL
WEIGHTED on Random Weights

	Deviance	(DF)	
Model 1	17.4645	(10)	
	Estimate	S.E.	P
Constant	-0.0733	0.0197	0.0040

NORTH AMERICA

	Deviance	(DF)	
Model 1	0.0001	(2)	
	Estimate	S.E.	P
Constant	-0.0826	0.0034	0.0017

WEIGHTED on DELTA Weights

	Deviance	(DF)	
Model 1	0.3662	(2)	
	Estimate	S.E.	P
Constant	-0.0859	0.0021	0.0006

RANDOM EFFECTS MODEL
WEIGHTED on Random Weights

	Deviance	(DF)	
Model 1	0.0584	(2)	
	Estimate	S.E.	P
Constant	-0.0862	0.0113	0.0169

EUROPE

	Deviance	(DF)	
Model 1	0.3693	(5)	
	Estimate	S.E.	P
Constant	-0.1484	0.1110	0.2388

FEMALES
NEVER SMOKERS OR NEVER AND LONG TERM EX SMOKERS
EXCLUDING THORNTON AS INCLUDED WITHIN HAMLING RESULTS

APPENDIX 8

Fruit/Vegetable/Tea consumption in SDs between lifelong nonsmokers exposed or unexposed to ETS at home
Meta-Analysis of Differences, 08-SEP-06

FIXED- AND RANDOM-EFFECTS META-ANALYSES OF DATA FOR FRUIT

EUROPE

Difference in SDs (DELTA)
WEIGHTED on DELTA Weights

	Deviance	(DF)	
Model 1	93.2811	(5)	
	Estimate	S.E.	P
Constant	-0.0503	0.0427	0.2912

RANDOM EFFECTS MODEL
WEIGHTED on Random Weights

	Deviance	(DF)	
Model 1	7.6951	(5)	
	Estimate	S.E.	P
Constant	-0.0581	0.0481	0.2808

NORTH AMERICA AND EUROPE

	Deviance	(DF)	
Model 1	0.3780	(8)	
	Estimate	S.E.	P
Constant	-0.1264	0.0725	0.1192

WEIGHTED on DELTA Weights

	Deviance	(DF)	
Model 1	104.0173	(8)	
	Estimate	S.E.	P
Constant	-0.0788	0.0160	0.0011

RANDOM EFFECTS MODEL
WEIGHTED on Random Weights

	Deviance	(DF)	
Model 1	11.7455	(8)	
	Estimate	S.E.	P
Constant	-0.0634	0.0249	0.0341

ASIA

	Deviance	(DF)	
Model 1	0.0240	(1)	
	Estimate	S.E.	P
Constant	-0.1913	0.1096	0.3310

WEIGHTED on DELTA Weights

	Deviance	(DF)	
Model 1	24.4494	(1)	
	Estimate	S.E.	P
Constant	-0.0904	0.0424	0.2795

FEMALES
NEVER SMOKERS OR NEVER AND LONG TERM EX SMOKERS
EXCLUDING THORNTON AS INCLUDED WITHIN HAMLING RESULTS

APPENDIX 8

Fruit/Vegetable/Tea consumption in SDs between lifelong nonsmokers exposed or unexposed to ETS at home
Meta-Analysis of Differences, 08-SEP-06

FIXED- AND RANDOM-EFFECTS META-ANALYSES OF DATA FOR FRUIT

ASIA
RANDOM EFFECTS MODEL

Difference in SDs (DELTA)
WEIGHTED on Random Weights

	Deviance	(DF)	
Model 1	1.0000	(1)	
	Estimate	S.E.	P
Constant	-0.1661	0.1066	0.3633

FEMALES
NEVER SMOKERS OR NEVER AND LONG TERM EX SMOKERS
EXCLUDING THORNTON AS INCLUDED WITHIN HAMLING RESULTS

APPENDIX 8

Fruit/Vegetable/Tea consumption in SDs between lifelong nonsmokers exposed or unexposed to ETS at home
Meta-Analysis of Differences, 08-SEP-06

FIXED- AND RANDOM-EFFECTS META-ANALYSES OF DATA FOR TEA

ALL STUDIES

Difference in SDs (DELTA)

	Deviance	(DF)	
Model 1	0.0084	(4)	
	Estimate	S.E.	P
Constant	-0.0724	0.0205	0.0241

WEIGHTED on DELTA Weights

	Deviance	(DF)	
Model 1	20.0740	(4)	
	Estimate	S.E.	P
Constant	-0.0671	0.0210	0.0330

RANDOM EFFECTS MODEL
WEIGHTED on Random Weights

	Deviance	(DF)	
Model 1	3.3026	(4)	
	Estimate	S.E.	P
Constant	-0.0655	0.0227	0.0446

NORTH AMERICA

	Deviance	(DF)	
Model 1	0.0000	(0)	
	Estimate	S.E.	P
Constant	-0.0194		

WEIGHTED on DELTA Weights

	Deviance	(DF)	
Model 1	-0.0000	(0)	
	Estimate	S.E.	P
Constant	-0.0194		

EUROPE

	Deviance	(DF)	
Model 1	0.0049	(3)	
	Estimate	S.E.	P
Constant	-0.0856	0.0201	0.0238

WEIGHTED on DELTA Weights

	Deviance	(DF)	
Model 1	10.0883	(3)	
	Estimate	S.E.	P
Constant	-0.0855	0.0202	0.0242

FEMALES
NEVER SMOKERS OR NEVER AND LONG TERM EX SMOKERS
EXCLUDING THORNTON AS INCLUDED WITHIN HAMLING RESULTS

APPENDIX 8

Fruit/Vegetable/Tea consumption in SDs between lifelong nonsmokers exposed or unexposed to ETS at home
Meta-Analysis of Differences, 08-SEP-06

FIXED- AND RANDOM-EFFECTS META-ANALYSES OF DATA FOR TEA

EUROPE
RANDOM EFFECTS MODEL

Difference in SDs (DELTA)
WEIGHTED on Random Weights

	Deviance	(DF)	
Model 1	1.8890	(3)	
	Estimate	S.E.	P
Constant	-0.0812	0.0262	0.0535

NORTH AMERICA AND EUROPE

	Deviance	(DF)	
Model 1	0.0084	(4)	
	Estimate	S.E.	P
Constant	-0.0724	0.0205	0.0241

WEIGHTED on DELTA Weights

	Deviance	(DF)	
Model 1	20.0740	(4)	
	Estimate	S.E.	P
Constant	-0.0671	0.0210	0.0330

RANDOM EFFECTS MODEL
WEIGHTED on Random Weights

	Deviance	(DF)	
Model 1	3.3026	(4)	
	Estimate	S.E.	P
Constant	-0.0655	0.0227	0.0446

FEMALES
NEVER SMOKERS OR NEVER AND LONG TERM EX SMOKERS
EXCLUDING THORNTON AS INCLUDED WITHIN HAMLING RESULTS

Appendix 9

Estimation of the standard deviation for years of education

1. Introduction

In our original work [1], we found seven studies which gave information on the SD for years of education among never smokers. As the results were quite consistent, we have not attempted to update this estimate based on more recent data. Nor, as the results were so similar by sex, have we attempted to re-estimate the SD specifically for females.

2. The studies

2.1 Cardenas *et al* [2]

The publication provides a breakdown of the number of never smokers by sex, ETS exposure and four levels of education. Based on the combined data by ETS exposure, and using assumed midpoints for each level of education, one can estimate the following:

SD (years) :	males	2.0189
	females	2.1207
	sexes combined	2.0795

2.2 Whitlock *et al* [3]

Based on the published percentage breakdown of never smokers by education, together with assumed midpoints in years for each level, one can estimate the following:

SD (years) :	sexes combined	2.7410

2.3 <u>HALS (UK Health and Lifestyle Survey)</u>

Data were available on the population distribution of education classified by 14 levels as: other, work related, degree, professional, nursing, teacher training, RSA etc., HNC/HND, ONC/OND, overseas, A Level, O Level, CSE grades 2-5 and none. Assigning relative year scores of, respectively, 5, 5, 8, 9, 7, 8, 5, 7, 5, 5, 5, 3, 3 and 1, gave:

SD (years) :	males	2.6454
	females	2.4790
	sexes combined	2.5528

2.4 <u>HALS 2 (UK Health and Lifestyle Survey Follow Up</u>

There were now 15 levels, the same as for HALS but, with the addition of apprenticeship, scored as 5. This gave:

SD (years) :	males	2.8063
	females	2.6198
	sexes combined	2.7213

2.5 <u>HSE 93 (Health Survey of England 1993)</u>

Here education levels and assigned relative scores were:
degree or equivalent (8), professional (9), A level or equivalent (5), O level or equivalent (3), CSE or equivalent (3), other (5) and no qualifications (1). This gave:

SD (years) :	males	2.7863
	females	2.7210
	sexes combined	2.7883

2.6 <u>HSE 94 (Health Survey of England 1994)</u>

Here education levels and assigned relative scores were:
degree or equivalent (8), higher below degree (7), A level or equivalent (5), GCSE or equivalent (3), foreign/other (5) and no qualifications (1). This gave:

SD (years) :	males	2.5179

	females	2.4014
	sexes combined	2.5033

2.7 HGPS (Hungarian General Practitioners Study)

Here education levels and assigned relative scores were: university (8), college (7), grammar school (5), vocational school (5) and elementary school (1). This gave:

SD (years) :	males	2.1349
	females	2.2689
	sexes combined	2.2698

3. Combined estimate

Averaging the seven values of SD for sexes combined gives a value of 2.522 years. The six values for females give a slightly lower mean of 2.435 years.

References

1. Fry JS, Lee PN. Revisiting the association between environmental tobacco smoke exposure and lung cancer risk. II. Adjustment for the potential confounding effects of fruit, vegetables, dietary fat and education. *Indoor Built Environ* 2001;**10**:20-39.

2. Cardenas VM, Thun MJ, Austin H, Lally CA, Clark WS, Greenberg RS, *et al*. Environmental tobacco smoke and lung cancer mortality in the American Cancer Society's Cancer Prevention Study II. *Cancer Causes Control* 1997;**8**:57-64.

3. Whitlock G, MacMahon S, Vander Hoorn S, Davis P, Jackson R, Norton R. Association of environmental tobacco smoke exposure with socioeconomic status in a population of 7725 New Zealanders. *Tob Control* 1998;**7**:276-80.

Appendix 10

Fuller details of the analyses relating ETS exposure at home to dietary fat consumption

APPENDIX 10

Dietary Fat consumption in SDs between lifelong nonsmokers exposed or unexposed to ETS at home
Meta-Analysis of Differences, 31-AUG-06

BASIC DATA USED IN META-ANALYSES - DIETARY FAT

Study Title	Continent	DELTA	St.Err. DELTA	WGT	WGTNS	WGTETS
Cardenas	US	-0.0307	0.0048	176320.0	71634.0	104686.0
Forastiere 2000	Europe	-0.0837	0.0471	1921.0	721.0	1200.0
Hamling (HALS2)	Europe	0.0782	0.0668	1265.0	974.0	291.0
Hamling (HSE93)	Europe	0.0660	0.0431	3664.0	3007.0	657.0
Hamling (HULS)	Europe	0.2551	0.0695	948.0	643.0	305.0
Hamling (HALS)	Europe	0.1898	0.0455	2351.0	1673.0	678.0
Koo (Hong Kong)	Asia	0.3532	0.1068	530.0	419.0	111.0
Koo (Sweden)	Europe	0.8087	0.2647	87.0	69.0	18.0
Koo (USA)	US	0.3578	0.1690	144.0	60.0	84.0
NHANES III	US	0.2337	0.0449	3171.0	2555.0	616.0
NHIS 2000	US	0.2218	0.0461	5063.0	4538.0	525.0
Reynolds 2004	US	0.0570	0.0097	42237.0	20950.0	21287.0

NOTES: DELTA SD DIFFERENCE IN DIETARY FAT CONSUMPTION ASSOCIATED WITH ETS EXPOSURE AT HOME
SE DELTA STANDARD ERROR OF DELTA
WGT TOTAL NUMBER OF FEMALES
WGTNS NUMBER OF FEMALES WITH NO ETS EXPOSURE
WGTETS NUMBER OF FEMALES WITH ETS EXPOSURE

FEMALES
NEVER SMOKERS OR NEVER AND LONG TERM EX SMOKERS
EXCLUDING BUTLER, EMMONS, LE MARCHAND AND THORNTON

APPENDIX 10

Dietary Fat consumption in SDs between lifelong nonsmokers exposed or unexposed to ETS at home
Meta-Analysis of Differences, 31-AUG-06

REGRESSION ESTIMATES, WEIGHTS AND OTHER RELEVANT DETAILS

Study Title	Country	DELTA	St.Err. DELTA	Z	WGT	RWGT	Expos	SMOKE
Cardenas	US	-0.0307	0.0048	-6.3313	176320.0	42531.0624	Fat	1
Forastiere 2000	Italy	-0.0837	0.0471	-1.7763	1921.0	450.3904	Meat	1
Hamling (HALS2)	UK	0.0782	0.0668	1.1705	1265.0	224.0585	Fried food	1
Hamling (HSE93)	UK	0.0660	0.0431	1.5326	3664.0	539.1919	Fried food	1
Hamling (HULS)	Hungary	0.2551	0.0695	3.6691	948.0	206.8724	Fried food	1
Hamling (HALS)	UK	0.1898	0.0455	4.1690	2351.0	482.4730	Fried food	1
Koo (Hong Kong)	Hong Kong	0.3532	0.1068	3.3087	530.0	87.7528	Fried food	1
Koo (Sweden)	Sweden	0.8087	0.2647	3.0555	87.0	14.2759	Fried food	1
Koo (USA)	US	0.3578	0.1690	2.1168	144.0	35.0000	Fat	1
NHANES III	US	0.2337	0.0449	5.2065	3171.0	496.3355	Fried food	1
NHIS 2000	US	0.2218	0.0461	4.8114	5063.0	470.5609	Fried food	1
Reynolds 2004	US	0.0570	0.0097	5.8570	42237.0	10558.5778	Meat	1

NOTES:
- DELTA — SD DIFFERENCE IN DIETARY FAT CONSUMPTION ASSOCIATED WITH ETS EXPOSURE AT HOME
- SE DELTA — STANDARD ERROR OF DELTA
- Z — RATIO OF DELTA TO ITS STANDARD ERROR (APPROXIMATE NORMAL STATISTIC)
- WGT — TOTAL NUMBER OF FEMALES FOR FIXED EFFECT MODELS
- RWGT — INVERSE OF THE VARIANCE OF DELTA FOR RANDOM EFFECTS MODELS
- SMOKE — 1 = NEVER SMOKERS, 2 = NEVER OR LONG-TERM EX-SMOKERS

FEMALES
NEVER SMOKERS OR NEVER AND LONG TERM EX SMOKERS
EXCLUDING BUTLER, EMMONS, LE MARCHAND AND THORNTON

APPENDIX 10

Dietary Fat consumption in SDs between lifelong nonsmokers exposed or unexposed to ETS at home
Meta-Analysis of Differences, 31-AUG-06

FIXED- AND RANDOM-EFFECTS META-ANALYSES OF DATA FOR DIETARY FAT

ALL STUDIES

Difference in SDs (DELTA)

	Deviance	(DF)	
Model 1	0.6096	(11)	
	Estimate	S.E.	P
Constant	0.2089	0.0680	0.0106

WEIGHTED on DELTA Weights

	Deviance	(DF)	
Model 1	1050.6533	(11)	
	Estimate	S.E.	P
Constant	0.0001	0.0200	0.9942

RANDOM EFFECTS MODEL
WEIGHTED on Random Weights

	Deviance	(DF)	
Model 1	22.3367	(11)	
	Estimate	S.E.	P
Constant	0.1310	0.0317	0.0017

NORTH AMERICA

	Deviance	(DF)	
Model 1	0.0950	(4)	
	Estimate	S.E.	P
Constant	0.1679	0.0689	0.0715

WEIGHTED on DELTA Weights

	Deviance	(DF)	
Model 1	738.8697	(4)	
	Estimate	S.E.	P
Constant	-0.0048	0.0285	0.8745

RANDOM EFFECTS MODEL
WEIGHTED on Random Weights

	Deviance	(DF)	
Model 1	8.4011	(4)	
	Estimate	S.E.	P
Constant	0.1188	0.0420	0.0476

EUROPE

	Deviance	(DF)	
Model 1	0.4848	(5)	
	Estimate	S.E.	P
Constant	0.2190	0.1271	0.1455

FEMALES
NEVER SMOKERS OR NEVER AND LONG TERM EX SMOKERS
EXCLUDING BUTLER, EMMONS, LE MARCHAND AND THORNTON

APPENDIX 10

Dietary Fat consumption in SDs between lifelong nonsmokers exposed or unexposed to ETS at home
Meta-Analysis of Differences, 31-AUG-06

FIXED- AND RANDOM-EFFECTS META-ANALYSES OF DATA FOR DIETARY FAT

EUROPE

Difference in SDs (DELTA)
WEIGHTED on DELTA Weights

	Deviance	(DF)	
Model 1	154.4125	(5)	
	Estimate	S.E.	P
Constant	0.0917	0.0549	0.1560

RANDOM EFFECTS MODEL
WEIGHTED on Random Weights

	Deviance	(DF)	
Model 1	8.6897	(5)	
	Estimate	S.E.	P
Constant	0.1302	0.0633	0.0946

NORTH AMERICA AND EUROPE

	Deviance	(DF)	
Model 1	0.5869	(10)	
	Estimate	S.E.	P
Constant	0.1958	0.0730	0.0231

WEIGHTED on DELTA Weights

	Deviance	(DF)	
Model 1	984.4441	(10)	
	Estimate	S.E.	P
Constant	-0.0006	0.0204	0.9756

RANDOM EFFECTS MODEL
WEIGHTED on Random Weights

	Deviance	(DF)	
Model 1	20.2451	(10)	
	Estimate	S.E.	P
Constant	0.1179	0.0319	0.0041

ASIA

	Deviance	(DF)	
Model 1	0.0000	(0)	
	Estimate	S.E.	P
Constant	0.3532		

WEIGHTED on DELTA Weights

	Deviance	(DF)	
Model 1	0.0000	(0)	
	Estimate	S.E.	P
Constant	0.3532		

FEMALES
NEVER SMOKERS OR NEVER AND LONG TERM EX SMOKERS
EXCLUDING BUTLER, EMMONS, LE MARCHAND AND THORNTON

APPENDIX 10

Dietary Fat consumption in SDs between lifelong nonsmokers exposed or unexposed to ETS at home
Meta-Analysis of Differences, 31-AUG-06

FIXED- AND RANDOM-EFFECTS META-ANALYSES OF DATA FOR DIETARY FAT

ASIA
RANDOM EFFECTS MODEL

Difference in SDs (DELTA)
WEIGHTED on Random Weights

	Deviance	(DF)	
Model 1	0.0000	(0)	
	Estimate	S.E.	P
Constant	0.3532	0.1068	

FEMALES
NEVER SMOKERS OR NEVER AND LONG TERM EX SMOKERS
EXCLUDING BUTLER, EMMONS, LE MARCHAND AND THORNTON

Appendix 11

Fuller details of the analyses relating ETS exposure at home to education

APPENDIX 11

Years of Education between lifelong nonsmokers exposed or unexposed to ETS at home
Meta-Analysis of Differences, 01-SEP-06

BASIC DATA USED IN META-ANALYSES - YEARS OF EDUCATION

Study Title	Continent	DELTA IN YRS	WGT	WGTNS	WGTETS
Cardenas	US	-0.3160	213154.0	71892.0	141262.0
Curtin 1999	Europe	-0.1920	779.0	698.0	81.0
Enstrom	US	-0.3300	25942.0	7339.0	18603.0
Forastiere 2000	Europe	-0.6422	1933.0	724.0	1209.0
Hamling (HALS2)	Europe	-0.3200	1265.0	974.0	291.0
Hamling (HSE93)	Europe	-0.5150	3664.0	3007.0	657.0
Hamling (HULS)	Europe	-0.4600	948.0	643.0	305.0
Hamling (HALS)	Europe	-0.3950	2351.0	1673.0	678.0
Koo (Hong Kong)	Asia	-0.5000	530.0	419.0	111.0
Koo (USA)	US	-0.4000	144.0	60.0	84.0
Matanoski	US	-0.5032	3791.0	1380.0	2411.0
NHANES III	US	-1.1239	3155.0	2543.0	612.0
NHIS 2000	US	-0.9940	5038.0	4515.0	523.0

NOTES: DELTA IN YRS = DIFFERENCE IN YEARS OF EDUCATION ASSOCIATED WITH ETS EXPOSURE AT HOME
WGT TOTAL NUMBER OF FEMALES
WGTNS NUMBER OF FEMALES WITH NO ETS EXPOSURE
WGTETS NUMBER OF FEMALES WITH ETS EXPOSURE

FEMALES
NEVER SMOKERS OR NEVER AND LONG TERM EX SMOKERS
EXCLUDE THORNTON AND BUTLER THROUGHOUT AS INCLUDED IN HAMLING AND NHANES III

APPENDIX 11

Years of Education between lifelong nonsmokers exposed or unexposed to ETS at home
Meta-Analysis of Differences, 01-SEP-06

REGRESSION ESTIMATES, WEIGHTS AND OTHER RELEVANT DETAILS

Study Title	Country	DELTA in YRS	St.Err. DELTA	Z	WGT	RWGT	SMOKE
Cardenas	US	-0.3160	0.0112	-28.3266	213154.0	8035.5295	1
Curtin 1999	Switzerland	-0.1920	0.2858	-0.6717	779.0	12.2407	1
Enstrom	US	-0.3300	0.0336	-9.8316	25942.0	887.6024	1
Forastiere 2000	Italy	-0.6422	0.1144	-5.6123	1933.0	76.3722	1
Hamling (HALS2)	UK	-0.3200	0.1627	-1.9671	1265.0	37.7888	1
Hamling (HSE93)	UK	-0.5150	0.1049	-4.9111	3664.0	90.9380	1
Hamling (HULS)	Hungary	-0.4600	0.1693	-2.7171	948.0	34.8903	1
Hamling (HALS)	UK	-0.3950	0.1109	-3.5632	2351.0	81.3720	1
Koo (Hong Kong)	Hong Kong	-0.5000	0.2599	-1.9235	530.0	14.8001	1
Koo (USA)	US	-0.4000	0.4116	-0.9718	144.0	5.9030	1
Matanoski	US	-0.5032	0.0822	-6.1221	3791.0	148.0214	1
NHANES III	US	-1.1239	0.1096	-10.2513	3155.0	83.1956	1
NHIS 2000	US	-0.9940	0.1125	-8.8377	5038.0	79.0503	1

NOTES: DELTA IN YRS = DIFFERENCE IN YEARS OF EDUCATION ASSOCIATED WITH ETS EXPOSURE AT HOME
SE DELTA STANDARD ERROR OF DELTA
Z RATIO OF DELTA TO ITS STANDARD ERROR (APPROXIMATE NORMAL STATISTIC)
WGT TOTAL NUMBER OF FEMALES FOR FIXED EFFECT MODELS
RWGT INVERSE OF THE VARIANCE OF DELTA FOR RANDOM EFFECTS MODELS
SMOKE 1 = NEVER SMOKERS, 2 = NEVER OR LONG-TERM EX-SMOKERS

FEMALES
NEVER SMOKERS OR NEVER AND LONG TERM EX SMOKERS
EXCLUDE THORNTON AND BUTLER THROUGHOUT AS INCLUDED IN HAMLING AND NHANES III

APPENDIX 11

Years of Education between lifelong nonsmokers exposed or unexposed to ETS at home
Meta-Analysis of Differences, 01-SEP-06

FIXED- AND RANDOM-EFFECTS META-ANALYSES OF DATA FOR YEARS OF EDUCATION

ALL STUDIES

Difference in Years (DELTA YR)

	Deviance	(DF)	
Model 1	0.8636	(12)	
	Estimate	S.E.	P
Constant	-0.5147	0.0744	0.0000

WEIGHTED on DELTA Weights

	Deviance	(DF)	
Model 1	4638.5472	(12)	
	Estimate	S.E.	P
Constant	-0.3493	0.0384	0.0000

RANDOM EFFECTS MODEL
WEIGHTED on Random Weights

	Deviance	(DF)	
Model 1	17.4962	(12)	
	Estimate	S.E.	P
Constant	-0.5337	0.0634	0.0000

NORTH AMERICA

	Deviance	(DF)	
Model 1	0.6319	(5)	
	Estimate	S.E.	P
Constant	-0.6112	0.1451	0.0084

WEIGHTED on DELTA Weights

	Deviance	(DF)	
Model 1	4316.2944	(5)	
	Estimate	S.E.	P
Constant	-0.3441	0.0586	0.0020

RANDOM EFFECTS MODEL
WEIGHTED on Random Weights

	Deviance	(DF)	
Model 1	12.1868	(5)	
	Estimate	S.E.	P
Constant	-0.6083	0.0946	0.0014

EUROPE

	Deviance	(DF)	
Model 1	0.1226	(5)	
	Estimate	S.E.	P
Constant	-0.4207	0.0639	0.0012

FEMALES
NEVER SMOKERS OR NEVER AND LONG TERM EX SMOKERS
EXCLUDE THORNTON AND BUTLER THROUGHOUT AS INCLUDED IN HAMLING AND NHANES III

APPENDIX 11

Years of Education between lifelong nonsmokers exposed or unexposed to ETS at home
Meta-Analysis of Differences, 01-SEP-06

FIXED- AND RANDOM-EFFECTS META-ANALYSES OF DATA FOR YEARS OF EDUCATION

EUROPE

Difference in Years (DELTA YR)
WEIGHTED on DELTA Weights

	Deviance	(DF)	
Model 1	165.9103	(5)	
	Estimate	S.E.	P
Constant	-0.4614	0.0551	0.0004

RANDOM EFFECTS MODEL
WEIGHTED on Random Weights

	Deviance	(DF)	
Model 1	4.6974	(5)	
	Estimate	S.E.	P
Constant	-0.4752	0.0548	0.0003

NORTH AMERICA AND EUROPE

	Deviance	(DF)	
Model 1	0.8633	(11)	
	Estimate	S.E.	P
Constant	-0.5159	0.0809	0.0001

WEIGHTED on DELTA Weights

	Deviance	(DF)	
Model 1	4626.4801	(11)	
	Estimate	S.E.	P
Constant	-0.3490	0.0401	0.0000

RANDOM EFFECTS MODEL
WEIGHTED on Random Weights

	Deviance	(DF)	
Model 1	17.2829	(11)	
	Estimate	S.E.	P
Constant	-0.5351	0.0651	0.0000

ASIA

	Deviance	(DF)	
Model 1	0.0000	(0)	
	Estimate	S.E.	P
Constant	-0.5000		

WEIGHTED on DELTA Weights

	Deviance	(DF)	
Model 1	0.0000	(0)	
	Estimate	S.E.	P
Constant	-0.5000		

FEMALES
NEVER SMOKERS OR NEVER AND LONG TERM EX SMOKERS
EXCLUDE THORNTON AND BUTLER THROUGHOUT AS INCLUDED IN HAMLING AND NHANES III

APPENDIX 11

Years of Education between lifelong nonsmokers exposed or unexposed to ETS at home
Meta-Analysis of Differences, 01-SEP-06

FIXED- AND RANDOM-EFFECTS META-ANALYSES OF DATA FOR YEARS OF EDUCATION

ASIA
RANDOM EFFECTS MODEL

Difference in Years (DELTA YR)
WEIGHTED on Random Weights

	Deviance	(DF)	
Model 1	0.0000	(0)	
	Estimate	S.E.	P
Constant	-0.5000	0.2599	

FEMALES
NEVER SMOKERS OR NEVER AND LONG TERM EX SMOKERS
EXCLUDE THORNTON AND BUTLER THROUGHOUT AS INCLUDED IN HAMLING AND NHANES III

Appendix 12

Estimation of intercorrelations within never smokers between fruit, vegetables, dietary fat and education

Published data on the extent of intercorrelations within never smokers between fruit, vegetables, dietary fat and education were not available in the literature. For the five studies HALS, HALS 2, HSE 93, HSE 94 and HULS referred to in Appendix 9 we have the data on computer. Education scores are as defined in Appendix C. The derivation of the variables used for fruit, vegetables and dietary fat are as given below. For this report we have added results from NHIS2000 and NHANES III and the possible confounder Tea.

Variable	Study	Derivation
Fruit	HALS	Answers for fresh fruit in summer, fresh fruit in winter and fruit juice, each coded 0 = never, 1 = less than once a week, 2 = once or twice a week, 3 = most days (3-6), 4 = once a day, 5 = more than once a day, were combined.
	HALS 2	As HALS
	HSE 93	Respondents were asked how often they usually ate fruit. Possible answers were more than once a day, once a day, 5-6 days a week, 3-4 days a week, 1-2 days a week, at least once a month, less than once a month or rarely/never
	HSE 94	Respondents were asked how often on average they ate fruit. Possible answers as HSE 93

Variable	Study	Derivation
	HULS	Answers for fresh fruit in summer, fresh fruit in winter and fruit juice, each coded 1 = never, 2 = more infrequently, 3 = monthly, 4 = weekly and 5 = several times per week, were combined.
	NHIS2000	Answers for frequency per week of eating fruit and drinking fruit juice were combined.
	NHANESIII	Answers for frequency per month of consuming Orange juice, etc, Other fruit juices, Citrus fruits, Melons, Peaches, nectarines and any other fruits were combined.
Vegetables	HALS	Answers for root vegetables (like carrots, turnips and parsnips), green vegetables and other cooked vegetables (including onions and mushrooms), each coded 0-5 as for fruit in HALS were combined.
	HALS 2	As HALS
	HSE 93	Respondents were asked how often they usually ate vegetables and salad. Possible answers as for fruit for HSE 93.
	HSE 94	Respondents were asked how often on average they ate vegetables or salad. Possible answers as for fruit for HSE 93.
	HULS	Answers for peas/beans and for cooked vegetables, coded 1-5 as for fruit in HULS were combined
	NHIS2000	Answers for frequency per week of eating salads and “other veg” (other than salads, potatoes, beans) were combined.
	NHANESIII	Answers for frequency per month of Carrots, Broccoli, Brussel sprouts/cauliflower, Spinach, greens, etc, Tossed salad, Cabbage, coleslaw, sauerkraut and Any other vegetables were combined.
Dietary fat	HALS	Answers for fried foods (other than chips), chips, eggs and sausages, each coded 0-5 as for fruit in HALS were combined
	HALS 2	As HALS

	HSE 93	Respondents were asked what type of cooking fat they usually used when frying food. Those replying that they did not eat fried food were compared with those who gave any other reply.
	HSE 94	As HSE 93
	HULS	Answers for fried potatoes, bacon, sausages, eggs, food fried in fat and food fried in vegetable oil, coded 1-5 as for fruit in HULS were combined.
	NHIS2000	Answers for frequency per week of eating bacon, fried potatoes and chips were combined.
	NHANESIII	Answers for frequency per month of eating bacon/sausage/processed meats and eggs were combined.
Tea	HALS	The answer for cups of tea drunk coded as: 0=none, 1=1 OR 2, 2=3 OR 4, 3=5 OR 6, 4= >6 was used.
	HALS 2	As HALS
	HSE 93	Respondents were asked whether they used sugar in their tea. Those replying that they did or did not use sugar in their tea were compared with those who answered “no tea”.
	HSE 94	As HSE 93
	HULS	The answer for tea drinking coded as: 1=never, 2=less often, 3=several times a week , 4=1-2 times a day, 5=3-5 times a day, 6=more than 5 times a day was used..
	NHIS2000	Nothing available on tea drinking
	NHANESIII	The answer to regular times drink tea a month was used.

Based on these definitions, the data available for never smokers gave Spearman rank correlations of:

	Sex	Correlation coefficients HALS	HALS 2	HSE 93	HSE 94	HULS	NHIS 2000	NHANES III
Fruit and vegetables	M	+0.2338	+0.2631	+0.2970	+0.3356	+0.1638	+0.3527	+0.3706
	F	+0.2324	+0.2146	+0.3584	+0.3901	+0.2774	+0.3365	+0.3860
	M+F	+0.2383	+0.2423	+0.3429	+0.3785	+0.2479	+0.3466	+0.3899
Fruit and dietary fat	M	-0.1997	-0.1890	-0.0831	-0.1171	+0.0111	-0.1449	-0.0449
	F	-0.1813	-0.2337	-0.0703	-0.0713	+0.0161	-0.1535	-0.0310
	M+F	-0.2162	-0.2428	-0.0826	-0.0927	+0.0040	-0.1624	-0.0618
Fruit and education	M	+0.1931	+0.1722	+0.0909	+0.0729	+0.1731	+0.0766	+0.0969
	F	+0.2720	+0.2199	+0.0845	+0.1119	+0.2012	+0.0510	+0.0594
	M+F	+0.2257	+0.1759	+0.0547	+0.0661	+0.1841	+0.0523	+0.0798
Vegetables and dietary fat	M	-0.1481	-0.0708	+0.0437	-0.0690	-0.0696	-0.0994	-0.0284
	F	-0.0435	-0.0976	-0.0223	-0.0406	-0.0104	-0.1051	-0.0572
	M+F	-0.0830	-0.1139	-0.0053	-0.0569	-0.0481	-0.1201	-0.0596
Vegetables and education	M	+0.0427	+0.0773	+0.1123	+0.1169	+0.1531	+0.1579	+0.1924
	F	+0.0680	+0.0244	+0.1156	+0.1640	+0.1744	+0.1787	+0.1873
	M+F	+0.0499	+0.0200	+0.0959	+0.1153	+0.1481	+0.1614	+0.1904
Dietary fat and education	M	-0.1437	-0.1634	-0.0249	+0.0018	-0.1388	-0.1339	-0.1496
	F	-0.0534	-0.0955	+0.0422	+0.0623	-0.0532	-0.0551	-0.1224
	M+F	-0.0329	-0.0707	+0.0334	+0.0562	-0.0321	-0.0682	-0.1379
Tea and Fruit	M	-0.0369	+0.0198	+0.0479	+0.0063	+0.1515		+0.0078
	F	-0.0819	-0.0987	+0.0021	+0.0327	+0.1063		-0.0050
	M+F	-0.0669	-0.0546	+0.0254	+0.0261	+0.1226		+0.0093
Tea and Vegetables	M	+0.0343	+0.0038	+0.0309	+0.0608	+0.1318		+0.1050
	F	+0.0469	+0.0269	+0.0368	+0.0032	+0.0392		+0.0861
	M+F	+0.0434	+0.0209	+0.0379	+0.0289	+0.0717		+0.0997
Tea and Dietary fat	M	+0.0615	+0.0542	-0.0109	+0.0502	+0.0118		+0.0368
	F	+0.0262	+0.0420	-0.0151	-0.0001	+0.0559		+0.0432
	M+F	+0.0282	+0.0360	-0.0158	+0.0157	+0.0224		+0.0297
Tea and Education	M	-0.1445	-0.0500	+0.0017	+0.0300	+0.0801		+0.0986
	F	-0.1727	-0.1186	-0.0732	-0.0674	+0.0519		+0.0672
	M+F	-0.1635	-0.1013	-0.0514	-0.0360	+0.0459		+0.0834

Averaging the estimates for the seven studies (six for tea) gives the following correlation matrices:

	Fruit	Vegetables	Dietary fat	Education	Tea
Sexes combined					
Fruit	1	+0.3122	-0.1221	+0.1198	+0.0103
Vegetables		1	-0.0696	+0.1116	+0.0504
Dietary fat			1	-0.0360	+0.0194
Education				1	-0.0372
Tea					1
Females					
Fruit	1	+0.3136	-0.1036	+0.1428	-0.0074
Vegetables		1	-0.0538	+0.1303	+0.0399
Dietary fat			1	-0.0393	+0.0254
Education				1	-0.0521
Tea					1

Appendix 13

Fuller details of the analyses relating lung cancer risk to the number of cigarettes smoked by the husband – adjusted for confounding

APPENDIX 13

ETS and Lung Cancer - Meta-Analysis of Dose Response Exposure (or nearest equivalent), 02-NOV-15

Female (Husband's smoking) - Number cigarettes smoked

BASIC DATA USED IN META-ANALYSES

CORRECTED FOR ALL CONFOUNDERS (FRUIT, VEG, FAT, EDUCATION)

Confounder Differences based on Random-effects Regression

Study title	Country	RR	RRL	RRU	CA1	CA0	CO1	CO0	NCigs
Akiba	Japan	1.2445	0.5935	2.4603	32.3061	13.8977	100.0036	53.5404	1.0000
Akiba	Japan	1.3667	0.6469	2.8791	24.8826	13.8977	70.1411	53.5404	2.1350
Akiba	Japan	1.7763	0.4821	6.8262	3.9868	13.8977	8.6465	53.5404	3.8390
Al-Zoughool	Canada	0.3781	0.1454	0.9500	5.8254	23.1997	114.7862	172.8264	1.8175
Asomaning	USA	0.8605	0.2868	2.5722	14.6969	5.6933	57.5722	19.1908	2.3157
Boffetta 2	7 countries	0.9258	0.4629	1.7590	24.7709	26.3647	53.4627	52.6801	1.8175
Boffetta	7 countries	0.9459	0.7284	1.2392	294.8059	119.5696	544.6561	208.9615	1.3380
Boffetta	7 countries	0.5119	0.3053	0.8352	24.5124	119.5696	83.6855	208.9615	2.5880
Boffetta	7 countries	1.1205	0.6940	1.8145	34.9477	119.5696	54.5068	208.9615	4.3060
Brenner	Canada	0.3669	0.2293	0.5778	52.0868	37.1284	509.8163	133.3216	1.8175
Brownson 1	USA	1.6368	0.3800	6.7227	3.7163	12.9813	6.1480	35.1516	2.3157
Brownson 2	USA	0.9258	0.7406	1.1110	252.8222	259.3830	710.6758	675.0201	2.3157
Buffler	USA	0.7396	0.3143	1.7565	31.1556	8.2177	157.5104	30.7264	2.3157
Butler	USA	1.8846	0.4478	7.9861	2.7079	5.8475	11312.3622	46036.4581	2.3157
Cardenas	USA	1.0817	0.4917	2.1635	9.8007	24.4347	13724.7269	37015.3350	1.0040
Cardenas	USA	1.1555	0.6740	2.1184	22.4840	24.4347	29476.3222	37015.3350	2.2670
Cardenas	USA	1.7682	0.9306	3.3503	15.1606	24.4347	12988.4812	37015.3350	4.3140
Chan	China	0.6911	0.3962	1.1979	32.0984	51.3674	65.5857	72.5338	1.8175
Choi	Korea	1.5212	0.8586	2.6784	46.7076	26.5178	85.9209	74.2033	1.8175
Correa	USA	1.9393	0.7589	4.9186	13.4489	8.1852	59.9862	70.8026	2.3157
De Waard	Netherlands	2.4134	0.7888	7.3716	18.1476	4.0628	119.7457	64.6974	1.8175
Du	China	0.6474	0.3132	1.3377	12.8183	29.1630	67.5830	99.5399	1.0000
Du	China	1.3456	0.7403	2.4457	28.6859	29.1630	72.7637	99.5399	2.6030
Enstrom	USA	0.8792	0.6173	1.2440	99.5426	45.1720	15160.4588	6048.9126	2.3157
EPIC Adulthood	Western Europe	0.8050	0.3163	2.0797	9.1566	8.2095	13824.9595	9978.3454	1.8175
Fang	China	1.7289	1.0452	2.8522	23.1266	106.5903	86.7806	691.5207	1.8175
Fontham	USA	1.2153	0.9798	1.5073	359.9461	188.3054	645.1049	410.1372	2.3157
Franco-Marina	Mexico	1.6789	0.8861	3.1900	21.0855	38.4105	39.8232	121.7972	1.8175
Gallegos	Mexico	7.6428	0.8120	71.9471	12.4466	0.8685	37.4502	19.9711	1.8175
Gao	China	1.2118	0.8084	1.8026	166.8487	49.3888	242.6102	87.0217	1.8175
Garfinkel 1	USA	1.2233	0.8284	1.8204	38.6886	68.7757	38183.9639	83033.4415	1.0040
Garfinkel 1	USA	0.9926	0.6858	1.4347	47.7308	68.7757	58057.4264	83033.4415	2.7520
Garfinkel 2	USA	0.8187	0.3900	1.7186	10.9472	44.8650	43.9941	147.6049	1.0040
Garfinkel 2	USA	1.0153	0.6021	1.7120	31.1601	44.8650	100.9717	147.6049	2.2670
Garfinkel 2	USA	1.7661	1.0055	3.1017	28.7183	44.8650	53.4991	147.6049	4.3140
GELAC study	Taiwan	1.2085	1.0133	1.4503	433.3120	553.0777	387.9471	598.4426	1.8175
Geng	China	1.3753	0.4814	3.9491	7.6110	15.0383	15.1355	41.1296	0.4850
Geng	China	1.8611	0.5726	6.0413	6.2132	15.0383	9.1308	41.1296	1.2730
Geng	China	2.4814	1.1180	5.5264	25.3040	15.0383	27.8895	41.1296	2.6030
Gorlova	USA	1.1196	0.6133	2.0445	64.7692	29.4836	65.8549	33.5632	2.3157
He	China	1.9353	0.2150	17.1461	4.7848	0.9525	325.1243	125.2529	1.8175
Hill (study 1)	New Zealand	0.9261	0.4538	1.8615	9.9833	33.8940	97100.6098	305305.5620	1.8175
Hill (study 2)	New Zealand	1.2818	0.7245	2.2385	14.7598	66.2900	66399.2973	382244.6030	1.8175
Hirayama	Japan	1.2898	0.8790	1.9012	134.7811	31.8596	61697.7438	18810.2083	0.8600
Hirayama	Japan	1.3849	0.8971	2.1426	55.4486	31.8596	23639.6065	18810.2083	2.6030
Hole	Scotland	1.2867	0.1188	14.1236	1.9716	1.0180	710.0530	471.7311	0.2080
Hole	Scotland	2.4050	0.2485	23.0556	2.7985	1.0180	539.2135	471.7311	2.4090
Humble 1	USA	1.7116	0.4659	6.6183	6.2089	7.6685	8.8324	18.6720	1.5820
Humble 1	USA	1.0772	0.2065	6.1851	2.5384	7.6685	5.7375	18.6720	3.3920
IARC: Kreuzer	Germany	0.7381	0.4613	1.1993	50.4570	47.3752	132.1228	91.5577	1.8175
ILCCO	International	1.1143	0.9843	1.2628	674.1443	642.6864	1936.2181	2056.8075	1.8175
Inoue	Japan	2.4961	0.2999	6.4145	6.9542	3.2640	11.5618	13.5454	1.0000
Inoue	Japan	2.8353	0.7708	14.0113	10.0664	3.2640	14.7340	13.5454	2.6030
Janerich	USA	0.6912	0.4332	1.1060	72.2145	70.4551	85.2073	57.4626	2.3157
Jee	Korea	1.9110	1.0511	3.7265	53.2411	11.6940	75964.3422	31885.8938	1.0000

APPENDIX 13

ETS and Lung Cancer - Meta-Analysis of Dose Response Exposure (or nearest equivalent), 02-NOV-15

Female (Husband's smoking) - Number cigarettes smoked

BASIC DATA USED IN META-ANALYSES

CORRECTED FOR ALL CONFOUNDERS (FRUIT, VEG, FAT, EDUCATION)

Confounder Differences based on Random-effects Regression

Study title	Country	RR	RRL	RRU	CA1	CA0	CO1	CO0	NCigs
Jee	Korea	1.3325	0.6218	2.9314	14.0793	11.6940	28810.7221	31885.8938	2.6030
Jiang	China	2.1540	1.0775	4.3071	46.1397	22.3122	33.5278	34.9242	1.8175
Johnson	Canada	1.1291	0.5834	2.1641	37.0982	13.1905	384.6107	154.4047	1.8175
Kabat 1	USA	0.7286	0.2306	2.2595	12.3346	11.2864	14.7632	9.8420	2.3157
Kabat 2	USA	0.7765	0.3977	1.5247	19.4487	27.2994	65.0841	70.9415	1.6540
Kabat 2	USA	0.9403	0.4347	2.0404	12.9858	27.2994	35.8864	70.9415	3.6380
Kalandidi	Greece	1.4817	0.7617	2.8822	33.3150	27.1036	37.8434	45.6170	1.3380
Kalandidi	Greece	1.6216	0.7569	3.4740	21.2715	27.1036	22.0782	45.6170	2.9020
Kalandidi	Greece	1.3398	0.4610	3.8942	7.5623	27.1036	9.4996	45.6170	5.3350
Kiyohara	Japan	0.9306	0.4315	2.0065	30.6501	18.0564	42.9740	23.5592	1.8175
Koo	China	2.2693	0.8960	5.7658	13.9994	20.4346	12.3757	40.9942	0.7080
Koo	China	1.6291	0.7584	3.5110	22.7910	20.4346	28.0655	40.9942	1.7670
Koo	China	1.0569	0.4085	2.6911	9.6675	20.4346	18.3504	40.9942	3.1830
Kurahashi	Japan	0.9872	0.4936	1.9744	11.6355	25.5372	46100.5282	99882.4769	1.0000
Kurahashi	Japan	1.3500	0.7990	2.2868	30.4653	25.5372	88262.7172	99882.4769	2.6030
Lagarde	Sweden	1.0670	0.7794	1.4660	81.3850	124.4428	285.3189	465.5203	1.8175
Lam T	China	2.1235	1.1105	4.0425	21.9002	87.4961	21.6819	183.9507	0.7080
Lam T	China	1.7327	1.1146	2.6881	54.3341	87.4961	65.9251	183.9507	1.7670
Lam T	China	1.8397	0.9510	3.5816	19.2153	87.4961	21.9591	183.9507	3.1830
Lam W	China	1.8821	1.0206	3.4833	35.8879	23.8383	63.7075	79.6455	1.8175
Layard	USA	0.5794	0.2193	1.5308	4.9321	25.6630	333.7028	1006.0621	0.8190
Layard	USA	0.5564	0.2481	1.2472	7.8190	25.6630	550.9362	1006.0621	2.6640
Lee	England	0.9259	0.3426	2.5093	17.3225	8.7320	36.6331	17.0985	1.8175
Lee C-H	Taiwan	1.7488	1.2064	2.5344	139.8914	60.7065	189.3708	143.7132	1.8175
Liang	China	1.3480	0.9429	1.9273	135.9199	87.9697	147.6092	128.7839	1.8175
Lim	Singapore	1.0417	0.8375	1.2958	192.8700	234.9654	604.5937	767.2917	1.8175
Lin	China	2.3492	1.5580	3.5411	97.4054	79.7760	72.1274	138.7715	1.8175
Liu Q	China	0.6766	0.2223	2.1264	6.0752	14.2963	16.7326	26.6411	1.0000
Liu Q	China	2.6542	1.0983	6.6814	23.1602	14.2963	16.2604	26.6411	2.6030
Liu Z	China	0.7120	0.2774	1.8124	33.9915	7.0534	133.7822	19.7653	1.8175
Lopez-Cima	Spain	0.9203	0.0019	472.5565	4.4400	0.1300	17.8800	0.5100	1.8175
Malats	7 Europe+Brazil	1.3973	0.7173	2.7108	34.8823	46.9569	23.5375	44.2744	1.8175
Masjedi	Iran	1.8745	0.9407	3.7349	20.3366	35.2603	28.3039	91.9876	1.8175
McGhee	China	1.2843	0.8748	1.8985	77.7328	78.6866	131.0764	170.4041	1.8175
Nishino	Japan	1.7389	0.6473	4.4439	9.6569	7.2427	22574.7158	29441.7074	1.8175
Ohno	Japan	0.9260	0.6204	1.3798	133.1635	54.1497	234.3878	88.2622	1.8175
Pershagen	Sweden	1.1143	0.6500	1.9500	34.7721	28.7573	138.8688	127.9726	1.8175
Rapiti	India	1.1140	0.4642	2.6922	12.2688	24.1237	18.6400	40.8307	1.8175
Ren	China	1.1140	0.9190	1.3553	629.7285	247.1442	784.9891	343.1922	1.8175
Rylander	Sweden	1.2731	0.5297	3.0666	7.7248	24.2485	41.6857	166.5886	1.8175
Schoenberg	USA	0.9997	0.6516	1.5328	65.8729	42.6241	283.3935	183.3283	2.3157
Schwartz	USA	1.0200	0.6676	1.5577	120.3787	68.4961	114.3430	66.3598	2.3157
Seki	Japan	1.2178	0.9203	1.5990	187.0033	83.9987	1085.8443	593.9890	1.8175
Shen	China	0.6372	0.2059	2.0291	10.4031	14.6297	12.0047	10.7566	0.4850
Shen	China	0.9964	0.3037	3.2076	11.7573	14.6297	8.6755	10.7566	1.2730
Shen	China	0.6289	0.2516	1.5813	31.6613	14.6297	37.0143	10.7566	2.6030
Shimizu	Japan	1.0011	0.5933	1.6871	49.4598	39.0906	89.5322	70.8413	1.8175
Sobue	Japan	1.0482	0.7236	1.5121	75.5276	61.2898	375.2953	319.2404	1.8175
Speize	USA	1.3927	0.2785	5.8492	27.2133	1.7651	199267.7570	17999.9996	2.3157
Stockwell	USA	1.4924	0.7462	2.7982	46.2689	20.2940	59.0480	38.6510	2.3157
Sun	China	1.0765	0.7424	1.5684	139.5003	89.5603	135.4456	93.6097	1.8175
Svensson	Sweden	1.2650	0.4930	3.2462	17.3624	7.2243	82.4503	43.3979	1.8175
Torres-Duran	Spain	0.6537	0.4235	1.0127	47.7852	88.9151	105.3666	128.1587	1.8175
Trichopoulos	Greece	0.5560	0.1198	2.5807	1.9983	25.0109	15.6698	109.0545	0.7080
Trichopoulos	Greece	2.3718	1.1985	4.6938	21.4020	25.0109	39.3454	109.0545	1.7670
Trichopoulos	Greece	3.6836	1.2183	11.1378	6.8442	25.0109	8.1014	109.0545	2.5880
Trichopoulos	Greece	1.6483	0.6156	4.4134	6.7756	25.0109	17.9239	109.0545	4.3060

APPENDIX 13

ETS and Lung Cancer - Meta-Analysis of Dose Response Exposure (or nearest equivalent), 02-NOV-15

Female (Husband's smoking) - Number cigarettes smoked

BASIC DATA USED IN META-ANALYSES

CORRECTED FOR ALL CONFOUNDERS (FRUIT, VEG, FAT, EDUCATION)

Confounder Differences based on Random-effects Regression

Study title	Country	RR	RRL	RRU	CA1	CA0	CO1	CO0	NCigs
Wang L	China	1.0025	0.5840	1.6546	123.0302	25.4928	250.2653	51.9849	1.8175
Wang S	China	2.3758	1.1832	4.7892	64.7972	15.4553	58.7229	33.2772	1.8175
Wang T	China	0.3430	0.1078	1.1367	4.1433	44.6388	13.0469	48.2112	0.4850
Wang T	China	1.2801	0.7017	2.3232	43.5895	44.6388	36.7766	48.2112	1.2730
Wang T	China	1.2558	0.6817	2.3053	40.4573	44.6388	34.7949	48.2112	2.6030
Wen	China	1.0244	0.6955	1.5132	66.5320	41.0532	40157.9157	25385.0005	1.8175
WHI-OS	USA	0.8130	0.4804	1.3766	25.1223	30.9005	42394.2679	42394.2680	2.3157
Wu	USA	1.1142	0.4643	3.0641	17.2537	10.3231	32.5009	21.6670	2.3157
Wu-Williams	China	0.6443	0.5523	0.8284	282.2162	358.6008	508.6544	416.4532	1.8175
Yang	USA	1.8726	1.0299	3.3988	66.4524	27.6907	54.8367	42.7897	2.3157
Yu	China	1.2708	0.6542	2.4710	109.5921	16.1126	145.2119	27.1308	1.8175
Zaridze	Russia	1.5995	1.0503	2.4282	65.3910	77.2268	87.5477	165.3792	0.7080
Zaridze	Russia	1.1971	0.7448	1.9330	38.7863	77.2268	69.3862	165.3792	2.2930
Zatloukal	Czech Republic	0.4416	0.1932	1.0028	6.5113	69.8279	140.8616	667.0534	1.8175
Zheng	China	2.3584	1.0184	5.4767	58.8146	7.1024	171.0207	48.7057	1.8175
Zhong	China	1.3856	0.8907	2.1773	97.2490	49.5870	112.1202	79.2127	0.7080
Zhong	China	0.8770	0.5847	1.3643	111.1948	49.5870	202.5346	79.2127	1.7670
Zhong	China	1.3363	0.6681	2.4817	23.1692	49.5870	27.6974	79.2127	3.1830

NOTES: RR,RL,RU RELATIVE RISKS AND LOWER AND UPPER CONFIDENCE INTERVALS

CA1,CA0 NUMBERS (OR PSEUDO-NUMBERS) OF EXPOSED AND UNEXPOSED CASES

CO1,CO0 NUMBERS (OR PSEUDO-NUMBERS) OF EXPOSED AND UNEXPOSED CONTROLS

NCIGS MIDPOINT OF NUMBER OF CIGARETTES SMOKED BY HUSBAND (IN UNITS OF 10)

Study title	Country	Beta	St.Err. Beta	Z	Weight	ETSse	FRU	VEG	FAT	EDU	TEA
Akiba	Japan	0.1373	0.1397	0.9828	51.2398	0.9896	0	0	0	0	0
Al-Zoughool	Canada	-0.5352	0.2634	-2.0319	14.4135	0.8916	0	0	0	1	0
Asomaning	USA	-0.0649	0.2417	-0.2685	17.1178	1.0091	0	0	0	0	0
Boffetta 2	7 countries	-0.0424	0.1874	-0.2263	28.4748	0.9130	0	0	0	0	0
Boffetta	7 countries	-0.0275	0.0533	-0.5159	352.0024	1.1768	0	0	0	0	0
Brenner	Canada	-0.5517	0.1297	-4.2537	59.4456	0.7374	0	0	0	0	0
Brownson 1	USA	0.2128	0.3165	0.6724	9.9828	0.8345	0	0	0	1	0
Brownson 2	USA	-0.0333	0.0447	-0.7450	500.4780	1.1579	0	0	0	0	0
Buffler	USA	-0.1303	0.1896	-0.6872	27.8178	0.8581	0	0	0	0	0
Butler	USA	0.2737	0.3174	0.8623	9.9263	0.9215	0	0	0	0	0
Cardenas	USA	0.1247	0.0733	1.7012	186.1196	1.4556	0	1	1	2	0
Chan	China	-0.2033	0.1553	-1.3091	41.4627	0.9109	0	0	0	0	0
Choi	Korea	0.2308	0.1597	1.4452	39.2094	0.9091	0	0	0	0	0
Correa	USA	0.2860	0.2059	1.3890	23.5878	1.1582	0	0	0	0	0
De Waard	Netherlands	0.4847	0.3137	1.5451	10.1618	0.8696	0	0	0	0	0
Du	China	0.1296	0.1167	1.1105	73.4274	1.0879	0	0	0	0	0
Enstrom	USA	-0.0556	0.0772	-0.7202	167.7897	1.0456	1	0	0	2	0
EPIC Adulthood	Western Europe	-0.1193	0.2644	-0.4512	14.3046	0.8968	1	1	1	2	0
Fang	China	0.3012	0.1409	2.1377	50.3707	0.5724	0	1	0	1	0
Fontham	USA	0.0842	0.0475	1.7726	443.2133	1.1293	1	1	0	2	0
Franco-Marina	Mexico	0.2851	0.1798	1.5857	30.9329	0.7856	0	0	0	0	0
Gallegos	Mexico	1.1190	0.6294	1.7779	2.5243	0.8730	0	0	0	0	0
Gao	China	0.1057	0.1126	0.9387	78.8721	0.8022	0	0	0	2	0
Garfinkel 1	USA	-0.0062	0.0684	-0.0906	213.7410	1.1963	0	0	0	0	0
Garfinkel 2	USA	0.1232	0.0647	1.9042	238.8864	1.5345	0	0	0	0	0

APPENDIX 13
ETS and Lung Cancer - Meta-Analysis of Dose Response Exposure (or nearest equivalent), 02-NOV-15
Female (Husband's smoking) - Number cigarettes smoked
BASIC DATA USED IN META-ANALYSES
CORRECTED FOR ALL CONFOUNDERS (FRUIT, VEG, FAT, EDUCATION)

Confounder Differences based on Random-effects Regression

Study title	Country	Beta	St.Err. Beta	Z	Weight	ETSse	FRU	VEG	FAT	EDU	TEA
GELAC study	Taiwan	0.1042	0.0503	2.0716	395.2429	0.8883	0	0	0	2	0
Geng	China	0.3361	0.1500	2.2407	44.4444	1.0478	0	0	0	0	0
Gorlova	USA	0.0488	0.1326	0.3680	56.8739	1.1005	0	0	0	1	0
He	China	0.3633	0.6146	0.5911	2.6474	0.8152	0	0	2	2	0
Hill (study 1)	New Zealand	-0.0422	0.1981	-0.2130	25.4819	0.7776	0	0	0	0	0
Hill (study 2)	New Zealand	0.1366	0.1583	0.8629	39.9060	0.6455	0	0	0	3	0
Hirayama	Japan	0.0885	0.0764	1.1584	171.3221	0.8998	0	0	0	0	0
Hole	Scotland	0.3163	0.3633	0.8706	7.5765	1.0530	0	0	0	0	0
Humble 1	USA	0.0769	0.2450	0.3139	16.6597	1.2885	0	0	0	0	0
IARC: Kreuzer	Germany	-0.1671	0.1341	-1.2461	55.6087	0.8957	0	0	0	0	0
ILCCO	International	0.0595	0.0350	1.7000	816.3265	0.9085	0	0	0	0	0
Inoue	Japan	0.3163	0.2648	1.1945	14.2615	1.1196	0	0	0	0	0
Janerich	USA	-0.1595	0.1033	-1.5440	93.7129	1.1397	0	0	0	0	0
Jee	Korea	0.0251	0.1468	0.1710	46.4032	0.9132	0	1	0	3	0
Jiang	China	0.4222	0.1945	2.1707	26.4339	0.9152	1	1	0	0	0
Johnson	Canada	0.0668	0.1840	0.3630	29.5369	0.8225	1	1	0	2	0
Kabat 1	USA	-0.1367	0.2514	-0.5438	15.8223	1.1579	0	0	0	0	0
Kabat 2	USA	-0.0289	0.1071	-0.2698	87.1808	1.3646	0	0	0	2	0
Kalandidi	Greece	0.0833	0.0906	0.9194	121.8270	1.5584	0	0	0	0	0
Kiyohara	Japan	-0.0396	0.2157	-0.1836	21.4931	0.8757	0	0	0	0	0
Koo	China	0.0299	0.1412	0.2118	50.1569	1.1884	0	0	0	2	0
Kurahashi	Japan	0.1207	0.1022	1.1810	95.7411	1.1771	0	0	0	0	0
Lagarde	Sweden	0.0357	0.0887	0.4025	127.1021	0.8828	0	0	0	3	0
Lam T	China	0.2311	0.0898	2.5735	124.0073	1.0055	0	0	0	0	0
Lam W	China	0.3479	0.1723	2.0192	33.6844	0.9063	0	0	0	0	0
Layard	USA	-0.2271	0.1543	-1.4718	42.0018	1.1466	0	0	0	0	0
Lee	England	-0.0423	0.2795	-0.1513	12.8008	0.8544	0	0	0	0	0
Lee C-H	Taiwan	0.3075	0.1042	2.9511	92.1010	0.9015	0	0	0	2	0
Liang	China	0.1643	0.1004	1.6365	99.2048	0.9083	0	0	0	0	0
Lim	Singapore	0.0225	0.0613	0.3670	266.1209	0.9027	0	0	0	0	0
Lin	China	0.4699	0.1152	4.0790	75.3520	0.8642	0	0	0	2	0
Liu Q	China	0.4022	0.1759	2.2865	32.3198	1.0561	0	0	0	2	0
Liu Z	China	-0.1869	0.2634	-0.7096	14.4135	0.6106	0	0	0	0	0
Lopez-Cima	Spain	-0.0039	1.7473	-0.0022	0.3275	0.3069	0	0	0	0	0
Malats	7 Europe+Brazil	0.1841	0.1866	0.9866	28.7195	0.8717	0	0	0	0	0
Masjedi	Iran	0.3457	0.1935	1.7866	26.7078	0.7742	0	0	0	0	0
McGhee	China	0.1377	0.1088	1.2656	84.4777	0.9025	0	0	0	2	0
Nishino	Japan	0.3044	0.2704	1.1257	13.6769	0.8950	1	1	1	0	0
Ohno	Japan	-0.0423	0.1122	-0.3770	79.4354	0.8114	0	0	0	0	0
Pershagen	Sweden	0.0595	0.1542	0.3859	42.0563	0.9097	0	0	0	0	0
Rapiti	India	0.0594	0.2467	0.2408	16.4309	0.8504	0	0	0	0	0
Ren	China	0.0594	0.0545	1.0899	336.6720	0.8365	0	0	0	0	0
Rylander	Sweden	0.1329	0.2465	0.5391	16.4576	0.7290	0	0	0	0	0
Schoenberg	USA	-0.0001	0.0942	-0.0011	112.6933	1.1321	0	1	0	2	0
Schwartz	USA	0.0085	0.0933	0.0911	114.8780	1.1194	0	0	0	0	0
Seki	Japan	0.1084	0.0775	1.3987	166.4932	0.8692	0	0	0	0	0
Shen	China	-0.1317	0.1572	-0.8378	40.4664	1.0903	0	0	0	0	0
Shimizu	Japan	0.0006	0.1467	0.0041	46.4665	0.9053	0	0	0	0	0
Sobue	Japan	0.0259	0.1035	0.2502	93.3511	0.9064	0	0	0	2	0
Speize	USA	0.1430	0.3354	0.4264	8.8894	0.6375	0	0	0	0	0
Stockwell	USA	0.1729	0.1456	1.1875	47.1712	1.1381	0	0	0	2	0
Sun	China	0.0406	0.1050	0.3867	90.7029	0.8954	0	0	0	2	0
Svensson	Sweden	0.1293	0.2646	0.4887	14.2830	0.8673	0	0	0	0	0
Torres-Duran	Spain	-0.2339	0.1224	-1.9109	66.7478	0.9064	0	0	0	0	0
Trichopoulos	Greece	0.2306	0.1063	2.1693	88.4980	1.3389	0	0	0	0	0
Wang L	China	0.0014	0.1462	0.0096	46.7849	0.6870	0	0	0	1	0
Wang S	China	0.4761	0.1962	2.4266	25.9778	0.8780	0	0	0	0	0

APPENDIX 13
ETS and Lung Cancer - Meta-Analysis of Dose Response Exposure (or nearest equivalent), 02-NOV-15
Female (Husband's smoking) - Number cigarettes smoked
BASIC DATA USED IN META-ANALYSES
CORRECTED FOR ALL CONFOUNDERS (FRUIT, VEG, FAT, EDUCATION)

Confounder Differences based on Random-effects Regression

Study title	Country	Beta	St.Err. Beta	Z	Weight	ETSse	FRU	VEG	FAT	EDU	TEA
Wang T	China	0.1247	0.1180	1.0568	71.8184	1.0379	0	0	0	0	0
Wen	China	0.0133	0.1091	0.1219	84.0138	0.8863	1	1	0	2	0
WHI-OS	USA	-0.0894	0.1160	-0.7707	74.3163	1.1579	0	0	0	0	0
Wu	USA	0.0467	0.2079	0.2246	23.1361	1.1449	0	0	0	0	0
Wu-Williams	China	-0.2418	0.0569	-4.2496	308.8698	0.9047	0	0	0	2	0
Yang	USA	0.2709	0.1315	2.0601	57.8294	1.1548	0	0	0	0	0
Yu	China	0.1319	0.1865	0.7072	28.7503	0.6640	1	1	0	2	0
Zaridze	Russia	0.0752	0.1061	0.7088	88.8320	0.8744	0	0	0	2	0
Zatloukal	Czech Republic	-0.4497	0.2312	-1.9451	18.7079	0.6900	0	0	0	2	0
Zheng	China	0.4721	0.2361	1.9996	17.9394	0.7567	0	0	0	0	0
Zhong	China	-0.0517	0.0880	-0.5875	129.1322	0.9343	1	0	0	1	0

```
NOTES: BETA      SLOPE OF LOG RR ON NCIGS

       SE BETA   STANDARD ERROR OF BETA

       Z         RATIO OF BETA TO ITS STANDARD ERROR (APPROXIMATE NORMAL STATISTIC)

       WEIGHT    INVERSE OF THE VARIANCE OF BETA

       ETSse     STANDARD ERROR OF ETS EXPOSURE OVER THE CONTROL GROUPS

       FRU = 1   DOSE-RESPONSE ANALYSIS ADJUSTED FOR FRUIT

       VEG = 1          "         "        "      " VEGETABLES

       FAT = 1          "         "        "      " FRUIT

       EDU = 1          "         "        "      " INCOME

           = 2          "         "        "      " EDUCATION

           = 3          "         "        "      " SOCIO-ECONOMIC STATUS

       TEA = 0   NO ADJUSTMENT (OR MATCHING) FOR TEA
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RANDOM-EFFECTS META-ANALYSES

Dose Response (Beta)
WEIGHTED on Beta
Weights

	Deviance	(DF)
Model 1	100.1628	(92)

	Estimate	S.E.	P	RR	95%CIl	95%CIu
Constant	0.0603	0.0174	+++	1.0622	1.0265	1.0991

SEPARATE RANDOM-EFFECTS META-ANALYSES BY REGION

NORTH AMERICA, EUROPE AND NEW ZEALAND

APPENDIX 13

ETS and Lung Cancer - Meta-Analysis of Dose Response Exposure (or nearest equivalent), 02-NOV-15

Female (Husband's smoking) - Number cigarettes smoked

CORRECTED FOR ALL CONFOUNDERS (FRUIT, VEG, FAT, EDUCATION)
SEPARATE RANDOM-EFFECTS META-ANALYSES BY REGION
Confounder Differences based on Random-effects Regression

Dose Response (Beta) WEIGHTED on Beta Weights

	Deviance	(DF)				
Model 1	52.3572	(48)				
	Estimate	**S.E.**	**P**	**RR**	**95%CIl**	**95%CIu**
Constant	0.0119	0.0232	N.S.	1.0120	0.9669	1.0591

ASIA

Dose Response (Beta) WEIGHTED on Beta Weights

	Deviance	(DF)				
Model 1	42.6111	(43)				
	Estimate	**S.E.**	**P**	**RR**	**95%CIl**	**95%CIu**
Constant	0.1074	0.0251	+++	1.1134	1.0599	1.1695

NORTH AMERICA

Dose Response (Beta) WEIGHTED on Beta Weights

	Deviance	(DF)				
Model 1	33.1519	(28)				
	Estimate	**S.E.**	**P**	**RR**	**95%CIl**	**95%CIu**
Constant	0.0059	0.0313	N.S.	1.0059	0.9460	1.0695

EUROPE AND NEW ZEALAND

Dose Response (Beta) WEIGHTED on Beta Weights

	Deviance	(DF)				
Model 1	18.9368	(19)				
	Estimate	**S.E.**	**P**	**RR**	**95%CIl**	**95%CIu**
Constant	0.0197	0.0332	N.S.	1.0199	0.9557	1.0884

CHINA AND HONG KONG

Dose Response (Beta) WEIGHTED on Beta Weights

	Deviance	(DF)				
Model 1	24.2339	(26)				
	Estimate	**S.E.**	**P**	**RR**	**95%CIl**	**95%CIu**
Constant	0.1191	0.0402	++	1.1265	1.0412	1.2188

REST OF ASIA

Dose Response (Beta) WEIGHTED on Beta Weights

	Deviance	(DF)				
Model 1	12.0573	(16)				
	Estimate	**S.E.**	**P**	**RR**	**95%CIl**	**95%CIu**
Constant	0.0902	0.0214	+++	1.0944	1.0495	1.1413

SEPARATE RANDOM-EFFECTS META-ANALYSES BY YEAR OF PUBLICATION

PUBLISHED IN 1980S

APPENDIX 13

ETS and Lung Cancer - Meta-Analysis of Dose Response Exposure (or nearest equivalent), 02-NOV-15

Female (Husband's smoking) - Number cigarettes smoked

CORRECTED FOR ALL CONFOUNDERS (FRUIT, VEG, FAT, EDUCATION)

SEPARATE RANDOM-EFFECTS META-ANALYSES BY YEAR OF PUBLICATION

Confounder Differences based on Random-effects Regression

Dose Response (Beta) WEIGHTED on Beta Weights

	Deviance	(DF)				
Model 1	22.1850	(25)				
	Estimate	**S.E.**	**P**	**RR**	**95%CIl**	**95%CIu**
Constant	0.1001	0.0254	+++	1.1053	1.0516	1.1616

PUBLISHED IN 1990S

Dose Response (Beta) WEIGHTED on Beta Weights

	Deviance	(DF)				
Model 1	26.8883	(26)				
	Estimate	**S.E.**	**P**	**RR**	**95%CIl**	**95%CIu**
Constant	0.0251	0.0299	N.S.	1.0254	0.9671	1.0873

PUBLISHED IN 2000S

Dose Response (Beta) WEIGHTED on Beta Weights

	Deviance	(DF)				
Model 1	24.7997	(25)				
	Estimate	**S.E.**	**P**	**RR**	**95%CIl**	**95%CIu**
Constant	0.0820	0.0316	+	1.0854	1.0203	1.1547

PUBLISHED IN 2010S

Dose Response (Beta) WEIGHTED on Beta Weights

	Deviance	(DF)				
Model 1	25.0319	(13)				
	Estimate	**S.E.**	**P**	**RR**	**95%CIl**	**95%CIu**
Constant	0.0312	0.0521	N.S.	1.0317	0.9315	1.1427

SEPARATE RANDOM-EFFECTS META-ANALYSES BY NUMBER OF LUNG CANCER CASES

<100 CASES

Dose Response (Beta) WEIGHTED on Beta Weights

	Deviance	(DF)				
Model 1	48.5972	(48)				
	Estimate	**S.E.**	**P**	**RR**	**95%CIl**	**95%CIu**
Constant	0.0958	0.0307	++	1.1005	1.0362	1.1688

100-199 CASES

Dose Response (Beta) WEIGHTED on Beta Weights

	Deviance	(DF)				
Model 1	24.2359	(21)				
	Estimate	**S.E.**	**P**	**RR**	**95%CIl**	**95%CIu**
Constant	0.0248	0.0351	N.S.	1.0251	0.9569	1.0982

200-399 CASES

APPENDIX 13

ETS and Lung Cancer - Meta-Analysis of Dose Response Exposure (or nearest equivalent), 02-NOV-15

Female (Husband's smoking) - Number cigarettes smoked

CORRECTED FOR ALL CONFOUNDERS (FRUIT, VEG, FAT, EDUCATION)

SEPARATE RANDOM-EFFECTS META-ANALYSES BY NUMBER OF LUNG CANCER CASES

Confounder Differences based on Random-effects Regression

Dose Response (Beta)
WEIGHTED on Beta
Weights

	Deviance	(DF)				
Model 1	12.7461	(12)				
	Estimate	**S.E.**	**P**	**RR**	**95%CIl**	**95%CIu**
Constant	0.1257	0.0356	++	1.1340	1.0575	1.2159

400+ CASES

Dose Response (Beta)
WEIGHTED on Beta
Weights

	Deviance	(DF)				
Model 1	8.6045	(8)				
	Estimate	**S.E.**	**P**	**RR**	**95%CIl**	**95%CIu**
Constant	0.0018	0.0337	N.S.	1.0018	0.9378	1.0701

SEPARATE RANDOM-EFFECTS META-ANALYSES BY DOSE-RESPONSE OR NOT

RESULTS FOR DOSE-RESPONSE

Dose Response (Beta)
WEIGHTED on Beta
Weights

	Deviance	(DF)				
Model 1	22.9394	(23)				
	Estimate	**S.E.**	**P**	**RR**	**95%CIl**	**95%CIu**
Constant	0.0789	0.0240	++	1.0821	1.0323	1.1343

NO RESULTS FOR DOSE-RESPONSE

Dose Response (Beta)
WEIGHTED on Beta
Weights

	Deviance	(DF)				
Model 1	75.8793	(68)				
	Estimate	**S.E.**	**P**	**RR**	**95%CIl**	**95%CIu**
Constant	0.0511	0.0224	+	1.0525	1.0072	1.0998

SEPARATE RANDOM-EFFECTS META-ANALYSES BY AGE ADJUSTMENT OR NOT

ADJUSTED (OR MATCHED) FOR AGE

Dose Response (Beta)
WEIGHTED on Beta
Weights

	Deviance	(DF)				
Model 1	78.6208	(74)				
	Estimate	**S.E.**	**P**	**RR**	**95%CIl**	**95%CIu**
Constant	0.0433	0.0183	+	1.0442	1.0075	1.0823

NOT ADJUSTED (OR MATCHED) FOR AGE

Dose Response (Beta)
WEIGHTED on Beta
Weights

	Deviance	(DF)				
Model 1	17.9777	(17)				
	Estimate	**S.E.**	**P**	**RR**	**95%CIl**	**95%CIu**
Constant	0.1552	0.0489	++	1.1678	1.0610	1.2854

APPENDIX 13

ETS and Lung Cancer - Meta-Analysis of Dose Response Exposure (or nearest equivalent), 02-NOV-15

Female (Husband's smoking) - Number cigarettes smoked

CORRECTED FOR ALL CONFOUNDERS (FRUIT, VEG, FAT, EDUCATION)
SEPARATE RANDOM-EFFECTS META-ANALYSES BY STUDY TYPE
Confounder Differences based on Random-effects Regression

CASE-CONTROL STUDIES

Dose Response (Beta)
WEIGHTED on Beta Weights

	Deviance	(DF)				
Model 1	86.8051	(76)				
	Estimate	**S.E.**	**P**	**RR**	**95%Cll**	**95%Clu**
Constant	0.0640	0.0202	++	1.0661	1.0247	1.1091

PROSPECTIVE STUDIES

Dose Response (Beta)
WEIGHTED on Beta Weights

	Deviance	(DF)				
Model 1	9.0154	(15)				
	Estimate	**S.E.**	**P**	**RR**	**95%Cll**	**95%Clu**
Constant	0.0423	0.0293	N.S.	1.0432	0.9849	1.1049

APPENDIX 13

ETS and Lung Cancer - Meta-Analysis of Dose Response Exposure (or nearest equivalent), 02-NOV-15

Female (Husband's smoking) - Number cigarettes smoked

BASIC DATA USED IN META-ANALYSES

CORRECTED FOR ALL CONFOUNDERS (FRUIT, VEG, FAT, EDUCATION)

Confounder Differences based on Unweighted Regression

Study title	Country	RR	RRL	RRU	CA1	CA0	CO1	CO0	NCigs
Akiba	Japan	1.2319	0.5875	2.4353	32.0215	13.9966	98.8294	53.2146	1.0000
Akiba	Japan	1.3371	0.6329	2.8169	24.6482	13.9966	70.0837	53.2146	2.1350
Akiba	Japan	1.7079	0.4636	6.5633	3.9502	13.9966	8.7934	53.2146	3.8390
Al-Zoughool	Canada	0.3675	0.1414	0.9235	5.7867	23.7058	116.6341	175.6089	1.8175
Asomaning	USA	0.8438	0.2813	2.5222	14.5188	5.7357	57.1888	19.0631	2.3157
Boffetta 2	7 countries	0.9079	0.4540	1.7251	24.5344	26.6261	53.4866	52.7034	1.8175
Boffetta	7 countries	0.9325	0.7180	1.2216	291.9057	120.6556	539.4406	207.9265	1.3380
Boffetta	7 countries	0.4980	0.2970	0.8125	24.4136	120.6556	84.4892	207.9265	2.5880
Boffetta	7 countries	1.0702	0.6629	1.7331	34.4810	120.6556	55.5232	207.9265	4.3060
Brenner	Canada	0.3583	0.2239	0.5643	51.4102	37.5223	508.1970	132.8993	1.8175
Brownson 1	USA	1.6073	0.3731	6.6014	3.6880	13.1193	6.1885	35.3829	2.3157
Brownson 2	USA	0.9080	0.7264	1.0896	250.3949	261.9390	710.8539	675.1895	2.3157
Buffler	USA	0.7250	0.3081	1.7219	30.7344	8.2720	156.0286	30.4465	2.3157
Butler	USA	1.8551	0.4408	7.8614	2.6945	5.9109	11378.5033	46305.6239	2.3157
Cardenas	USA	1.0808	0.4913	2.1615	9.7956	24.4663	13710.1547	37009.0067	1.0040
Cardenas	USA	1.1531	0.6727	2.1140	22.4573	24.4663	29459.3599	37009.0067	2.2670
Cardenas	USA	1.7612	0.9270	3.3371	15.1485	24.4663	13010.4092	37009.0067	4.3140
Chan	China	0.6763	0.3877	1.1722	31.7760	51.9629	65.7975	72.7655	1.8175
Choi	Korea	1.4974	0.8452	2.6365	46.3017	26.7043	85.6628	73.9803	1.8175
Correa	USA	1.9125	0.7484	4.8506	13.3395	8.2323	59.8137	70.5985	2.3157
De Waard	Netherlands	2.3826	0.7788	7.2777	17.9715	4.0747	118.8676	64.2135	1.8175
Du	China	0.6415	0.3104	1.3256	12.7768	29.4462	67.2710	99.4621	1.0000
Du	China	1.3143	0.7231	2.3887	28.3921	29.4462	72.9705	99.4621	2.6030
Enstrom	USA	0.8707	0.6113	1.2319	98.8728	45.3096	15104.7020	6026.6660	2.3157
EPIC Adulthood	Western Europe	0.8079	0.3174	2.0870	9.1737	8.1959	13827.6589	9980.2937	1.8175
Fang	China	1.6999	1.0276	2.8044	23.0079	107.8524	87.5455	697.6159	1.8175
Fontham	USA	1.2042	0.9709	1.4936	358.1363	189.0750	643.8831	409.3588	2.3157
Franco-Marina	Mexico	1.6525	0.8721	3.1397	20.9371	38.7509	39.9519	122.1906	1.8175
Gallegos	Mexico	7.6059	0.8081	71.6002	12.3890	0.8690	37.2406	19.8689	1.8175
Gao	China	1.1905	0.7942	1.7711	165.1832	49.7671	241.1659	86.5037	1.8175
Garfinkel 1	USA	1.2118	0.8206	1.8033	38.4333	69.5965	37884.0966	83128.8648	1.0040
Garfinkel 1	USA	0.9672	0.6682	1.3980	47.3436	69.5965	58467.9686	83128.8648	2.7520
Garfinkel 2	USA	0.8136	0.3876	1.7079	10.9351	45.3065	43.7756	147.5620	1.0040
Garfinkel 2	USA	1.0011	0.5938	1.6882	30.9723	45.3065	100.7610	147.5620	2.2670
Garfinkel 2	USA	1.7195	0.9790	3.0200	28.4386	45.3065	53.8661	147.5620	4.3140
GELAC study	Taiwan	1.1876	0.9957	1.4251	429.5290	557.9300	388.3676	599.0914	1.8175
Geng	China	1.3704	0.4796	3.9351	7.6113	15.1506	15.0373	41.0202	0.4850
Geng	China	1.8437	0.5673	5.9850	6.2052	15.1506	9.1124	41.0202	1.2730
Geng	China	2.4344	1.0968	5.4217	25.0537	15.1506	27.8640	41.0202	2.6030
Gorlova	USA	1.0978	0.6014	2.0047	64.1258	29.7697	65.6052	33.4361	2.3157
He	China	1.9068	0.2119	16.8937	4.7255	0.9548	321.8918	124.0108	1.8175
Hill (study 1)	New Zealand	0.9085	0.4452	1.8261	9.9402	34.4009	98126.9101	308532.4770	1.8175
Hill (study 2)	New Zealand	1.2592	0.7117	2.1991	14.7126	67.2600	67155.2890	386596.6640	1.8175
Hirayama	Japan	1.2756	0.8693	1.8803	132.6188	31.9820	60485.3131	18606.3559	0.8600
Hirayama	Japan	1.3393	0.8676	2.0721	55.0817	31.9820	23927.2078	18606.3559	2.6030
Hole	Scotland	1.2842	0.1185	14.0971	1.9594	1.0213	700.6571	469.0125	0.2080
Hole	Scotland	2.3531	0.2431	22.5586	2.7741	1.0213	541.4089	469.0125	2.4090
Humble 1	USA	1.6911	0.4604	6.5389	6.1690	7.7504	8.8006	18.6978	1.5820
Humble 1	USA	1.0497	0.2012	6.0270	2.5191	7.7504	5.7895	18.6978	3.3920
IARC: Kreuzer	Germany	0.7227	0.4517	1.1743	49.9242	47.8713	132.0740	91.5205	1.8175
ILCCO	International	1.0943	0.9667	1.2402	668.0227	648.4615	1935.7082	2056.2662	1.8175
Inoue	Japan	2.4794	0.2979	6.3715	6.9277	3.2815	11.4707	13.4718	1.0000
Inoue	Japan	2.7861	0.7574	13.7683	9.9655	3.2815	14.6841	13.4718	2.6030
Janerich	USA	0.6765	0.4239	1.0824	71.4397	71.2188	85.1997	57.4594	2.3157
Jee	Korea	1.8900	1.0395	3.6854	52.4080	11.7349	74535.1073	31542.4492	1.0000

APPENDIX 13
ETS and Lung Cancer - Meta-Analysis of Dose Response Exposure (or nearest equivalent), 02-NOV-15
Female (Husband's smoking) - Number cigarettes smoked
BASIC DATA USED IN META-ANALYSES
CORRECTED FOR ALL CONFOUNDERS (FRUIT, VEG, FAT, EDUCATION)

Confounder Differences based on Unweighted Regression

Study title	Country	RR	RRL	RRU	CA1	CA0	CO1	CO0	NCigs
Jee	Korea	1.2945	0.6041	2.8480	14.0204	11.7349	29111.4232	31542.4492	2.6030
Jiang	China	2.1396	1.0703	4.2783	45.9815	22.3857	33.4861	34.8810	1.8175
Johnson	Canada	1.1185	0.5779	2.1438	36.8555	13.2280	383.0457	153.7734	1.8175
Kabat 1	USA	0.7133	0.2257	2.2120	12.2042	11.4069	14.7570	9.8379	2.3157
Kabat 2	USA	0.7658	0.3922	1.5036	19.3066	27.6230	64.8107	71.0122	1.6540
Kabat 2	USA	0.9120	0.4216	1.9789	12.8638	27.6230	36.2604	71.0122	3.6380
Kalandidi	Greece	1.4677	0.7545	2.8550	33.1549	27.3773	37.5775	45.5403	1.3380
Kalandidi	Greece	1.5885	0.7415	3.4032	21.1035	27.3773	22.0988	45.5403	2.9020
Kalandidi	Greece	1.2901	0.4439	3.7495	7.4655	27.3773	9.6262	45.5403	5.3350
Kiyohara	Japan	0.9128	0.4232	1.9681	30.3445	18.2254	42.8536	23.4931	1.8175
Koo	China	2.2547	0.8903	5.7287	13.9928	20.6639	12.3014	40.9590	0.7080
Koo	China	1.6030	0.7462	3.4548	22.6007	20.6639	27.9457	40.9590	1.7670
Koo	China	1.0266	0.3968	2.6140	9.5795	20.6639	18.4957	40.9590	3.1830
Kurahashi	Japan	0.9797	0.4898	1.9593	11.5927	25.7458	45823.3524	99696.5110	1.0000
Kurahashi	Japan	1.3234	0.7832	2.2417	30.1736	25.7458	88290.0534	99696.5110	2.6030
Lagarde	Sweden	1.0476	0.7652	1.4393	80.7295	125.7321	286.1976	466.9540	1.8175
Lam T	China	2.1111	1.1040	4.0189	21.8945	88.3192	21.6337	184.2308	0.7080
Lam T	China	1.7075	1.0984	2.6490	53.9829	88.3192	65.9468	184.2308	1.7670
Lam T	China	1.7918	0.9262	3.4883	19.0280	88.3192	22.1524	184.2308	3.1830
Lam W	China	1.8556	1.0063	3.4343	35.6166	23.9923	63.5828	79.4785	1.8175
Layard	USA	0.5736	0.2171	1.5155	4.9141	26.1559	333.1671	1017.2345	0.8190
Layard	USA	0.5385	0.2402	1.2072	7.7717	26.1559	561.2447	1017.2345	2.6640
Lee	England	0.9082	0.3360	2.4613	17.1380	8.8076	36.4793	17.0267	1.8175
Lee C-H	Taiwan	1.7232	1.1887	2.4972	138.7314	61.1004	188.6513	143.1723	1.8175
Liang	China	1.3258	0.9273	1.8955	134.7658	88.6848	147.3204	128.5292	1.8175
Lim	Singapore	1.0226	0.8221	1.2720	191.1832	237.2758	605.4748	768.4100	1.8175
Lin	China	2.3186	1.5377	3.4951	96.7685	80.2971	72.0803	138.6808	1.8175
Liu Q	China	0.6722	0.2209	2.1127	6.0686	14.3969	16.6691	26.5824	1.0000
Liu Q	China	2.6098	1.0799	6.5694	22.9670	14.3969	16.2491	26.5824	2.6030
Liu Z	China	0.6981	0.2720	1.7769	33.5726	7.0994	132.6204	19.5769	1.8175
Lopez-Cima	Spain	0.9034	0.0018	463.8697	4.0861	0.1303	16.4938	0.4751	1.8175
Malats	7 Europe+Brazil	1.3744	0.7055	2.6663	34.5893	47.3391	23.5632	44.3227	1.8175
Masjedi	Iran	1.8459	0.9263	3.6780	20.1917	35.5511	28.3782	92.2290	1.8175
McGhee	China	1.2626	0.8600	1.8664	77.0808	79.3574	131.0967	170.4110	1.8175
Nishino	Japan	1.7428	0.6487	4.4539	9.6689	7.2360	22580.3437	29451.2300	1.8175
Ohno	Japan	0.9084	0.6086	1.3535	131.7553	54.6185	233.2154	87.8218	1.8175
Pershagen	Sweden	1.0943	0.6384	1.9151	34.4421	29.0037	138.6860	127.8041	1.8175
Rapiti	India	1.0940	0.4558	2.6439	12.1667	24.3566	18.7097	40.9770	1.8175
Ren	China	1.0940	0.9025	1.3310	623.6700	249.2599	781.4232	341.6555	1.8175
Rylander	Sweden	1.2509	0.5205	3.0132	7.6819	24.5410	42.0108	167.8887	1.8175
Schoenberg	USA	0.9830	0.6406	1.5071	65.2460	42.9386	282.5774	182.8004	2.3157
Schwartz	USA	1.0010	0.6552	1.5289	119.2632	69.1432	114.0605	66.1961	2.3157
Seki	Japan	1.1967	0.9044	1.5713	184.9258	84.5313	1079.6542	590.6028	1.8175
Shen	China	0.6338	0.2048	2.0185	10.4266	14.8139	11.9012	10.7172	0.4850
Shen	China	0.9827	0.2995	3.1635	11.7434	14.8139	8.6449	10.7172	1.2730
Shen	China	0.6114	0.2446	1.5372	31.2151	14.8139	36.9367	10.7172	2.6030
Shimizu	Japan	0.9824	0.5822	1.6556	48.9778	39.4504	89.4063	70.7481	1.8175
Sobue	Japan	1.0290	0.7103	1.4843	74.7850	61.8217	374.7180	318.7490	1.8175
Speize	USA	1.3681	0.2736	5.7459	26.7333	1.7671	199042.3290	17999.9999	2.3157
Stockwell	USA	1.4687	0.7344	2.7539	45.8663	20.4412	58.8212	38.5025	2.3157
Sun	China	1.0570	0.7289	1.5399	138.2260	90.3815	135.1828	93.4259	1.8175
Svensson	Sweden	1.2434	0.4846	3.1907	17.1712	7.2690	81.9598	43.1402	1.8175
Torres-Duran	Spain	0.6394	0.4143	0.9907	47.3098	89.9918	105.8300	128.7224	1.8175
Trichopoulos	Greece	0.5536	0.1193	2.5694	1.9980	25.2287	15.6037	109.0797	0.7080
Trichopoulos	Greece	2.3461	1.1855	4.6430	21.2811	25.2287	39.2191	109.0797	1.7670
Trichopoulos	Greece	3.6253	1.1990	10.9617	6.8119	25.2287	8.1241	109.0797	2.5880
Trichopoulos	Greece	1.6051	0.5994	4.2978	6.7308	25.2287	18.1304	109.0797	4.3060

APPENDIX 13

ETS and Lung Cancer - Meta-Analysis of Dose Response Exposure (or nearest equivalent), 02-NOV-15

Female (Husband's smoking) - Number cigarettes smoked

BASIC DATA USED IN META-ANALYSES

CORRECTED FOR ALL CONFOUNDERS (FRUIT, VEG, FAT, EDUCATION)

Confounder Differences based on Unweighted Regression

Study title	Country	RR	RRL	RRU	CA1	CA0	CO1	CO0	NCigs
Wang L	China	0.9823	0.5722	1.6213	121.5182	25.6949	248.0620	51.5245	1.8175
Wang S	China	2.3456	1.1682	4.7283	64.3204	15.5387	58.4360	33.1129	1.8175
Wang T	China	0.3413	0.1073	1.1313	4.1476	45.1031	12.9702	48.1451	0.4850
Wang T	China	1.2641	0.6929	2.2942	43.3947	45.1031	36.6430	48.1451	1.2730
Wang T	China	1.2240	0.6644	2.2468	40.0045	45.1031	34.8891	48.1451	2.6030
Wen	China	1.0145	0.6887	1.4984	65.7569	41.3547	40209.7119	25653.8566	1.8175
WHI-OS	USA	0.7966	0.4707	1.3487	24.8946	31.2522	42488.1071	42488.1086	2.3157
Wu	USA	1.0943	0.4559	3.0093	17.0855	10.4092	32.4034	21.6025	2.3157
Wu-Williams	China	0.6302	0.5402	0.8103	279.1820	362.6829	509.4853	417.1337	1.8175
Yang	USA	1.8462	1.0154	3.3508	65.9625	27.8799	54.6616	42.6530	2.3157
Yu	China	1.2592	0.6482	2.4484	108.9520	16.1756	144.5202	27.0171	1.8175
Zaridze	Russia	1.5851	1.0408	2.4063	65.0738	78.0610	87.0319	165.4851	0.7080
Zaridze	Russia	1.1625	0.7233	1.8772	38.3856	78.0610	70.0025	165.4851	2.2930
Zatloukal	Czech Republic	0.4319	0.1890	0.9808	6.4934	71.1961	143.3555	678.8575	1.8175
Zheng	China	2.3248	1.0039	5.3988	58.1774	7.1246	169.4385	48.2403	1.8175
Zhong	China	1.3772	0.8854	2.1642	96.9932	49.9230	111.3394	78.9246	0.7080
Zhong	China	0.8639	0.5759	1.3438	110.3006	49.9230	201.8494	78.9246	1.7670
Zhong	China	1.3005	0.6502	2.4151	22.9677	49.9230	27.9209	78.9246	3.1830

NOTES: RR,RL,RU RELATIVE RISKS AND LOWER AND UPPER CONFIDENCE INTERVALS

CA1,CA0 NUMBERS (OR PSEUDO-NUMBERS) OF EXPOSED AND UNEXPOSED CASES

CO1,CO0 NUMBERS (OR PSEUDO-NUMBERS) OF EXPOSED AND UNEXPOSED CONTROLS

NCIGS MIDPOINT OF NUMBER OF CIGARETTES SMOKED BY HUSBAND (IN UNITS OF 10)

Study title	Country	Beta	St.Err. Beta	Z	Weight	ETSse	FRU	VEG	FAT	EDU	TEA
Akiba	Japan	0.1273	0.1398	0.9106	51.1665	0.9896	0	0	0	0	0
Al-Zoughool	Canada	-0.5507	0.2634	-2.0907	14.4135	0.8916	0	0	0	1	0
Asomaning	USA	-0.0734	0.2417	-0.3037	17.1178	1.0091	0	0	0	0	0
Boffetta 2	7 countries	-0.0531	0.1874	-0.2834	28.4748	0.9130	0	0	0	0	0
Boffetta	7 countries	-0.0382	0.0532	-0.7180	353.3269	1.1768	0	0	0	0	0
Brenner	Canada	-0.5647	0.1297	-4.3539	59.4456	0.7374	0	0	0	0	0
Brownson 1	USA	0.2049	0.3165	0.6474	9.9828	0.8345	0	0	0	1	0
Brownson 2	USA	-0.0417	0.0447	-0.9329	500.4780	1.1579	0	0	0	0	0
Buffler	USA	-0.1389	0.1896	-0.7326	27.8178	0.8581	0	0	0	0	0
Butler	USA	0.2669	0.3174	0.8409	9.9263	0.9215	0	0	0	0	0
Cardenas	USA	0.1238	0.0733	1.6889	186.1196	1.4556	0	1	1	2	0
Chan	China	-0.2152	0.1553	-1.3857	41.4627	0.9109	0	0	0	0	0
Choi	Korea	0.2221	0.1597	1.3907	39.2094	0.9091	0	0	0	0	0
Correa	USA	0.2800	0.2059	1.3599	23.5878	1.1582	0	0	0	0	0
De Waard	Netherlands	0.4777	0.3137	1.5228	10.1618	0.8696	0	0	0	0	0
Du	China	0.1200	0.1167	1.0283	73.4274	1.0879	0	0	0	0	0
Enstrom	USA	-0.0598	0.0772	-0.7746	167.7897	1.0456	1	0	0	2	0
EPIC Adulthood	Western Europe	-0.1174	0.2644	-0.4440	14.3046	0.8968	1	1	1	2	0
Fang	China	0.2919	0.1409	2.0717	50.3707	0.5724	0	1	0	1	0
Fontham	USA	0.0803	0.0475	1.6905	443.2133	1.1293	1	1	0	2	0
Franco-Marina	Mexico	0.2764	0.1798	1.5373	30.9329	0.7856	0	0	0	0	0
Gallegos	Mexico	1.1163	0.6294	1.7736	2.5243	0.8730	0	0	0	0	0
Gao	China	0.0960	0.1126	0.8526	78.8721	0.8022	0	0	0	2	0
Garfinkel 1	USA	-0.0152	0.0684	-0.2222	213.7410	1.1963	0	0	0	0	0
Garfinkel 2	USA	0.1168	0.0647	1.8053	238.8864	1.5345	0	0	0	0	0

APPENDIX 13

ETS and Lung Cancer - Meta-Analysis of Dose Response Exposure (or nearest equivalent), 02-NOV-15

Female (Husband's smoking) - Number cigarettes smoked

BASIC DATA USED IN META-ANALYSES

CORRECTED FOR ALL CONFOUNDERS (FRUIT, VEG, FAT, EDUCATION)

Confounder Differences based on Unweighted Regression

Study title	Country	Beta	St.Err. Beta	Z	Weight	ETSse	FRU	VEG	FAT	EDU	TEA
GELAC study	Taiwan	0.0946	0.0503	1.8807	395.2429	0.8883	0	0	0	2	0
Geng	China	0.3289	0.1501	2.1912	44.3852	1.0478	0	0	0	0	0
Gorlova	USA	0.0403	0.1326	0.3039	56.8739	1.1005	0	0	0	1	0
He	China	0.3551	0.6146	0.5778	2.6474	0.8152	0	0	2	2	0
Hill (study 1)	New Zealand	-0.0528	0.1981	-0.2665	25.4819	0.7776	0	0	0	0	0
Hill (study 2)	New Zealand	0.1268	0.1583	0.8010	39.9060	0.6455	0	0	0	3	0
Hirayama	Japan	0.0760	0.0765	0.9935	170.8745	0.8998	0	0	0	0	0
Hole	Scotland	0.3075	0.3643	0.8441	7.5350	1.0530	0	0	0	0	0
Humble 1	USA	0.0695	0.2448	0.2839	16.6870	1.2885	0	0	0	0	0
IARC: Kreuzer	Germany	-0.1787	0.1341	-1.3326	55.6087	0.8957	0	0	0	0	0
ILCCO	International	0.0496	0.0350	1.4171	816.3265	0.9085	0	0	0	0	0
Inoue	Japan	0.3103	0.2651	1.1705	14.2292	1.1196	0	0	0	0	0
Janerich	USA	-0.1688	0.1033	-1.6341	93.7129	1.1397	0	0	0	0	0
Jee	Korea	0.0153	0.1469	0.1042	46.3400	0.9132	0	1	0	3	0
Jiang	China	0.4185	0.1945	2.1517	26.4339	0.9152	1	1	0	0	0
Johnson	Canada	0.0616	0.1840	0.3348	29.5369	0.8225	1	1	0	2	0
Kabat 1	USA	-0.1459	0.2514	-0.5804	15.8223	1.1579	0	0	0	0	0
Kabat 2	USA	-0.0375	0.1070	-0.3505	87.3439	1.3646	0	0	0	2	0
Kalandidi	Greece	0.0764	0.0906	0.8433	121.8270	1.5584	0	0	0	0	0
Kiyohara	Japan	-0.0502	0.2157	-0.2327	21.4931	0.8757	0	0	0	0	0
Koo	China	0.0216	0.1411	0.1531	50.2280	1.1884	0	0	0	2	0
Kurahashi	Japan	0.1129	0.1022	1.1047	95.7411	1.1771	0	0	0	0	0
Lagarde	Sweden	0.0256	0.0887	0.2886	127.1021	0.8828	0	0	0	3	0
Lam T	China	0.2230	0.0898	2.4833	124.0073	1.0055	0	0	0	0	0
Lam W	China	0.3401	0.1723	1.9739	33.6844	0.9063	0	0	0	0	0
Layard	USA	-0.2398	0.1543	-1.5541	42.0018	1.1466	0	0	0	0	0
Lee	England	-0.0530	0.2795	-0.1896	12.8008	0.8544	0	0	0	0	0
Lee C-H	Taiwan	0.2994	0.1042	2.8733	92.1010	0.9015	0	0	0	2	0
Liang	China	0.1552	0.1004	1.5458	99.2048	0.9083	0	0	0	0	0
Lim	Singapore	0.0123	0.0613	0.2007	266.1209	0.9027	0	0	0	0	0
Lin	China	0.4627	0.1152	4.0165	75.3520	0.8642	0	0	0	2	0
Liu Q	China	0.3953	0.1760	2.2460	32.2831	1.0561	0	0	0	2	0
Liu Z	China	-0.1978	0.2634	-0.7509	14.4135	0.6106	0	0	0	0	0
Lopez-Cima	Spain	-0.0559	1.7473	-0.0320	0.3275	0.3069	0	0	0	0	0
Malats	7 Europe+Brazil	0.1750	0.1866	0.9378	28.7195	0.8717	0	0	0	0	0
Masjedi	Iran	0.3373	0.1935	1.7432	26.7078	0.7742	0	0	0	0	0
McGhee	China	0.1283	0.1088	1.1792	84.4777	0.9025	0	0	0	2	0
Nishino	Japan	0.3056	0.2704	1.1302	13.6769	0.8950	1	1	1	0	0
Ohno	Japan	-0.0529	0.1122	-0.4715	79.4354	0.8114	0	0	0	0	0
Pershagen	Sweden	0.0496	0.1542	0.3217	42.0563	0.9097	0	0	0	0	0
Rapiti	India	0.0494	0.2467	0.2002	16.4309	0.8504	0	0	0	0	0
Ren	China	0.0494	0.0545	0.9064	336.6720	0.8365	0	0	0	0	0
Rylander	Sweden	0.1232	0.2465	0.4998	16.4576	0.7290	0	0	0	0	0
Schoenberg	USA	-0.0074	0.0942	-0.0786	112.6933	1.1321	0	1	0	2	0
Schwartz	USA	0.0005	0.0933	0.0054	114.8780	1.1194	0	0	0	0	0
Seki	Japan	0.0988	0.0775	1.2748	166.4932	0.8692	0	0	0	0	0
Shen	China	-0.1426	0.1574	-0.9060	40.3637	1.0903	0	0	0	0	0
Shimizu	Japan	-0.0098	0.1467	-0.0668	46.4665	0.9053	0	0	0	0	0
Sobue	Japan	0.0157	0.1035	0.1517	93.3511	0.9064	0	0	0	2	0
Speize	USA	0.1353	0.3354	0.4034	8.8894	0.6375	0	0	0	0	0
Stockwell	USA	0.1660	0.1456	1.1401	47.1712	1.1381	0	0	0	2	0
Sun	China	0.0305	0.1050	0.2905	90.7029	0.8954	0	0	0	2	0
Svensson	Sweden	0.1199	0.2646	0.4531	14.2830	0.8673	0	0	0	0	0
Torres-Duran	Spain	-0.2460	0.1224	-2.0098	66.7478	0.9064	0	0	0	0	0
Trichopoulos	Greece	0.2247	0.1062	2.1158	88.6647	1.3389	0	0	0	0	0
Wang L	China	-0.0098	0.1462	-0.0670	46.7849	0.6870	0	0	0	1	0
Wang S	China	0.4691	0.1962	2.3909	25.9778	0.8780	0	0	0	0	0

APPENDIX 13

ETS and Lung Cancer - Meta-Analysis of Dose Response Exposure (or nearest equivalent), 02-NOV-15

Female (Husband's smoking) - Number cigarettes smoked

BASIC DATA USED IN META-ANALYSES

CORRECTED FOR ALL CONFOUNDERS (FRUIT, VEG, FAT, EDUCATION)

Confounder Differences based on Unweighted Regression

Study title	Country	Beta	St.Err. Beta	Z	Weight	ETSse	FRU	VEG	FAT	EDU	TEA
Wang T	China	0.1147	0.1180	0.9720	71.8184	1.0379	0	0	0	0	0
Wen	China	0.0079	0.1091	0.0724	84.0138	0.8863	1	1	0	2	0
WHI-OS	USA	-0.0982	0.1160	-0.8466	74.3163	1.1579	0	0	0	0	0
Wu	USA	0.0389	0.2079	0.1871	23.1361	1.1449	0	0	0	0	0
Wu-Williams	China	-0.2540	0.0569	-4.4640	308.8698	0.9047	0	0	0	2	0
Yang	USA	0.2648	0.1315	2.0137	57.8294	1.1548	0	0	0	0	0
Yu	China	0.1268	0.1865	0.6799	28.7503	0.6640	1	1	0	2	0
Zaridze	Russia	0.0630	0.1061	0.5938	88.8320	0.8744	0	0	0	2	0
Zatloukal	Czech Republic	-0.4619	0.2312	-1.9978	18.7079	0.6900	0	0	0	2	0
Zheng	China	0.4642	0.2361	1.9661	17.9394	0.7567	0	0	0	0	0
Zhong	China	-0.0597	0.0880	-0.6784	129.1322	0.9343	1	0	0	1	0

```
NOTES: BETA      SLOPE OF LOG RR ON NCIGS

       SE BETA   STANDARD ERROR OF BETA

       Z         RATIO OF BETA TO ITS STANDARD ERROR (APPROXIMATE NORMAL STATISTIC)

       WEIGHT    INVERSE OF THE VARIANCE OF BETA

       ETSse     STANDARD ERROR OF ETS EXPOSURE OVER THE CONTROL GROUPS

       FRU = 1   DOSE-RESPONSE ANALYSIS ADJUSTED FOR FRUIT

       VEG = 1          "         "        "      " VEGETABLES

       FAT = 1          "         "        "      " FRUIT

       EDU = 1          "         "        "      " INCOME

           = 2          "         "        "      " EDUCATION

           = 3          "         "        "      " SOCIO-ECONOMIC STATUS

       TEA = 0   NO ADJUSTMENT (OR MATCHING) FOR TEA
```

RANDOM-EFFECTS META-ANALYSES

Dose Response (Beta)
WEIGHTED on Beta
Weights

	Deviance	(DF)
Model 1	100.4349	(92)

	Estimate	S.E.	P	RR	95%CIl	95%CIu
Constant	0.0518	0.0176	++	1.0531	1.0175	1.0900

SEPARATE RANDOM-EFFECTS META-ANALYSES BY REGION

NORTH AMERICA, EUROPE AND NEW ZEALAND

APPENDIX 13
ETS and Lung Cancer - Meta-Analysis of Dose Response Exposure (or nearest equivalent), 02-NOV-15
Female (Husband's smoking) - Number cigarettes smoked

CORRECTED FOR ALL CONFOUNDERS (FRUIT, VEG, FAT, EDUCATION)
SEPARATE RANDOM-EFFECTS META-ANALYSES BY REGION
Confounder Differences based on Unweighted Regression

Dose Response (Beta) WEIGHTED on Beta Weights

	Deviance	(DF)				
Model 1	52.4877	(48)				
	Estimate	**S.E.**	**P**	**RR**	**95%CIl**	**95%CIu**
Constant	0.0038	0.0236	N.S.	1.0038	0.9585	1.0512

ASIA

Dose Response (Beta) WEIGHTED on Beta Weights

	Deviance	(DF)				
Model 1	42.7222	(43)				
	Estimate	**S.E.**	**P**	**RR**	**95%CIl**	**95%CIu**
Constant	0.0985	0.0253	+++	1.1035	1.0502	1.1595

NORTH AMERICA

Dose Response (Beta) WEIGHTED on Beta Weights

	Deviance	(DF)				
Model 1	33.2840	(28)				
	Estimate	**S.E.**	**P**	**RR**	**95%CIl**	**95%CIu**
Constant	-0.0015	0.0317	N.S.	0.9985	0.9383	1.0625

EUROPE AND NEW ZEALAND

Dose Response (Beta) WEIGHTED on Beta Weights

	Deviance	(DF)				
Model 1	18.9289	(19)				
	Estimate	**S.E.**	**P**	**RR**	**95%CIl**	**95%CIu**
Constant	0.0103	0.0337	N.S.	1.0104	0.9458	1.0794

CHINA AND HONG KONG

Dose Response (Beta) WEIGHTED on Beta Weights

	Deviance	(DF)				
Model 1	24.2569	(26)				
	Estimate	**S.E.**	**P**	**RR**	**95%CIl**	**95%CIu**
Constant	0.1105	0.0405	+	1.1168	1.0317	1.2090

REST OF ASIA

Dose Response (Beta) WEIGHTED on Beta Weights

	Deviance	(DF)				
Model 1	12.2994	(16)				
	Estimate	**S.E.**	**P**	**RR**	**95%CIl**	**95%CIu**
Constant	0.0804	0.0214	++	1.0838	1.0393	1.1302

SEPARATE RANDOM-EFFECTS META-ANALYSES BY YEAR OF PUBLICATION

PUBLISHED IN 1980S

APPENDIX 13

ETS and Lung Cancer - Meta-Analysis of Dose Response Exposure (or nearest equivalent), 02-NOV-15

Female (Husband's smoking) - Number cigarettes smoked

CORRECTED FOR ALL CONFOUNDERS (FRUIT, VEG, FAT, EDUCATION)

SEPARATE RANDOM-EFFECTS META-ANALYSES BY YEAR OF PUBLICATION

Confounder Differences based on Unweighted Regression

Dose Response (Beta)
WEIGHTED on Beta
Weights

	Deviance	(DF)				
Model 1	22.4865	(25)				
	Estimate	**S.E.**	**P**	**RR**	**95%CIl**	**95%CIu**
Constant	0.0915	0.0254	++	1.0958	1.0426	1.1517

PUBLISHED IN 1990S

Dose Response (Beta)
WEIGHTED on Beta
Weights

	Deviance	(DF)				
Model 1	26.8458	(26)				
	Estimate	**S.E.**	**P**	**RR**	**95%CIl**	**95%CIu**
Constant	0.0171	0.0303	N.S.	1.0172	0.9586	1.0795

PUBLISHED IN 2000S

Dose Response (Beta)
WEIGHTED on Beta
Weights

	Deviance	(DF)				
Model 1	24.8602	(25)				
	Estimate	**S.E.**	**P**	**RR**	**95%CIl**	**95%CIu**
Constant	0.0739	0.0316	+	1.0767	1.0120	1.1456

PUBLISHED IN 2010S

Dose Response (Beta)
WEIGHTED on Beta
Weights

	Deviance	(DF)				
Model 1	25.1730	(13)				
	Estimate	**S.E.**	**P**	**RR**	**95%CIl**	**95%CIu**
Constant	0.0213	0.0524	N.S.	1.0216	0.9218	1.1322

SEPARATE RANDOM-EFFECTS META-ANALYSES BY NUMBER OF LUNG CANCER CASES

<100 CASES

Dose Response (Beta)
WEIGHTED on Beta
Weights

	Deviance	(DF)				
Model 1	48.6581	(48)				
	Estimate	**S.E.**	**P**	**RR**	**95%CIl**	**95%CIu**
Constant	0.0873	0.0310	++	1.0913	1.0270	1.1596

100-199 CASES

Dose Response (Beta)
WEIGHTED on Beta
Weights

	Deviance	(DF)				
Model 1	24.2840	(21)				
	Estimate	**S.E.**	**P**	**RR**	**95%CIl**	**95%CIu**
Constant	0.0160	0.0353	N.S.	1.0161	0.9482	1.0890

200-399 CASES

APPENDIX 13
ETS and Lung Cancer - Meta-Analysis of Dose Response Exposure (or nearest equivalent), 02-NOV-15
Female (Husband's smoking) - Number cigarettes smoked

CORRECTED FOR ALL CONFOUNDERS (FRUIT, VEG, FAT, EDUCATION)
SEPARATE RANDOM-EFFECTS META-ANALYSES BY NUMBER OF LUNG CANCER CASES
Confounder Differences based on Unweighted Regression

Dose Response (Beta)
WEIGHTED on Beta
Weights

	Deviance	(DF)				
Model 1	12.7550	(12)				
	Estimate	**S.E.**	**P**	**RR**	**95%CIl**	**95%CIu**
Constant	0.1173	0.0359	++	1.1245	1.0481	1.2064

400+ CASES
Dose Response (Beta)
WEIGHTED on Beta
Weights

	Deviance	(DF)				
Model 1	8.6142	(8)				
	Estimate	**S.E.**	**P**	**RR**	**95%CIl**	**95%CIu**
Constant	-0.0075	0.0340	N.S.	0.9925	0.9285	1.0609

SEPARATE RANDOM-EFFECTS META-ANALYSES BY DOSE-RESPONSE OR NOT

RESULTS FOR DOSE-RESPONSE
Dose Response (Beta)
WEIGHTED on Beta
Weights

	Deviance	(DF)				
Model 1	22.9359	(23)				
	Estimate	**S.E.**	**P**	**RR**	**95%CIl**	**95%CIu**
Constant	0.0709	0.0244	++	1.0734	1.0233	1.1260

NO RESULTS FOR DOSE-RESPONSE
Dose Response (Beta)
WEIGHTED on Beta
Weights

	Deviance	(DF)				
Model 1	76.1192	(68)				
	Estimate	**S.E.**	**P**	**RR**	**95%CIl**	**95%CIu**
Constant	0.0425	0.0226	(+)	1.0434	0.9982	1.0906

SEPARATE RANDOM-EFFECTS META-ANALYSES BY AGE ADJUSTMENT OR NOT

ADJUSTED (OR MATCHED) FOR AGE
Dose Response (Beta)
WEIGHTED on Beta
Weights

	Deviance	(DF)				
Model 1	78.8157	(74)				
	Estimate	**S.E.**	**P**	**RR**	**95%CIl**	**95%CIu**
Constant	0.0346	0.0184	(+)	1.0352	0.9985	1.0733

NOT ADJUSTED (OR MATCHED) FOR AGE
Dose Response (Beta)
WEIGHTED on Beta
Weights

	Deviance	(DF)				
Model 1	18.0100	(17)				
	Estimate	**S.E.**	**P**	**RR**	**95%CIl**	**95%CIu**
Constant	0.1470	0.0493	++	1.1584	1.0517	1.2759

APPENDIX 13

ETS and Lung Cancer - Meta-Analysis of Dose Response Exposure (or nearest equivalent), 02-NOV-15

Female (Husband's smoking) - Number cigarettes smoked

CORRECTED FOR ALL CONFOUNDERS (FRUIT, VEG, FAT, EDUCATION)
SEPARATE RANDOM-EFFECTS META-ANALYSES BY STUDY TYPE
Confounder Differences based on Unweighted Regression

CASE-CONTROL STUDIES

Dose Response (Beta)
WEIGHTED on Beta Weights

	Deviance	(DF)
Model 1	87.0939	(76)

	Estimate	S.E.	P	RR	95%Cll	95%Clu
Constant	0.0551	0.0203	++	1.0567	1.0154	1.0996

PROSPECTIVE STUDIES

Dose Response (Beta)
WEIGHTED on Beta Weights

	Deviance	(DF)
Model 1	9.1010	(15)

	Estimate	S.E.	P	RR	95%Cll	95%Clu
Constant	0.0353	0.0293	N.S.	1.0359	0.9780	1.0972

BASIC DATA USED IN META-ANALYSES
Confounder Differences based on Weighted Regression

Study title	Country	RR	RRL	RRU	CA1	CA0	CO1	CO0	NCigs
Akiba	Japan	1.2716	0.6064	2.5138	32.9157	13.6954	102.5296	54.2461	1.0000
Akiba	Japan	1.4309	0.6773	3.0144	25.3841	13.6954	70.2675	54.2461	2.1350
Akiba	Japan	1.9292	0.5236	7.4136	4.0667	13.6954	8.3496	54.2461	3.8390
Al-Zoughool	Canada	0.3873	0.1489	0.9731	5.8592	22.7805	113.2615	170.5310	1.8175
Asomaning	USA	0.8948	0.2983	2.6747	15.0537	5.6119	58.3256	19.4555	2.3157
Boffetta 2	7 countries	0.9624	0.4812	1.8286	25.2505	25.8565	53.4290	52.6541	1.8175
Boffetta	7 countries	0.9729	0.7491	1.2745	300.5669	117.4921	555.0822	211.0956	1.3380
Boffetta	7 countries	0.5405	0.3224	0.8818	24.7088	117.4921	82.1398	211.0956	2.5880
Boffetta	7 countries	1.2265	0.7597	1.9862	35.9070	117.4921	52.6004	211.0956	4.3060
Brenner	Canada	0.3836	0.2397	0.6041	53.3979	36.4071	513.1855	134.2032	1.8175
Brownson 1	USA	1.6702	0.3877	6.8599	3.7483	12.8263	6.1047	34.8906	2.3157
Brownson 2	USA	0.9624	0.7699	1.1549	257.7637	254.3963	710.6132	674.9606	2.3157
Buffler	USA	0.7694	0.3270	1.8274	31.9940	8.1137	160.4382	31.3056	2.3157
Butler	USA	1.9496	0.4633	8.2617	2.7549	5.6395	11258.4102	44931.4800	2.3157
Cardenas	USA	1.0865	0.4939	2.1730	9.8248	24.2859	13794.2232	37046.5496	1.0040
Cardenas	USA	1.1669	0.6807	2.1394	22.6115	24.2859	29557.6327	37046.5496	2.2670
Cardenas	USA	1.8017	0.9482	3.4137	15.2183	24.2859	12885.0589	37046.5496	4.3140
Chan	China	0.7205	0.4131	1.2489	32.7317	50.2503	65.1984	72.1180	1.8175
Choi	Korea	1.5735	0.8881	2.7705	47.5938	26.1249	86.4967	74.7078	1.8175
Correa	USA	2.0012	0.7831	5.0755	13.7009	8.0810	60.3953	71.2867	2.3157
De Waard	Netherlands	2.4867	0.8128	7.5957	18.5718	4.0353	121.8822	65.8552	1.8175
Du	China	0.6598	0.3193	1.3634	12.9067	28.5795	68.2583	99.7310	1.0000
Du	China	1.4141	0.7780	2.5701	29.3228	28.5795	72.3623	99.7310	2.6030
Enstrom	USA	0.9153	0.6426	1.2950	102.3603	44.6218	15397.9997	6143.6945	2.3157
EPIC Adulthood	Western Europe	0.8181	0.3214	2.1135	9.2352	8.1474	13838.0422	9987.7881	1.8175
Fang	China	1.7655	1.0673	2.9125	23.2756	105.0574	85.8547	684.1428	1.8175
Fontham	USA	1.2607	1.0164	1.5637	367.3426	185.2550	650.2239	413.4094	2.3157
Franco-Marina	Mexico	1.7372	0.9168	3.3006	21.4092	37.6932	39.5599	120.9918	1.8175
Gallegos	Mexico	7.7917	0.8279	73.3491	12.6605	0.8665	38.0460	20.2897	1.8175
Gao	China	1.2567	0.8384	1.8696	170.3614	48.6226	245.6881	88.1249	1.8175
Garfinkel 1	USA	1.2465	0.8441	1.8551	39.2090	67.1921	38802.4064	82888.9390	1.0040
Garfinkel 1	USA	1.0452	0.7221	1.5108	48.5239	67.1921	57271.4185	82888.9390	2.7520
Garfinkel 2	USA	0.8297	0.3953	1.7417	10.9728	43.9390	44.4808	147.7767	1.0040
Garfinkel 2	USA	1.0464	0.6206	1.7644	31.5672	43.9390	101.4627	147.7767	2.2670
Garfinkel 2	USA	1.8704	1.0649	3.2849	29.3325	43.9390	52.7450	147.7767	4.3140
GELAC study	Taiwan	1.2531	1.0507	1.5037	441.2388	543.1790	387.1716	597.2463	1.8175
Geng	China	1.3870	0.4854	3.9826	7.6104	14.7783	15.3728	41.4037	0.4850
Geng	China	1.9027	0.5855	6.1766	6.2316	14.7783	9.1755	41.4037	1.2730

APPENDIX 13

ETS and Lung Cancer - Meta-Analysis of Dose Response Exposure (or nearest equivalent), 02-NOV-15

Female (Husband's smoking) - Number cigarettes smoked

BASIC DATA USED IN META-ANALYSES

CORRECTED FOR ALL CONFOUNDERS (FRUIT, VEG, FAT, EDUCATION)

Confounder Differences based on Weighted Regression

Study title	Country	RR	RRL	RRU	CA1	CA0	CO1	CO0	NCigs
Geng	China	2.5964	1.1698	5.7825	25.9090	14.7783	27.9568	41.4037	2.6030
Gorlova	USA	1.1431	0.6262	2.0875	65.4588	29.1841	66.1274	33.7022	2.3157
He	China	1.9995	0.2222	17.7155	4.9184	0.9476	332.4202	128.0597	1.8175
Hill (study 1)	New Zealand	0.9625	0.4716	1.9345	9.2204	47.1364	89096.7424	438382.9990	1.8175
Hill (study 2)	New Zealand	1.3296	0.7515	2.3220	13.7118	100.9314	59267.4677	580058.9990	1.8175
Hirayama	Japan	1.3194	0.8991	1.9449	139.2859	31.6197	64217.9119	19234.2967	0.8600
Hirayama	Japan	1.4833	0.9609	2.2950	56.1909	31.6197	23043.4219	19234.2967	2.6030
Hole	Scotland	1.2929	0.1193	14.1916	1.9955	1.0119	745.8631	489.0005	0.2080
Hole	Scotland	2.5425	0.2627	24.3745	2.8464	1.0119	540.9916	489.0005	2.4090
Humble 1	USA	1.7549	0.4777	6.7857	6.2924	7.5034	8.9004	18.6255	1.5820
Humble 1	USA	1.1365	0.2178	6.5252	2.5791	7.5034	5.6333	18.6255	3.3920
IARC: Kreuzer	Germany	0.7689	0.4806	1.2494	51.5202	46.4289	132.2822	91.6591	1.8175
ILCCO	International	1.1562	1.0213	1.3103	686.9177	631.1243	1937.9992	2058.6995	1.8175
Inoue	Japan	2.5357	0.3047	6.5162	7.0172	3.2234	11.7815	13.7230	1.0000
Inoue	Japan	2.9538	0.8030	14.5971	10.3089	3.2234	14.8581	13.7230	2.6030
Janerich	USA	0.7206	0.4515	1.1529	73.7279	69.0069	85.2447	57.4906	2.3157
Jee	Korea	1.9590	1.0775	3.8201	55.1323	11.6068	79204.2659	32665.7680	1.0000
Jee	Korea	1.4213	0.6633	3.1269	14.2079	11.6068	28133.3730	32665.7680	2.6030
Jiang	China	2.2212	1.1111	4.4414	46.8692	21.9807	33.7224	35.1285	1.8175
Johnson	Canada	1.1723	0.6057	2.2469	38.0890	13.0441	391.0607	157.0000	1.8175
Kabat 1	USA	0.7592	0.2402	2.3544	12.5909	11.0566	14.7797	9.8532	2.3157
Kabat 2	USA	0.7982	0.4088	1.5671	19.7337	26.6782	65.6459	70.8358	1.6540
Kabat 2	USA	0.9989	0.4618	2.1675	13.2330	26.6782	35.1741	70.8358	3.6380
Kalandidi	Greece	1.5114	0.7769	2.9400	33.6516	26.5485	38.4057	45.7930	1.3380
Kalandidi	Greece	1.6929	0.7902	3.6268	21.6275	26.5485	22.0361	45.7930	2.9020
Kalandidi	Greece	1.4502	0.4990	4.2149	7.7729	26.5485	9.2453	45.7930	5.3350
Kiyohara	Japan	0.9673	0.4485	2.0856	31.2722	17.7244	43.2294	23.6992	1.8175
Koo	China	2.2994	0.9079	5.8422	14.0140	19.9779	12.5303	41.0736	0.7080
Koo	China	1.6835	0.7837	3.6282	23.1888	19.9779	28.3188	41.0736	1.7670
Koo	China	1.1213	0.4334	2.8551	9.8519	19.9779	18.0637	41.0736	3.1830
Kurahashi	Japan	1.0032	0.5016	2.0064	11.7267	25.1091	46701.1484	100318.9190	1.0000
Kurahashi	Japan	1.4079	0.8332	2.3848	31.0978	25.1091	88249.4397	100318.9190	2.6030
Lagarde	Sweden	1.1077	0.8091	1.5219	82.7456	121.8814	283.6545	462.8046	1.8175
Lam T	China	2.1509	1.1248	4.0945	21.9109	85.7387	21.7898	183.3936	0.7080
Lam T	China	1.7889	1.1507	2.7752	55.1081	85.7387	65.8917	183.3936	1.7670
Lam T	China	1.9485	1.0072	3.7935	19.6338	85.7387	21.5529	183.3936	3.1830
Lam W	China	1.9428	1.0536	3.5956	36.5191	23.4947	64.0121	80.0092	1.8175
Layard	USA	0.5903	0.2234	1.5597	4.9663	24.7822	334.7831	986.2429	0.8190
Layard	USA	0.5913	0.2637	1.3254	7.9098	24.7822	532.3830	986.2429	2.6640
Lee	England	0.9624	0.3561	2.6082	17.6991	8.5840	36.9534	17.2488	1.8175
Lee C-H	Taiwan	1.8066	1.2463	2.6181	142.4840	59.8518	191.0150	144.9575	1.8175
Liang	China	1.3961	0.9765	1.9960	138.3888	86.4852	148.2595	129.3526	1.8175
Lim	Singapore	1.0816	0.8696	1.3454	196.3580	230.3882	603.0546	765.3383	1.8175
Lin	China	2.4214	1.6059	3.6500	98.8983	78.5820	72.2491	139.0056	1.8175
Liu Q	China	0.6875	0.2259	2.1606	6.0909	14.0533	16.8932	26.7960	1.0000
Liu Q	China	2.7669	1.1449	6.9649	23.6401	14.0533	16.2911	26.7960	2.6030
Liu Z	China	0.7406	0.2885	1.8852	34.8910	6.9609	136.4191	20.1563	1.8175
Lopez-Cima	Spain	0.9559	0.0019	490.8038	4.4400	0.1300	17.8800	0.5100	1.8175
Malats	7 Europe+Brazil	1.4470	0.7428	2.8071	35.5082	46.1590	23.4880	44.1812	1.8175

APPENDIX 13

ETS and Lung Cancer - Meta-Analysis of Dose Response Exposure (or nearest equivalent), 02-NOV-15

Female (Husband's smoking) - Number cigarettes smoked

BASIC DATA USED IN META-ANALYSES

CORRECTED FOR ALL CONFOUNDERS (FRUIT, VEG, FAT, EDUCATION)

Confounder Differences based on Weighted Regression

Study title	Country	RR	RRL	RRU	CA1	CA0	CO1	CO0	NCigs
Masjedi	Iran	1.9381	0.9726	3.8618	20.6569	34.6368	28.1508	91.4843	1.8175
McGhee	China	1.3307	0.9064	1.9672	79.1348	77.2979	131.0884	170.3957	1.8175
Nishino	Japan	1.7588	0.6547	4.4946	9.7201	7.2075	22613.0418	29490.4513	1.8175
Ohno	Japan	0.9624	0.6448	1.4340	136.0420	53.2267	236.8403	89.1844	1.8175
Pershagen	Sweden	1.1562	0.6744	2.0233	35.4620	28.2648	139.3002	128.3702	1.8175
Rapiti	India	1.1561	0.4817	2.7938	12.4824	23.6478	18.5082	40.5359	1.8175
Ren	China	1.1560	0.9537	1.4065	642.3280	242.9116	792.4520	346.4448	1.8175
Rylander	Sweden	1.3203	0.5493	3.1802	7.8158	23.6575	41.0340	163.9839	1.8175
Schoenberg	USA	1.0380	0.6765	1.5914	67.2978	41.9406	285.3298	184.5809	2.3157
Schwartz	USA	1.0592	0.6933	1.6178	122.6661	67.2068	114.9490	66.7098	2.3157
Seki	Japan	1.2627	0.9543	1.6579	191.4078	82.9216	1099.1764	601.2820	1.8175
Shen	China	0.6437	0.2080	2.0498	10.3573	14.2816	12.2101	10.8371	0.4850
Shen	China	1.0234	0.3119	3.2942	11.7817	14.2816	8.7361	10.8371	1.2730
Shen	China	0.6642	0.2657	1.6699	32.5424	14.2816	37.1800	10.8371	2.6030
Shimizu	Japan	1.0399	0.6162	1.7524	50.4434	38.3814	89.8114	71.0614	1.8175
Sobue	Japan	1.0883	0.7512	1.5699	77.0685	60.2364	376.6325	320.3781	1.8175
Speize	USA	1.4449	0.2890	6.0687	28.2213	1.7610	199635.6750	18000.0001	2.3157
Stockwell	USA	1.5442	0.7721	2.8954	47.1445	19.9846	59.5496	38.9806	2.3157
Sun	China	1.1174	0.7706	1.6279	142.1290	87.9089	136.0265	94.0113	1.8175
Svensson	Sweden	1.3112	0.5110	3.3647	17.7699	7.1332	83.5169	43.9574	1.8175
Torres-Duran	Spain	0.6819	0.4418	1.0564	48.7174	86.8946	104.5315	127.1309	1.8175
Trichopoulos	Greece	0.5616	0.1210	2.6065	1.9990	24.5165	15.8256	109.0024	0.7080
Trichopoulos	Greece	2.4315	1.2286	4.8120	21.6863	24.5165	39.6544	109.0024	1.7670
Trichopoulos	Greece	3.8202	1.2634	11.5509	6.9185	24.5165	8.0519	109.0024	2.5880
Trichopoulos	Greece	1.7512	0.6540	4.6890	6.8811	24.5165	17.4698	109.0024	4.3060
Wang L	China	1.0237	0.5964	1.6897	124.6322	25.2866	252.6180	52.4709	1.8175
Wang S	China	2.4481	1.2192	4.9348	65.9373	15.2630	59.4155	33.6691	1.8175
Wang T	China	0.3464	0.1089	1.1482	4.1342	43.6881	13.2108	48.3635	0.4850
Wang T	China	1.3142	0.7204	2.3850	43.9974	43.6881	37.0621	48.3635	1.2730
Wang T	China	1.3251	0.7193	2.4325	41.4250	43.6881	34.6080	48.3635	2.6030
Wen	China	1.0645	0.7227	1.5724	67.7498	40.6048	40676.2827	25951.5464	1.8175
WHI-OS	USA	0.8462	0.5001	1.4328	25.5828	30.2311	42236.1346	42236.1355	2.3157
Wu	USA	1.1562	0.4817	3.1795	17.6039	10.1507	32.7100	21.8066	2.3157
Wu-Williams	China	0.6722	0.5762	0.8643	288.1329	350.9420	507.2717	415.3210	1.8175
Yang	USA	1.9331	1.0632	3.5085	67.5647	27.2734	55.2415	43.1055	2.3157
Yu	China	1.3190	0.6790	2.5647	111.9749	15.8711	147.6714	27.6068	1.8175
Zaridze	Russia	1.6294	1.0699	2.4735	66.0426	75.5701	88.6221	165.2289	0.7080
Zaridze	Russia	1.2710	0.7908	2.0524	39.6265	75.5701	68.1692	165.2289	2.2930
Zatloukal	Czech Republic	0.4608	0.2016	1.0464	6.5469	67.2813	136.2322	645.1210	1.8175
Zheng	China	2.4351	1.0515	5.6549	60.2875	7.0534	174.6988	49.7712	1.8175
Zhong	China	1.4006	0.9004	2.2010	97.7115	48.9977	113.5310	79.7372	0.7080
Zhong	China	0.9010	0.6007	1.4015	112.8185	48.9977	203.7757	79.7372	1.7670
Zhong	China	1.4027	0.7014	2.6051	23.5377	48.9977	27.3070	79.7372	3.1830

NOTES: RR,RL,RU RELATIVE RISKS AND LOWER AND UPPER CONFIDENCE INTERVALS

CA1,CA0 NUMBERS (OR PSEUDO-NUMBERS) OF EXPOSED AND UNEXPOSED CASES

CO1,CO0 NUMBERS (OR PSEUDO-NUMBERS) OF EXPOSED AND UNEXPOSED CONTROLS

NCIGS MIDPOINT OF NUMBER OF CIGARETTES SMOKED BY HUSBAND (IN UNITS OF 10)

APPENDIX 13

ETS and Lung Cancer - Meta-Analysis of Dose Response Exposure (or nearest equivalent), 02-NOV-15

Female (Husband's smoking) - Number cigarettes smoked

BASIC DATA USED IN META-ANALYSES

CORRECTED FOR ALL CONFOUNDERS (FRUIT, VEG, FAT, EDUCATION)

Confounder Differences based on Weighted Regression

Study title	**Country**	**Beta**	**St.Err. Beta**	**Z**	**Weight**	**ETSse**	**FRU**	**VEG**	**FAT**	**EDU**	**TEA**
Akiba	Japan	0.1585	0.1396	1.1354	51.3132	0.9896	0	0	0	0	0
Al-Zoughool	Canada	-0.5220	0.2634	-1.9818	14.4135	0.8916	0	0	0	1	0
Asomaning	USA	-0.0480	0.2417	-0.1986	17.1178	1.0091	0	0	0	0	0
Boffetta 2	7 countries	-0.0211	0.1874	-0.1126	28.4748	0.9130	0	0	0	0	0
Boffetta	7 countries	-0.0064	0.0533	-0.1201	352.0024	1.1768	0	0	0	0	0
Brenner	Canada	-0.5272	0.1297	-4.0648	59.4456	0.7374	0	0	0	0	0
Brownson 1	USA	0.2215	0.3165	0.6998	9.9828	0.8345	0	0	0	1	0
Brownson 2	USA	-0.0165	0.0447	-0.3691	500.4780	1.1579	0	0	0	0	0
Buffler	USA	-0.1132	0.1896	-0.5970	27.8178	0.8581	0	0	0	0	0
Butler	USA	0.2883	0.3174	0.9083	9.9263	0.9215	0	0	0	0	0
Cardenas	USA	0.1291	0.0733	1.7613	186.1196	1.4556	0	1	1	2	0
Chan	China	-0.1804	0.1553	-1.1616	41.4627	0.9109	0	0	0	0	0
Choi	Korea	0.2494	0.1597	1.5617	39.2094	0.9091	0	0	0	0	0
Correa	USA	0.2996	0.2059	1.4551	23.5878	1.1582	0	0	0	0	0
De Waard	Netherlands	0.5012	0.3137	1.5977	10.1618	0.8696	0	0	0	0	0
Du	China	0.1500	0.1166	1.2864	73.5534	1.0879	0	0	0	0	0
Enstrom	USA	-0.0382	0.0772	-0.4948	167.7897	1.0456	1	0	0	2	0
EPIC Adulthood	Western Europe	-0.1104	0.2644	-0.4175	14.3046	0.8968	1	1	1	2	0
Fang	China	0.3127	0.1409	2.2193	50.3707	0.5724	0	1	0	1	0
Fontham	USA	0.1000	0.0475	2.1053	443.2133	1.1293	1	1	0	2	0
Franco-Marina	Mexico	0.3039	0.1798	1.6902	30.9329	0.7856	0	0	0	0	0
Gallegos	Mexico	1.1296	0.6294	1.7947	2.5243	0.8730	0	0	0	0	0
Gao	China	0.1257	0.1126	1.1163	78.8721	0.8022	0	0	0	2	0
Garfinkel 1	USA	0.0118	0.0683	0.1728	214.3673	1.1963	0	0	0	0	0
Garfinkel 2	USA	0.1371	0.0647	2.1190	238.8864	1.5345	0	0	0	0	0
GELAC study	Taiwan	0.1241	0.0503	2.4672	395.2429	0.8883	0	0	0	2	0
Geng	China	0.3531	0.1497	2.3587	44.6228	1.0478	0	0	0	0	0
Gorlova	USA	0.0578	0.1326	0.4359	56.8739	1.1005	0	0	0	1	0
He	China	0.3812	0.6146	0.6202	2.6474	0.8152	0	0	2	2	0
Hill (study 1)	New Zealand	-0.0211	0.1981	-0.1065	25.4819	0.7776	0	0	0	0	0
Hill (study 2)	New Zealand	0.1567	0.1583	0.9899	39.9060	0.6455	0	0	0	3	0
Hirayama	Japan	0.1140	0.0760	1.5000	173.1302	0.8998	0	0	0	0	0
Hole	Scotland	0.3390	0.3614	0.9380	7.6564	1.0530	0	0	0	0	0
Humble 1	USA	0.0920	0.2453	0.3751	16.6190	1.2885	0	0	0	0	0
IARC: Kreuzer	Germany	-0.1446	0.1341	-1.0783	55.6087	0.8957	0	0	0	0	0
ILCCO	International	0.0799	0.0350	2.2829	816.3265	0.9085	0	0	0	0	0
Inoue	Japan	0.3301	0.2640	1.2504	14.3480	1.1196	0	0	0	0	0
Janerich	USA	-0.1415	0.1033	-1.3698	93.7129	1.1397	0	0	0	0	0
Jee	Korea	0.0470	0.1465	0.3208	46.5934	0.9132	0	1	0	3	0
Jiang	China	0.4391	0.1945	2.2576	26.4339	0.9152	1	1	0	0	0
Johnson	Canada	0.0875	0.1840	0.4755	29.5369	0.8225	1	1	0	2	0
Kabat 1	USA	-0.1190	0.2514	-0.4733	15.8223	1.1579	0	0	0	0	0
Kabat 2	USA	-0.0118	0.1072	-0.1101	87.0183	1.3646	0	0	0	2	0
Kalandidi	Greece	0.0977	0.0907	1.0772	121.5585	1.5584	0	0	0	0	0
Kiyohara	Japan	-0.0183	0.2157	-0.0848	21.4931	0.8757	0	0	0	0	0
Koo	China	0.0467	0.1413	0.3305	50.0859	1.1884	0	0	0	2	0
Kurahashi	Japan	0.1371	0.1020	1.3441	96.1169	1.1771	0	0	0	0	0
Lagarde	Sweden	0.0563	0.0887	0.6347	127.1021	0.8828	0	0	0	3	0
Lam T	China	0.2486	0.0900	2.7622	123.4568	1.0055	0	0	0	0	0
Lam W	China	0.3654	0.1723	2.1207	33.6844	0.9063	0	0	0	0	0
Layard	USA	-0.2035	0.1544	-1.3180	41.9474	1.1466	0	0	0	0	0
Lee	England	-0.0211	0.2795	-0.0755	12.8008	0.8544	0	0	0	0	0
Lee C-H	Taiwan	0.3254	0.1042	3.1228	92.1010	0.9015	0	0	0	2	0
Liang	China	0.1836	0.1004	1.8287	99.2048	0.9083	0	0	0	0	0
Lim	Singapore	0.0432	0.0613	0.7047	266.1209	0.9027	0	0	0	0	0
Lin	China	0.4866	0.1152	4.2240	75.3520	0.8642	0	0	0	2	0
Liu Q	China	0.4193	0.1759	2.3837	32.3198	1.0561	0	0	0	2	0

APPENDIX 13

ETS and Lung Cancer - Meta-Analysis of Dose Response Exposure (or nearest equivalent), 02-NOV-15

Female (Husband's smoking) - Number cigarettes smoked

BASIC DATA USED IN META-ANALYSES

CORRECTED FOR ALL CONFOUNDERS (FRUIT, VEG, FAT, EDUCATION)

Confounder Differences based on Weighted Regression

Study title	Country	Beta	St.Err. Beta	Z	Weight	ETSse	FRU	VEG	FAT	EDU	TEA
Liu Z	China	-0.1652	0.2634	-0.6272	14.4135	0.6106	0	0	0	0	0
Lopez-Cima	Spain	-0.0039	1.7473	-0.0022	0.3275	0.3069	0	0	0	0	0
Malats	7 Europe+Brazil	0.2033	0.1866	1.0895	28.7195	0.8717	0	0	0	0	0
Masjedi	Iran	0.3641	0.1935	1.8817	26.7078	0.7742	0	0	0	0	0
McGhee	China	0.1572	0.1088	1.4449	84.4777	0.9025	0	0	0	2	0
Nishino	Japan	0.3107	0.2704	1.1490	13.6769	0.8950	1	1	1	0	0
Ohno	Japan	-0.0211	0.1122	-0.1881	79.4354	0.8114	0	0	0	0	0
Pershagen	Sweden	0.0799	0.1542	0.5182	42.0563	0.9097	0	0	0	0	0
Rapiti	India	0.0798	0.2467	0.3235	16.4309	0.8504	0	0	0	0	0
Ren	China	0.0798	0.0545	1.4642	336.6720	0.8365	0	0	0	0	0
Rylander	Sweden	0.1529	0.2465	0.6203	16.4576	0.7290	0	0	0	0	0
Schoenberg	USA	0.0161	0.0942	0.1709	112.6933	1.1321	0	1	0	2	0
Schwartz	USA	0.0249	0.0933	0.2669	114.8780	1.1194	0	0	0	0	0
Seki	Japan	0.1283	0.0775	1.6555	166.4932	0.8692	0	0	0	0	0
Shen	China	-0.1105	0.1567	-0.7052	40.7251	1.0903	0	0	0	0	0
Shimizu	Japan	0.0215	0.1467	0.1466	46.4665	0.9053	0	0	0	0	0
Sobue	Japan	0.0466	0.1035	0.4502	93.3511	0.9064	0	0	0	2	0
Speize	USA	0.1589	0.3354	0.4738	8.8894	0.6375	0	0	0	0	0
Stockwell	USA	0.1876	0.1456	1.2885	47.1712	1.1381	0	0	0	2	0
Sun	China	0.0611	0.1050	0.5819	90.7029	0.8954	0	0	0	2	0
Svensson	Sweden	0.1491	0.2646	0.5635	14.2830	0.8673	0	0	0	0	0
Torres-Duran	Spain	-0.2107	0.1224	-1.7214	66.7478	0.9064	0	0	0	0	0
Trichopoulos	Greece	0.2441	0.1064	2.2942	88.3317	1.3389	0	0	0	0	0
Wang L	China	0.0129	0.1462	0.0882	46.7849	0.6870	0	0	0	1	0
Wang S	China	0.4926	0.1962	2.5107	25.9778	0.8780	0	0	0	0	0
Wang T	China	0.1455	0.1180	1.2331	71.8184	1.0379	0	0	0	0	0
Wen	China	0.0344	0.1091	0.3153	84.0138	0.8863	1	1	0	2	0
WHI-OS	USA	-0.0721	0.1160	-0.6216	74.3163	1.1579	0	0	0	0	0
Wu	USA	0.0627	0.2079	0.3016	23.1361	1.1449	0	0	0	0	0
Wu-Williams	China	-0.2185	0.0569	-3.8401	308.8698	0.9047	0	0	0	2	0
Yang	USA	0.2846	0.1315	2.1643	57.8294	1.1548	0	0	0	0	0
Yu	China	0.1523	0.1865	0.8166	28.7503	0.6640	1	1	0	2	0
Zaridze	Russia	0.0999	0.1061	0.9416	88.8320	0.8744	0	0	0	2	0
Zatloukal	Czech Republic	-0.4263	0.2312	-1.8439	18.7079	0.6900	0	0	0	2	0
Zheng	China	0.4897	0.2361	2.0741	17.9394	0.7567	0	0	0	0	0
Zhong	China	-0.0375	0.0879	-0.4266	129.4262	0.9343	1	0	0	1	0

NOTES: BETA SLOPE OF LOG RR ON NCIGS

SE BETA STANDARD ERROR OF BETA

Z RATIO OF BETA TO ITS STANDARD ERROR (APPROXIMATE NORMAL STATISTIC)

WEIGHT INVERSE OF THE VARIANCE OF BETA

ETSse STANDARD ERROR OF ETS EXPOSURE OVER THE CONTROL GROUPS

FRU = 1 DOSE-RESPONSE ANALYSIS ADJUSTED FOR FRUIT

VEG = 1 " " " " VEGETABLES

FAT = 1 " " " " FRUIT

EDU = 1 " " " " INCOME

APPENDIX 13

ETS and Lung Cancer - Meta-Analysis of Dose Response Exposure (or nearest equivalent), 02-NOV-15

Female (Husband's smoking) - Number cigarettes smoked

BASIC DATA USED IN META-ANALYSES

CORRECTED FOR ALL CONFOUNDERS (FRUIT, VEG, FAT, EDUCATION)

Confounder Differences based on Weighted Regression

= 2 " " " " EDUCATION

= 3 " " " " SOCIO-ECONOMIC STATUS

TEA = 0 NO ADJUSTMENT (OR MATCHING) FOR TEA

RANDOM-EFFECTS META-ANALYSES

Dose Response (Beta)
WEIGHTED on Beta
Weights

	Deviance	(DF)				
Model 1	99.9135	(92)				
	Estimate	**S.E.**	**P**	**RR**	**95%Cll**	**95%Clu**
Constant	0.0785	0.0173	+++	1.0816	1.0456	1.1189

SEPARATE RANDOM-EFFECTS META-ANALYSES BY REGION

NORTH AMERICA, EUROPE AND NEW ZEALAND

Dose Response (Beta)
WEIGHTED on Beta
Weights

	Deviance	(DF)				
Model 1	52.1885	(48)				
	Estimate	**S.E.**	**P**	**RR**	**95%Cll**	**95%Clu**
Constant	0.0292	0.0228	N.S.	1.0296	0.9845	1.0767

ASIA

Dose Response (Beta)
WEIGHTED on Beta
Weights

	Deviance	(DF)				
Model 1	42.5047	(43)				
	Estimate	**S.E.**	**P**	**RR**	**95%Cll**	**95%Clu**
Constant	0.1263	0.0249	+++	1.1346	1.0806	1.1913

NORTH AMERICA

Dose Response (Beta)
WEIGHTED on Beta
Weights

	Deviance	(DF)				
Model 1	32.9888	(28)				
	Estimate	**S.E.**	**P**	**RR**	**95%Cll**	**95%Clu**
Constant	0.0218	0.0308	N.S.	1.0220	0.9622	1.0856

EUROPE AND NEW ZEALAND

Dose Response (Beta)
WEIGHTED on Beta
Weights

	Deviance	(DF)				
Model 1	18.9500	(19)				
	Estimate	**S.E.**	**P**	**RR**	**95%Cll**	**95%Clu**
Constant	0.0390	0.0323	N.S.	1.0398	0.9760	1.1078

CHINA AND HONG KONG

APPENDIX 13
ETS and Lung Cancer - Meta-Analysis of Dose Response Exposure (or nearest equivalent), 02-NOV-15
Female (Husband's smoking) - Number cigarettes smoked

CORRECTED FOR ALL CONFOUNDERS (FRUIT, VEG, FAT, EDUCATION)
SEPARATE RANDOM-EFFECTS META-ANALYSES BY REGION
Confounder Differences based on Weighted Regression

Dose Response (Beta)
WEIGHTED on Beta Weights

	Deviance	(DF)				
Model 1	24.2452	(26)				
	Estimate	**S.E.**	**P**	**RR**	**95%CIl**	**95%CIu**
Constant	0.1375	0.0399	++	1.1474	1.0612	1.2406

REST OF ASIA
Dose Response (Beta)
WEIGHTED on Beta Weights

	Deviance	(DF)				
Model 1	11.7311	(16)				
	Estimate	**S.E.**	**P**	**RR**	**95%CIl**	**95%CIu**
Constant	0.1105	0.0214	+++	1.1169	1.0711	1.1647

SEPARATE RANDOM-EFFECTS META-ANALYSES BY YEAR OF PUBLICATION

PUBLISHED IN 1980S
Dose Response (Beta)
WEIGHTED on Beta Weights

	Deviance	(DF)				
Model 1	21.8337	(25)				
	Estimate	**S.E.**	**P**	**RR**	**95%CIl**	**95%CIu**
Constant	0.1180	0.0254	+++	1.1253	1.0707	1.1826

PUBLISHED IN 1990S
Dose Response (Beta)
WEIGHTED on Beta Weights

	Deviance	(DF)				
Model 1	26.9389	(26)				
	Estimate	**S.E.**	**P**	**RR**	**95%CIl**	**95%CIu**
Constant	0.0425	0.0294	N.S.	1.0434	0.9849	1.1053

PUBLISHED IN 2000S
Dose Response (Beta)
WEIGHTED on Beta Weights

	Deviance	(DF)				
Model 1	24.7633	(25)				
	Estimate	**S.E.**	**P**	**RR**	**95%CIl**	**95%CIu**
Constant	0.0997	0.0312	++	1.1048	1.0392	1.1746

PUBLISHED IN 2010S
Dose Response (Beta)
WEIGHTED on Beta Weights

	Deviance	(DF)				
Model 1	24.9852	(13)				
	Estimate	**S.E.**	**P**	**RR**	**95%CIl**	**95%CIu**
Constant	0.0512	0.0519	N.S.	1.0525	0.9507	1.1651

SEPARATE RANDOM-EFFECTS META-ANALYSES BY NUMBER OF LUNG CANCER CASES

<100 CASES

APPENDIX 13
ETS and Lung Cancer - Meta-Analysis of Dose Response Exposure (or nearest equivalent), 02-NOV-15
Female (Husband's smoking) - Number cigarettes smoked

CORRECTED FOR ALL CONFOUNDERS (FRUIT, VEG, FAT, EDUCATION)
SEPARATE RANDOM-EFFECTS META-ANALYSES BY NUMBER OF LUNG CANCER CASES
Confounder Differences based on Weighted Regression

Dose Response (Beta)
WEIGHTED on Beta
Weights

	Deviance	(DF)				
Model 1	48.5651	(48)				
	Estimate	**S.E.**	**P**	**RR**	**95%Cll**	**95%Clu**
Constant	0.1139	0.0305	+++	1.1206	1.0556	1.1896

100-199 CASES
Dose Response (Beta)
WEIGHTED on Beta
Weights

	Deviance	(DF)				
Model 1	24.1632	(21)				
	Estimate	**S.E.**	**P**	**RR**	**95%Cll**	**95%Clu**
Constant	0.0431	0.0347	N.S.	1.0441	0.9754	1.1176

200-399 CASES
Dose Response (Beta)
WEIGHTED on Beta
Weights

	Deviance	(DF)				
Model 1	12.7630	(12)				
	Estimate	**S.E.**	**P**	**RR**	**95%Cll**	**95%Clu**
Constant	0.1433	0.0355	++	1.1541	1.0766	1.2371

400+ CASES
Dose Response (Beta)
WEIGHTED on Beta
Weights

	Deviance	(DF)				
Model 1	8.5946	(8)				
	Estimate	**S.E.**	**P**	**RR**	**95%Cll**	**95%Clu**
Constant	0.0211	0.0334	N.S.	1.0214	0.9567	1.0904

SEPARATE RANDOM-EFFECTS META-ANALYSES BY DOSE-RESPONSE OR NOT

RESULTS FOR DOSE-RESPONSE
Dose Response (Beta)
WEIGHTED on Beta
Weights

	Deviance	(DF)				
Model 1	22.9708	(23)				
	Estimate	**S.E.**	**P**	**RR**	**95%Cll**	**95%Clu**
Constant	0.0959	0.0237	+++	1.1007	1.0508	1.1529

NO RESULTS FOR DOSE-RESPONSE
Dose Response (Beta)
WEIGHTED on Beta
Weights

	Deviance	(DF)				
Model 1	75.6145	(68)				
	Estimate	**S.E.**	**P**	**RR**	**95%Cll**	**95%Clu**
Constant	0.0695	0.0223	++	1.0720	1.0262	1.1199

SEPARATE RANDOM-EFFECTS META-ANALYSES BY AGE ADJUSTMENT OR NOT

ADJUSTED (OR MATCHED) FOR AGE

APPENDIX 13

ETS and Lung Cancer - Meta-Analysis of Dose Response Exposure (or nearest equivalent), 02-NOV-15

Female (Husband's smoking) - Number cigarettes smoked

CORRECTED FOR ALL CONFOUNDERS (FRUIT, VEG, FAT, EDUCATION)

SEPARATE RANDOM-EFFECTS META-ANALYSES BY AGE ADJUSTMENT OR NOT

Confounder Differences based on Weighted Regression

Dose Response (Beta)
WEIGHTED on Beta
Weights

	Deviance	(DF)				
Model 1	78.4330	(74)				
	Estimate	**S.E.**	**P**	**RR**	**95%Cll**	**95%Clu**
Constant	0.0616	0.0181	++	1.0635	1.0264	1.1019

NOT ADJUSTED (OR MATCHED) FOR AGE

Dose Response (Beta)
WEIGHTED on Beta
Weights

	Deviance	(DF)				
Model 1	17.9590	(17)				
	Estimate	**S.E.**	**P**	**RR**	**95%Cll**	**95%Clu**
Constant	0.1727	0.0485	++	1.1885	1.0807	1.3070

SEPARATE RANDOM-EFFECTS META-ANALYSES BY STUDY TYPE

CASE-CONTROL STUDIES

Dose Response (Beta)
WEIGHTED on Beta
Weights

	Deviance	(DF)				
Model 1	86.5417	(76)				
	Estimate	**S.E.**	**P**	**RR**	**95%Cll**	**95%Clu**
Constant	0.0824	0.0200	+++	1.0859	1.0441	1.1293

PROSPECTIVE STUDIES

Dose Response (Beta)
WEIGHTED on Beta
Weights

	Deviance	(DF)				
Model 1	8.7293	(15)				
	Estimate	**S.E.**	**P**	**RR**	**95%Cll**	**95%Clu**
Constant	0.0593	0.0293	(+)	1.0611	1.0019	1.1238

Appendix 14

Fuller details of the analyses relating lung cancer risk to the number of cigarettes smoked by the husband – adjusted for different confounders

APPENDIX 14

ETS and Lung Cancer - Meta-Analysis of Dose Response Exposure (or nearest equivalent), 05-NOV-15

Female (Husband's smoking) - Number cigarettes smoked

CORRECTED FOR NO CONFOUNDERS (BACK CORRECTED FOR FRUIT, VEG, FAT, EDUCATION)

RANDOM-EFFECTS META-ANALYSES

Confounder Differences based on Random-effects Regression

Dose Response (Beta)
WEIGHTED on Beta
Weights

	Deviance	(DF)
Model 1	99.5875	(92)

	Estimate	S.E.	P(+)	RR	95%Cll	95%Clu
Constant	0.0983	0.0172	0.0000 +++	1.1033	1.0668	1.1412

SEPARATE RANDOM-EFFECTS META-ANALYSES BY REGION

NORTH AMERICA, EUROPE AND NEW ZEALAND

Dose Response (Beta)
WEIGHTED on Beta
Weights

	Deviance	(DF)
Model 1	51.9185	(48)

	Estimate	S.E.	P(+)	RR	95%Cll	95%Clu
Constant	0.0479	0.0226	0.0198 +	1.0490	1.0035	1.0966

ASIA

Dose Response (Beta)
WEIGHTED on Beta
Weights

	Deviance	(DF)
Model 1	42.4160	(43)

	Estimate	S.E.	P(+)	RR	95%Cll	95%Clu
Constant	0.1471	0.0247	0.0000 +++	1.1585	1.1037	1.2160

CORRECTED FOR FRUIT

RANDOM-EFFECTS META-ANALYSES

	Deviance	(DF)
Model 1	99.6216	(92)

	Estimate	S.E.	P(+)	RR	95%Cll	95%Clu
Constant	0.0930	0.0172	0.0000 +++	1.0974	1.0610	1.1351

SEPARATE RANDOM-EFFECTS META-ANALYSES BY REGION

NORTH AMERICA, EUROPE AND NEW ZEALAND

Dose Response (Beta)
WEIGHTED on Beta
Weights

	Deviance	(DF)
Model 1	51.9565	(48)

	Estimate	S.E.	P(+)	RR	95%Cll	95%Clu
Constant	0.0428	0.0227	0.0326 +	1.0438	0.9984	1.0912

ASIA

Dose Response (Beta)
WEIGHTED on Beta
Weights

	Deviance	(DF)
Model 1	42.4254	(43)

	Estimate	S.E.	P(+)	RR	95%Cll	95%Clu
Constant	0.1415	0.0247	0.0000 +++	1.1519	1.0974	1.2092

APPENDIX 14

ETS and Lung Cancer - Meta-Analysis of Dose Response Exposure (or nearest equivalent), 05-NOV-15

Female (Husband's smoking) - Number cigarettes smoked

CORRECTED FOR VEGETABLES

RANDOM-EFFECTS META-ANALYSES

Confounder Differences based on Random-effects Regression

Dose Response (Beta)
WEIGHTED on Beta
Weights

	Deviance	(DF)				
Model 1	99.6037	(92)				
	Estimate	**S.E.**	**P(+)**	**RR**	**95%Cll**	**95%Clu**
Constant	0.0948	0.0172	0.0000 +++	1.0994	1.0629	1.1371

SEPARATE RANDOM-EFFECTS META-ANALYSES BY REGION

NORTH AMERICA, EUROPE AND NEW ZEALAND

Dose Response (Beta)
WEIGHTED on Beta
Weights

	Deviance	(DF)				
Model 1	51.9405	(48)				
	Estimate	**S.E.**	**P(+)**	**RR**	**95%Cll**	**95%Clu**
Constant	0.0445	0.0227	0.0277 +	1.0455	1.0001	1.0930

ASIA

Dose Response (Beta)
WEIGHTED on Beta
Weights

	Deviance	(DF)				
Model 1	42.4195	(43)				
	Estimate	**S.E.**	**P(+)**	**RR**	**95%Cll**	**95%Clu**
Constant	0.1433	0.0247	0.0000 +++	1.1541	1.0995	1.2114

CORRECTED FOR DIETARY FAT

RANDOM-EFFECTS META-ANALYSES

	Deviance	(DF)				
Model 1	99.7287	(92)				
	Estimate	**S.E.**	**P(+)**	**RR**	**95%Cll**	**95%Clu**
Constant	0.0855	0.0173	0.0000 +++	1.0893	1.0530	1.1267

SEPARATE RANDOM-EFFECTS META-ANALYSES BY REGION

NORTH AMERICA, EUROPE AND NEW ZEALAND

Dose Response (Beta)
WEIGHTED on Beta
Weights

	Deviance	(DF)				
Model 1	52.0384	(48)				
	Estimate	**S.E.**	**P(+)**	**RR**	**95%Cll**	**95%Clu**
Constant	0.0358	0.0228	0.0615 (+)	1.0364	0.9911	1.0838

ASIA

Dose Response (Beta)
WEIGHTED on Beta
Weights

	Deviance	(DF)				
Model 1	42.4595	(43)				
	Estimate	**S.E.**	**P(+)**	**RR**	**95%Cll**	**95%Clu**
Constant	0.1336	0.0248	0.0000 +++	1.1430	1.0887	1.1999

APPENDIX 14
ETS and Lung Cancer - Meta-Analysis of Dose Response Exposure (or nearest equivalent), 05-NOV-15
Female (Husband's smoking) - Number cigarettes smoked

CORRECTED FOR YEARS OF EDUCATION
RANDOM-EFFECTS META-ANALYSES
Confounder Differences based on Random-effects Regression

Dose Response (Beta)
WEIGHTED on Beta
Weights

	Deviance	(DF)				
Model 1	100.0416	(92)				
	Estimate	**S.E.**	**P(+)**	**RR**	**95%Cll**	**95%Clu**
Constant	0.0741	0.0174	0.0000 +++	1.0770	1.0409	1.1143

SEPARATE RANDOM-EFFECTS META-ANALYSES BY REGION

NORTH AMERICA, EUROPE AND NEW ZEALAND
Dose Response (Beta)
WEIGHTED on Beta
Weights

	Deviance	(DF)				
Model 1	52.2502	(48)				
	Estimate	**S.E.**	**P(+)**	**RR**	**95%Cll**	**95%Clu**
Constant	0.0249	0.0231	0.1432	1.0252	0.9799	1.0726

ASIA
Dose Response (Beta)
WEIGHTED on Beta
Weights

	Deviance	(DF)				
Model 1	42.5631	(43)				
	Estimate	**S.E.**	**P(+)**	**RR**	**95%Cll**	**95%Clu**
Constant	0.1219	0.0250	0.0000 +++	1.1297	1.0757	1.1864

Appendix 15

Fuller details of the analyses relating lung cancer risk to the number of cigarettes smoked by the husband – adjusted for confounding and corrected for misclassification

APPENDIX 15

ETS and Lung Cancer - Meta-Analysis of Dose Response Exposure (or nearest equivalent), 02-NOV-15

Female (Husband's smoking) - Number cigarettes smoked

BASIC DATA USED IN META-ANALYSES

CORRECTED FOR ALL CONFOUNDERS (FRUIT, VEG, FAT, EDUCATION) AND MISCLASSIFICATION

Confounder Differences based on Random-effects Regression

Misclassification: Additive, Concordance: 3.0, MissP: US:0.025, EU:0.025, ASIA:0.1

Study title	Country	RR	RRL	RRU	CA1	CA0	CO1	CO0	NCigs
Akiba	Japan	1.2250	0.5758	2.4570	31.6486	13.3026	97.3255	50.1121	1.0000
Akiba	Japan	1.3213	0.6064	2.8708	21.7111	13.3026	61.9014	50.1121	2.1350
Akiba	Japan	1.6716	0.4292	6.7909	3.5991	13.3026	8.1107	50.1121	3.8390
Al-Zoughool	Canada	0.3781	0.1454	0.9500	5.8254	23.1997	114.7862	172.8264	1.8175
Asomaning	USA	0.7052	0.2036	2.4340	10.1767	4.8105	42.3161	14.1053	2.3157
Boffetta 2	7 countries	0.8827	0.4291	1.7249	22.2843	24.8758	49.3062	48.5844	1.8175
Boffetta	7 countries	0.9210	0.7062	1.2115	281.0705	117.7671	519.3988	200.4223	1.3380
Boffetta	7 countries	0.4861	0.2876	0.7995	23.5618	117.7671	82.4956	200.4223	2.5880
Boffetta	7 countries	1.0280	0.6282	1.6875	32.0392	117.7671	53.0390	200.4223	4.3060
Brenner	Canada	0.3600	0.2227	0.5729	49.3372	35.8372	486.7258	127.2832	1.8175
Brownson 1	USA	1.5973	0.3437	7.0771	3.3188	11.8804	5.5959	31.9960	2.3157
Brownson 2	USA	0.7791	0.6054	0.9626	177.6702	216.6047	547.0494	519.6031	2.3157
Buffler	USA	0.5757	0.2193	1.5260	20.7987	7.0473	111.3956	21.7308	2.3157
Butler	USA	1.8748	0.4333	8.1692	2.5564	5.8749	10684.6215	46036.4581	2.3157
Cardenas	USA	1.0388	0.4608	2.1293	9.4162	21.5567	12746.8904	30314.9200	1.0040
Cardenas	USA	1.0546	0.5820	2.0435	17.7504	21.5567	23670.0266	30314.9200	2.2670
Cardenas	USA	1.4859	0.7038	3.1284	10.1451	21.5567	9601.3378	30314.9200	4.3140
Chan	China	0.5770	0.3028	1.0926	21.9501	42.0751	50.3097	55.6394	1.8175
Choi	Korea	1.5122	0.8433	2.6950	44.6429	25.4949	82.2979	71.0744	1.8175
Correa	USA	1.6775	0.5025	5.5573	7.4822	5.2646	35.3438	41.7168	2.3157
De Waard	Netherlands	2.3925	0.7481	7.6383	16.6986	3.7656	110.3945	59.5596	1.8175
Du	China	0.6284	0.2986	1.3223	12.4403	27.1541	64.3059	88.2071	1.0000
Du	China	1.2454	0.6535	2.3733	23.0298	27.1541	60.0670	88.2071	2.6030
Enstrom	USA	0.8498	0.5904	1.2150	91.6780	43.0465	14113.8871	5631.3380	2.3157
EPIC Adulthood	Western Europe	0.7663	0.2868	2.0778	8.0734	7.6040	12480.4207	9007.9648	1.8175
Fang	China	1.6667	0.9462	2.9279	18.0655	86.3718	69.8685	556.7551	1.8175
Fontham	USA	1.0807	0.8534	1.3683	281.0843	165.3565	525.2900	333.9428	2.3157
Franco-Marina	Mexico	1.6665	0.8681	3.2081	20.1830	37.0399	38.3021	117.1444	1.8175
Gallegos	Mexico	7.7639	0.7766	77.6351	11.9694	0.8220	35.9781	19.1835	1.8175
Gao	China	1.1514	0.7520	1.7496	146.2061	45.5461	215.1445	77.1721	1.8175
Garfinkel 1	USA	1.2132	0.8185	1.8121	37.7535	68.2125	37881.2240	83033.4407	1.0040
Garfinkel 1	USA	0.9703	0.6636	1.4168	43.8551	68.2125	55019.0249	83033.4407	2.7520
Garfinkel 2	USA	0.8004	0.3777	1.6963	10.8139	42.7699	42.4813	134.4876	1.0040
Garfinkel 2	USA	0.9650	0.5602	1.6624	28.2911	42.7699	92.1882	134.4876	2.2670
Garfinkel 2	USA	1.6032	0.8764	2.9330	23.5346	42.7699	46.1583	134.4876	4.3140
GELAC study	Taiwan	1.2038	1.0080	1.4464	426.3321	546.3179	382.5433	590.1068	1.8175
Geng	China	1.3540	0.4589	4.0153	8.0254	12.2026	14.9129	30.7030	0.4850
Geng	China	1.7864	0.5051	6.3105	5.6913	12.2026	8.0159	30.7030	1.2730
Geng	China	2.2822	0.8651	6.0417	14.5204	12.2026	16.0084	30.7030	2.6030
Gorlova	USA	1.0258	0.5446	1.9329	55.9792	27.8119	58.5454	29.8377	2.3157
He	China	1.9335	0.2100	17.5216	4.6842	0.9333	318.3379	122.6386	1.8175
Hill (study 1)	New Zealand	0.8640	0.3944	1.8639	8.1210	29.5542	83376.4846	262151.7920	1.8175
Hill (study 2)	New Zealand	1.2403	0.6773	2.2417	13.0362	60.5078	60250.2175	346845.8420	1.8175
Hirayama	Japan	1.2660	0.8551	1.8828	131.4233	30.2957	59711.7028	17426.3211	0.8600
Hirayama	Japan	1.3091	0.8255	2.0806	44.0309	30.2957	19347.2799	17426.3211	2.6030
Hole	Scotland	1.2784	0.1146	14.4496	2.2765	0.9197	735.0286	379.6062	0.2080
Hole	Scotland	2.2320	0.1643	30.0296	1.4615	0.9197	270.2718	379.6062	2.4090
Humble 1	USA	1.4363	0.3160	6.8716	4.3305	6.2408	6.5629	13.5844	1.5820
Humble 1	USA	0.7396	0.0898	6.7038	1.3717	6.2408	4.0371	13.5844	3.3920
IARC: Kreuzer	Germany	0.7041	0.4319	1.1658	45.6188	44.8997	122.2457	84.7131	1.8175
ILCCO	International	1.0680	0.9376	1.2180	598.3979	595.1750	1754.9844	1864.2864	1.8175
Inoue	Japan	2.4941	0.2953	6.5034	7.0521	3.1454	11.6901	13.0044	1.0000
Inoue	Japan	2.8293	0.7405	14.5224	9.2749	3.1454	13.5530	13.0044	2.6030
Janerich	USA	0.5698	0.3414	0.9537	54.5764	64.5944	71.1726	48.0000	2.3157
Jee	Korea	1.9047	1.0403	3.7404	52.3798	11.4243	76754.2569	31885.8937	1.0000

APPENDIX 15
ETS and Lung Cancer - Meta-Analysis of Dose Response Exposure (or nearest equivalent), 02-NOV-15
Female (Husband's smoking) - Number cigarettes smoked
BASIC DATA USED IN META-ANALYSES
CORRECTED FOR ALL CONFOUNDERS (FRUIT, VEG, FAT, EDUCATION) AND MISCLASSIFICATION

Confounder Differences based on Random-effects Regression
Misclassification: Additive, Concordance: 3.0, MissP: US:0.025, EU:0.025, ASIA:0.1

Study title	Country	RR	RRL	RRU	CA1	CA0	CO1	CO0	NCigs
Jee	Korea	1.3210	0.6053	2.9599	13.0754	11.4243	27625.7441	31885.8937	2.6030
Jiang	China	2.1188	1.0240	4.3850	41.5224	20.4142	30.3356	31.6002	1.8175
Johnson	Canada	0.9418	0.4387	2.0021	24.4416	10.4187	266.6129	107.0339	1.8175
Kabat 1	USA	0.6449	0.1891	2.1585	10.1964	10.5406	12.9607	8.6404	2.3157
Kabat 2	USA	0.6913	0.3364	1.4285	16.2561	25.0686	55.9052	59.5971	1.6540
Kabat 2	USA	0.7281	0.3008	1.7679	8.8570	25.0686	28.9188	59.5971	3.6380
Kalandidi	Greece	1.4757	0.7562	2.8800	33.0569	26.8513	37.5135	44.9668	1.3380
Kalandidi	Greece	1.6075	0.7450	3.4682	20.7495	26.8513	21.6167	44.9668	2.9020
Kalandidi	Greece	1.3185	0.4478	3.8822	7.3224	26.8513	9.3004	44.9668	5.3350
Kiyohara	Japan	0.8946	0.4030	1.9856	27.8928	17.0927	39.6918	21.7600	1.8175
Koo	China	2.2255	0.8602	5.7765	13.8417	18.4039	12.2243	36.1719	0.7080
Koo	China	1.5517	0.6849	3.5272	19.2721	18.4039	24.4108	36.1719	1.7670
Koo	China	0.9682	0.3400	2.7135	7.5085	18.4039	15.2429	36.1719	3.1830
Kurahashi	Japan	0.9730	0.4805	1.9701	11.4717	23.5712	45011.2531	89985.0011	1.0000
Kurahashi	Japan	1.3000	0.7451	2.2739	25.8929	23.5712	76037.7810	89985.0011	2.6030
Lagarde	Sweden	0.9696	0.6838	1.3796	63.2567	106.4451	235.2410	383.8143	1.8175
Lam T	China	2.0811	1.0713	4.0246	21.2413	77.3622	20.9598	158.8644	0.7080
Lam T	China	1.6476	1.0190	2.6584	44.3633	77.3622	55.2934	158.8644	1.7670
Lam T	China	1.6800	0.8091	3.5107	15.0297	77.3622	18.3708	158.8644	3.1830
Lam W	China	1.7958	0.9144	3.5394	28.7838	20.0385	52.0768	65.1050	1.8175
Layard	USA	0.5476	0.1992	1.5054	4.5765	23.0287	314.7188	867.1538	0.8190
Layard	USA	0.4629	0.1814	1.1812	5.5050	23.0287	447.7772	867.1538	2.6640
Lee	England	0.7937	0.2629	2.4021	12.8975	7.5852	28.7986	13.4422	1.8175
Lee C-H	Taiwan	1.7413	1.1980	2.5302	137.5717	59.9638	186.4757	141.5308	1.8175
Liang	China	1.2947	0.8891	1.8854	120.4261	81.1490	132.8977	115.9459	1.8175
Lim	Singapore	0.9835	0.7792	1.2413	164.9149	212.8086	533.7783	677.4196	1.8175
Lin	China	2.3484	1.5567	3.5417	97.1473	79.6072	71.9436	138.4466	1.8175
Liu Q	China	0.6496	0.2038	2.1377	5.8999	12.8810	15.1804	21.5290	1.0000
Liu Q	China	2.3873	0.8763	6.7740	16.3959	12.8810	11.4789	21.5290	2.6030
Liu Z	China	0.6771	0.2563	1.7741	30.9482	6.7524	122.8863	18.1539	1.8175
Lopez-Cima	Spain	0.9918	0.0020	516.1995	4.4400	0.1300	17.8800	0.5100	1.8175
Malats	7 Europe+Brazil	1.3514	0.6777	2.6839	31.9973	44.5412	22.0121	41.4100	1.8175
Masjedi	Iran	1.8668	0.9243	3.7703	19.5258	33.9927	27.2456	88.5485	1.8175
McGhee	China	1.1967	0.7852	1.8364	62.4297	67.8190	109.1511	141.8961	1.8175
Nishino	Japan	1.7095	0.6029	4.6109	8.5766	6.5430	20197.0200	26340.7383	1.8175
Ohno	Japan	0.8921	0.5898	1.3470	122.1938	51.5800	217.4490	81.8878	1.8175
Pershagen	Sweden	1.0657	0.6040	1.9194	30.6690	26.5211	125.0118	115.2029	1.8175
Rapiti	India	1.0647	0.4144	2.7543	10.3492	21.2928	16.2061	35.4998	1.8175
Ren	China	1.0652	0.8720	1.3061	568.5658	233.3501	717.8939	313.8535	1.8175
Rylander	Sweden	1.1265	0.3955	3.2152	5.2239	18.5324	30.9725	123.7757	1.8175
Schoenberg	USA	0.8030	0.4839	1.3315	41.7109	33.6023	196.7178	127.2573	2.3157
Schwartz	USA	0.8950	0.5683	1.4090	98.2426	63.7044	98.0406	56.8992	2.3157
Seki	Japan	1.1863	0.8870	1.5744	170.4146	78.5818	997.6725	545.7565	1.8175
Shen	China	0.6287	0.2020	2.0132	10.7543	14.3007	12.1254	10.1370	0.4850
Shen	China	0.9620	0.2890	3.1419	11.6700	14.3007	8.5987	10.1370	1.2730
Shen	China	0.5853	0.2273	1.5158	27.7840	14.3007	33.6473	10.1370	2.6030
Shimizu	Japan	0.9488	0.5448	1.6502	42.7843	35.6814	79.3349	62.7761	1.8175
Sobue	Japan	0.9939	0.6679	1.4725	63.8256	54.6273	324.9210	276.3901	1.8175
Speize	USA	1.2129	0.1982	6.2355	17.9257	1.3921	191085.9790	17999.9996	2.3157
Stockwell	USA	1.3665	0.6460	2.7099	37.4768	17.9517	49.1718	32.1870	2.3157
Sun	China	1.0239	0.6941	1.5177	124.3069	83.9003	123.1175	85.0866	1.8175
Svensson	Sweden	1.1740	0.4252	3.2419	14.2522	6.3896	69.2226	36.4344	1.8175
Torres-Duran	Spain	0.6463	0.4168	1.0060	46.5362	87.5827	103.3773	125.7388	1.8175
Trichopoulos	Greece	0.5557	0.1196	2.5822	1.9964	24.8229	15.6397	108.0606	0.7080
Trichopoulos	Greece	2.3682	1.1930	4.7009	21.1990	24.8229	38.9686	108.0606	1.7670
Trichopoulos	Greece	3.6754	1.2102	11.1626	6.7874	24.8229	8.0392	108.0606	2.5880
Trichopoulos	Greece	1.6422	0.6088	4.4297	6.6599	24.8229	17.6544	108.0606	4.3060

APPENDIX 15

ETS and Lung Cancer - Meta-Analysis of Dose Response Exposure (or nearest equivalent), 02-NOV-15

Female (Husband's smoking) - Number cigarettes smoked

BASIC DATA USED IN META-ANALYSES

CORRECTED FOR ALL CONFOUNDERS (FRUIT, VEG, FAT, EDUCATION) AND MISCLASSIFICATION

Confounder Differences based on Random-effects Regression

Misclassification: Additive, Concordance: 3.0, MissP: US:0.025, EU:0.025, ASIA:0.1

Study title	Country	RR	RRL	RRU	CA1	CA0	CO1	CO0	NCigs
Wang L	China	0.9999	0.5801	1.6571	120.9278	25.1222	246.1163	51.1247	1.8175
Wang S	China	2.3678	1.1689	4.8149	63.0826	15.0977	57.2065	32.4180	1.8175
Wang T	China	0.3385	0.1057	1.1286	4.1513	42.9454	12.7668	44.7041	0.4850
Wang T	China	1.2364	0.6671	2.2799	41.5552	42.9454	34.9849	44.7041	1.2730
Wang T	China	1.1698	0.6147	2.2184	34.5078	42.9454	30.7076	44.7041	2.6030
Wen	China	0.9733	0.6436	1.4760	56.5661	36.7369	34826.8416	22015.0700	1.8175
WHI-OS	USA	0.7019	0.3801	1.2969	17.3473	24.7147	31829.6929	31829.6925	2.3157
Wu	USA	1.0462	0.4060	3.0890	14.4214	9.1902	27.8285	18.5533	2.3157
Wu-Williams	China	0.5572	0.4637	0.7378	200.4975	294.6000	392.9882	321.7532	1.8175
Yang	USA	1.7515	0.9131	3.3536	54.0619	24.0846	45.5198	35.5184	2.3157
Yu	China	1.2523	0.6391	2.4567	105.8333	15.7878	140.4981	26.2477	1.8175
Zaridze	Russia	1.5988	1.0491	2.4287	65.2664	76.8224	87.4091	164.4926	0.7080
Zaridze	Russia	1.1953	0.7421	1.9345	38.3428	76.8224	68.6835	164.4926	2.2930
Zatloukal	Czech Republic	0.2425	0.0558	1.0467	1.9370	37.8273	73.3734	347.4615	1.8175
Zheng	China	2.3300	0.9633	5.6515	52.6772	6.4382	153.3764	43.6779	1.8175
Zhong	China	1.3592	0.8687	2.1484	98.3459	47.7688	112.9660	74.5783	0.7080
Zhong	China	0.8359	0.5492	1.3195	98.0746	47.7688	183.1710	74.5783	1.7670
Zhong	China	1.2256	0.5969	2.3368	20.5457	47.7688	26.1721	74.5783	3.1830

NOTES: RR,RL,RU RELATIVE RISKS AND LOWER AND UPPER CONFIDENCE INTERVALS

CA1,CA0 NUMBERS (OR PSEUDO-NUMBERS) OF EXPOSED AND UNEXPOSED CASES

CO1,CO0 NUMBERS (OR PSEUDO-NUMBERS) OF EXPOSED AND UNEXPOSED CONTROLS

NCIGS MIDPOINT OF NUMBER OF CIGARETTES SMOKED BY HUSBAND (IN UNITS OF 10)

Study title	Country	Beta	St.Err. Beta	Z	Weight	ETSse	FRU	VEG	FAT	EDU	TEA
Akiba	Japan	0.1220	0.1456	0.8379	47.1712	0.9896	0	0	0	0	0
Al-Zoughool	Canada	-0.5352	0.2634	-2.0319	14.4135	0.8916	0	0	0	1	0
Asomaning	USA	-0.1508	0.2733	-0.5518	13.3882	1.0091	0	0	0	0	0
Boffetta 2	7 countries	-0.0686	0.1953	-0.3513	26.2178	0.9130	0	0	0	0	0
Boffetta	7 countries	-0.0490	0.0545	-0.8991	336.6720	1.1768	0	0	0	0	0
Brenner	Canada	-0.5621	0.1326	-4.2391	56.8739	0.7374	0	0	0	0	0
Brownson 1	USA	0.2022	0.3332	0.6068	9.0072	0.8345	0	0	0	1	0
Brownson 2	USA	-0.1078	0.0511	-2.1096	382.9642	1.1579	0	0	0	0	0
Buffler	USA	-0.2384	0.2137	-1.1156	21.8973	0.8581	0	0	0	0	0
Butler	USA	0.2714	0.3235	0.8389	9.5555	0.9215	0	0	0	0	0
Cardenas	USA	0.0807	0.0841	0.9596	141.3865	1.4556	0	1	1	2	0
Chan	China	-0.3026	0.1801	-1.6802	30.8299	0.9109	0	0	0	0	0
Choi	Korea	0.2276	0.1631	1.3955	37.5917	0.9091	0	0	0	0	0
Correa	USA	0.2234	0.2647	0.8440	14.2722	1.1582	0	0	0	0	0
De Waard	Netherlands	0.4800	0.3261	1.4719	9.4037	0.8696	0	0	0	0	0
Du	China	0.0956	0.1262	0.7575	62.7887	1.0879	0	0	0	0	0
Enstrom	USA	-0.0703	0.0795	-0.8843	158.2216	1.0456	1	0	0	2	0
EPIC Adulthood	Western Europe	-0.1464	0.2779	-0.5268	12.9486	0.8968	1	1	1	2	0
Fang	China	0.2811	0.1586	1.7724	39.7552	0.5724	0	1	0	1	0
Fontham	USA	0.0335	0.0520	0.6442	369.8225	1.1293	1	1	0	2	0
Franco-Marina	Mexico	0.2810	0.1835	1.5313	29.6980	0.7856	0	0	0	0	0
Gallegos	Mexico	1.1276	0.6463	1.7447	2.3940	0.8730	0	0	0	0	0
Gao	China	0.0776	0.1185	0.6549	71.2137	0.8022	0	0	0	2	0
Garfinkel 1	USA	-0.0131	0.0703	-0.1863	202.3435	1.1963	0	0	0	0	0
Garfinkel 2	USA	0.0979	0.0689	1.4209	210.6500	1.5345	0	0	0	0	0

APPENDIX 15

ETS and Lung Cancer - Meta-Analysis of Dose Response Exposure (or nearest equivalent), 02-NOV-15

Female (Husband's smoking) - Number cigarettes smoked

BASIC DATA USED IN META-ANALYSES

CORRECTED FOR ALL CONFOUNDERS (FRUIT, VEG, FAT, EDUCATION) AND MISCLASSIFICATION

Confounder Differences based on Random-effects Regression

Misclassification: Additive, Concordance: 3.0, MissP: US:0.025, EU:0.025, ASIA:0.1

Study title	Country	Beta	St.Err. Beta	Z	Weight	ETSse	FRU	VEG	FAT	EDU	TEA
GELAC study	Taiwan	0.1021	0.0507	2.0138	389.0309	0.8883	0	0	0	2	0
Geng	China	0.3058	0.1831	1.6701	29.8279	1.0478	0	0	0	0	0
Gorlova	USA	0.0110	0.1395	0.0789	51.3868	1.1005	0	0	0	1	0
He	China	0.3628	0.6209	0.5843	2.5939	0.8152	0	0	2	2	0
Hill (study 1)	New Zealand	-0.0804	0.2180	-0.3688	21.0420	0.7776	0	0	0	0	0
Hill (study 2)	New Zealand	0.1185	0.1680	0.7054	35.4308	0.6455	0	0	0	3	0
Hirayama	Japan	0.0700	0.0832	0.8413	144.4619	0.8998	0	0	0	0	0
Hole	Scotland	0.2824	0.4379	0.6449	5.2149	1.0530	0	0	0	0	0
Humble 1	USA	-0.0149	0.3014	-0.0494	11.0081	1.2885	0	0	0	0	0
IARC: Kreuzer	Germany	-0.1931	0.1394	-1.3852	51.4606	0.8957	0	0	0	0	0
ILCCO	International	0.0362	0.0367	0.9864	742.4511	0.9085	0	0	0	0	0
Inoue	Japan	0.3147	0.2722	1.1561	13.4966	1.1196	0	0	0	0	0
Janerich	USA	-0.2429	0.1132	-2.1458	78.0382	1.1397	0	0	0	0	0
Jee	Korea	0.0270	0.1510	0.1788	43.8577	0.9132	0	1	0	3	0
Jiang	China	0.4131	0.2042	2.0230	23.9822	0.9152	1	1	0	0	0
Johnson	Canada	-0.0330	0.2131	-0.1549	22.0208	0.8225	1	1	0	2	0
Kabat 1	USA	-0.1894	0.2682	-0.7062	13.9022	1.1579	0	0	0	0	0
Kabat 2	USA	-0.1048	0.1210	-0.8661	68.3013	1.3646	0	0	0	2	0
Kalandidi	Greece	0.0807	0.0916	0.8810	119.1816	1.5584	0	0	0	0	0
Kiyohara	Japan	-0.0613	0.2238	-0.2739	19.9655	0.8757	0	0	0	0	0
Koo	China	0.0071	0.1538	0.0462	42.2754	1.1884	0	0	0	2	0
Kurahashi	Japan	0.1059	0.1086	0.9751	84.7892	1.1771	0	0	0	0	0
Lagarde	Sweden	-0.0170	0.0985	-0.1726	103.0689	0.8828	0	0	0	3	0
Lam T	China	0.2048	0.0984	2.0813	103.2785	1.0055	0	0	0	0	0
Lam W	China	0.3221	0.1900	1.6953	27.7008	0.9063	0	0	0	0	0
Layard	USA	-0.3026	0.1784	-1.6962	31.4203	1.1466	0	0	0	0	0
Lee	England	-0.1271	0.3105	-0.4093	10.3723	0.8544	0	0	0	0	0
Lee C-H	Taiwan	0.3052	0.1049	2.9094	90.8760	0.9015	0	0	0	2	0
Liang	China	0.1421	0.1055	1.3469	89.8452	0.9083	0	0	0	0	0
Lim	Singapore	-0.0092	0.0654	-0.1407	233.8000	0.9027	0	0	0	0	0
Lin	China	0.4697	0.1154	4.0702	75.0911	0.8642	0	0	0	2	0
Liu Q	China	0.3532	0.2000	1.7660	25.0000	1.0561	0	0	0	2	0
Liu Z	China	-0.2146	0.2716	-0.7901	13.5563	0.6106	0	0	0	0	0
Lopez-Cima	Spain	-0.0039	1.7473	-0.0022	0.3275	0.3069	0	0	0	0	0
Malats	7 Europe+Brazil	0.1657	0.1932	0.8577	26.7908	0.8717	0	0	0	0	0
Masjedi	Iran	0.3435	0.1973	1.7410	25.6889	0.7742	0	0	0	0	0
McGhee	China	0.0988	0.1192	0.8289	70.3797	0.9025	0	0	0	2	0
Nishino	Japan	0.2950	0.2855	1.0333	12.2684	0.8950	1	1	1	0	0
Ohno	Japan	-0.0628	0.1159	-0.5418	74.4446	0.8114	0	0	0	0	0
Pershagen	Sweden	0.0350	0.1623	0.2157	37.9632	0.9097	0	0	0	0	0
Rapiti	India	0.0345	0.2658	0.1298	14.1544	0.8504	0	0	0	0	0
Ren	China	0.0348	0.0567	0.6138	311.0526	0.8365	0	0	0	0	0
Rylander	Sweden	0.0655	0.2941	0.2227	11.5614	0.7290	0	0	0	0	0
Schoenberg	USA	-0.0947	0.1115	-0.8493	80.4360	1.1321	0	1	0	2	0
Schwartz	USA	-0.0479	0.1000	-0.4790	100.0000	1.1194	0	0	0	0	0
Seki	Japan	0.0940	0.0805	1.1677	154.3150	0.8692	0	0	0	0	0
Shen	China	-0.1561	0.1623	-0.9618	37.9632	1.0903	0	0	0	0	0
Shimizu	Japan	-0.0289	0.1556	-0.1857	41.3029	0.9053	0	0	0	0	0
Sobue	Japan	-0.0034	0.1110	-0.0306	81.1622	0.9064	0	0	0	2	0
Speize	USA	0.0834	0.3799	0.2195	6.9289	0.6375	0	0	0	0	0
Stockwell	USA	0.1349	0.1580	0.8538	40.0577	1.1381	0	0	0	2	0
Sun	China	0.0130	0.1098	0.1184	82.9460	0.8954	0	0	0	2	0
Svensson	Sweden	0.0883	0.2851	0.3097	12.3028	0.8673	0	0	0	0	0
Torres-Duran	Spain	-0.2402	0.1237	-1.9418	65.3523	0.9064	0	0	0	0	0
Trichopoulos	Greece	0.2307	0.1069	2.1581	87.5074	1.3389	0	0	0	0	0
Wang L	China	-0.0001	0.1473	-0.0007	46.0887	0.6870	0	0	0	1	0
Wang S	China	0.4742	0.1987	2.3865	25.3282	0.8780	0	0	0	0	0

APPENDIX 15

ETS and Lung Cancer - Meta-Analysis of Dose Response Exposure (or nearest equivalent), 02-NOV-15

Female (Husband's smoking) - Number cigarettes smoked

BASIC DATA USED IN META-ANALYSES

CORRECTED FOR ALL CONFOUNDERS (FRUIT, VEG, FAT, EDUCATION) AND MISCLASSIFICATION

Confounder Differences based on Random-effects Regression

Misclassification: Additive, Concordance: 3.0, MissP: US:0.025, EU:0.025, ASIA:0.1

Study title	Country	Beta	St.Err. Beta	Z	Weight	ETSse	FRU	VEG	FAT	EDU	TEA
Wang T	China	0.1005	0.1241	0.8098	64.9316	1.0379	0	0	0	0	0
Wen	China	-0.0149	0.1165	-0.1279	73.6798	0.8863	1	1	0	2	0
WHI-OS	USA	-0.1529	0.1352	-1.1309	54.7075	1.1579	0	0	0	0	0
Wu	USA	0.0195	0.2236	0.0872	20.0012	1.1449	0	0	0	0	0
Wu-Williams	China	-0.3218	0.0652	-4.9356	235.2366	0.9047	0	0	0	2	0
Yang	USA	0.2420	0.1433	1.6888	48.6976	1.1548	0	0	0	0	0
Yu	China	0.1238	0.1890	0.6550	27.9947	0.6640	1	1	0	2	0
Zaridze	Russia	0.0749	0.1066	0.7026	88.0006	0.8744	0	0	0	2	0
Zatloukal	Czech Republic	-0.7795	0.4114	-1.8947	5.9084	0.6900	0	0	0	2	0
Zheng	China	0.4654	0.2483	1.8743	16.2198	0.7567	0	0	0	0	0
Zhong	China	-0.0806	0.0911	-0.8847	120.4934	0.9343	1	0	0	1	0

NOTES: BETA SLOPE OF LOG RR ON NCIGS

SE BETA STANDARD ERROR OF BETA

Z RATIO OF BETA TO ITS STANDARD ERROR (APPROXIMATE NORMAL STATISTIC)

WEIGHT INVERSE OF THE VARIANCE OF BETA

ETSse STANDARD ERROR OF ETS EXPOSURE OVER THE CONTROL GROUPS

FRU = 1 DOSE-RESPONSE ANALYSIS ADJUSTED FOR FRUIT

VEG = 1 " " " " VEGETABLES

FAT = 1 " " " " FRUIT

EDU = 1 " " " " INCOME

= 2 " " " " EDUCATION

= 3 " " " " SOCIO-ECONOMIC STATUS

TEA = 0 NO ADJUSTMENT (OR MATCHING) FOR TEA

RANDOM-EFFECTS META-ANALYSES

Dose Response (Beta)
WEIGHTED on Beta
Weights

	Deviance	(DF)				
Model 1	98.5113	(92)				
	Estimate	**S.E.**	**P**	**RR**	**95%CIl**	**95%CIu**
Constant	0.0311	0.0189	N.S.	1.0316	0.9942	1.0705

SEPARATE RANDOM-EFFECTS META-ANALYSES BY REGION

NORTH AMERICA, EUROPE AND NEW ZEALAND

APPENDIX 15

ETS and Lung Cancer - Meta-Analysis of Dose Response Exposure (or nearest equivalent), 02-NOV-15

Female (Husband's smoking) - Number cigarettes smoked

CORRECTED FOR ALL CONFOUNDERS (FRUIT, VEG, FAT, EDUCATION) AND MISCLASSIFICATION
SEPARATE RANDOM-EFFECTS META-ANALYSES BY REGION
Confounder Differences based on Random-effects Regression
Misclassification: Additive, Concordance: 3.0, MissP: US:0.025, EU:0.025, ASIA:0.1

Dose Response (Beta)
WEIGHTED on Beta Weights

	Deviance	(DF)				
Model 1	51.0323	(48)				
	Estimate	**S.E.**	**P**	**RR**	**95%Cll**	**95%Clu**
Constant	-0.0260	0.0248	N.S.	0.9743	0.9281	1.0228

ASIA

Dose Response (Beta)
WEIGHTED on Beta Weights

	Deviance	(DF)				
Model 1	42.6701	(43)				
	Estimate	**S.E.**	**P**	**RR**	**95%Cll**	**95%Clu**
Constant	0.0849	0.0268	++	1.0886	1.0329	1.1474

NORTH AMERICA

Dose Response (Beta)
WEIGHTED on Beta Weights

	Deviance	(DF)				
Model 1	31.6340	(28)				
	Estimate	**S.E.**	**P**	**RR**	**95%Cll**	**95%Clu**
Constant	-0.0440	0.0335	N.S.	0.9569	0.8961	1.0220

EUROPE AND NEW ZEALAND

Dose Response (Beta)
WEIGHTED on Beta Weights

	Deviance	(DF)				
Model 1	18.7655	(19)				
	Estimate	**S.E.**	**P**	**RR**	**95%Cll**	**95%Clu**
Constant	0.0027	0.0343	N.S.	1.0028	0.9375	1.0726

CHINA AND HONG KONG

Dose Response (Beta)
WEIGHTED on Beta Weights

	Deviance	(DF)				
Model 1	24.1653	(26)				
	Estimate	**S.E.**	**P**	**RR**	**95%Cll**	**95%Clu**
Constant	0.0902	0.0430	+	1.0944	1.0060	1.1905

REST OF ASIA

Dose Response (Beta)
WEIGHTED on Beta Weights

	Deviance	(DF)				
Model 1	13.4119	(16)				
	Estimate	**S.E.**	**P**	**RR**	**95%Cll**	**95%Clu**
Constant	0.0760	0.0223	++	1.0789	1.0329	1.1271

SEPARATE RANDOM-EFFECTS META-ANALYSES BY YEAR OF PUBLICATION

PUBLISHED IN 1980S

APPENDIX 15

ETS and Lung Cancer - Meta-Analysis of Dose Response Exposure (or nearest equivalent), 02-NOV-15

Female (Husband's smoking) - Number cigarettes smoked

CORRECTED FOR ALL CONFOUNDERS (FRUIT, VEG, FAT, EDUCATION) AND MISCLASSIFICATION
SEPARATE RANDOM-EFFECTS META-ANALYSES BY YEAR OF PUBLICATION
Confounder Differences based on Random-effects Regression
Misclassification: Additive, Concordance: 3.0, MissP: US:0.025, EU:0.025, ASIA:0.1

Dose Response (Beta)
WEIGHTED on Beta Weights

	Deviance	(DF)
Model 1	22.7360	(25)

	Estimate	S.E.	P	RR	95%CIl	95%CIu
Constant	0.0721	0.0274	+	1.0747	1.0186	1.1339

PUBLISHED IN 1990S

Dose Response (Beta)
WEIGHTED on Beta Weights

	Deviance	(DF)
Model 1	27.2923	(26)

	Estimate	S.E.	P	RR	95%CIl	95%CIu
Constant	-0.0124	0.0327	N.S.	0.9876	0.9263	1.0530

PUBLISHED IN 2000S

Dose Response (Beta)
WEIGHTED on Beta Weights

	Deviance	(DF)
Model 1	24.6857	(25)

	Estimate	S.E.	P	RR	95%CIl	95%CIu
Constant	0.0595	0.0327	(+)	1.0613	0.9954	1.1317

PUBLISHED IN 2010S

Dose Response (Beta)
WEIGHTED on Beta Weights

	Deviance	(DF)
Model 1	24.1716	(13)

	Estimate	S.E.	P	RR	95%CIl	95%CIu
Constant	0.0139	0.0542	N.S.	1.0140	0.9117	1.1277

SEPARATE RANDOM-EFFECTS META-ANALYSES BY NUMBER OF LUNG CANCER CASES

<100 CASES

Dose Response (Beta)
WEIGHTED on Beta Weights

	Deviance	(DF)
Model 1	48.6015	(48)

	Estimate	S.E.	P	RR	95%CIl	95%CIu
Constant	0.0693	0.0330	+	1.0718	1.0046	1.1435

100-199 CASES

Dose Response (Beta)
WEIGHTED on Beta Weights

	Deviance	(DF)
Model 1	23.6793	(21)

	Estimate	S.E.	P	RR	95%CIl	95%CIu
Constant	-0.0064	0.0360	N.S.	0.9936	0.9259	1.0662

200-399 CASES

APPENDIX 15

ETS and Lung Cancer - Meta-Analysis of Dose Response Exposure (or nearest equivalent), 02-NOV-15

Female (Husband's smoking) - Number cigarettes smoked

CORRECTED FOR ALL CONFOUNDERS (FRUIT, VEG, FAT, EDUCATION) AND MISCLASSIFICATION
SEPARATE RANDOM-EFFECTS META-ANALYSES BY NUMBER OF LUNG CANCER CASES
Confounder Differences based on Random-effects Regression
Misclassification: Additive, Concordance: 3.0, MissP: US:0.025, EU:0.025, ASIA:0.1

Dose Response (Beta)
WEIGHTED on Beta
Weights

	Deviance	(DF)				
Model 1	12.5714	(12)				
	Estimate	**S.E.**	**P**	**RR**	**95%CIl**	**95%CIu**
Constant	0.1052	0.0402	+	1.1109	1.0268	1.2020

400+ CASES

Dose Response (Beta)
WEIGHTED on Beta
Weights

	Deviance	(DF)				
Model 1	8.9817	(8)				
	Estimate	**S.E.**	**P**	**RR**	**95%CIl**	**95%CIu**
Constant	-0.0348	0.0387	N.S.	0.9658	0.8953	1.0419

SEPARATE RANDOM-EFFECTS META-ANALYSES BY DOSE-RESPONSE OR NOT

RESULTS FOR DOSE-RESPONSE

Dose Response (Beta)
WEIGHTED on Beta
Weights

	Deviance	(DF)				
Model 1	22.8304	(23)				
	Estimate	**S.E.**	**P**	**RR**	**95%CIl**	**95%CIu**
Constant	0.0514	0.0239	+	1.0528	1.0046	1.1032

NO RESULTS FOR DOSE-RESPONSE

Dose Response (Beta)
WEIGHTED on Beta
Weights

	Deviance	(DF)				
Model 1	74.1281	(68)				
	Estimate	**S.E.**	**P**	**RR**	**95%CIl**	**95%CIu**
Constant	0.0206	0.0246	N.S.	1.0208	0.9728	1.0712

SEPARATE RANDOM-EFFECTS META-ANALYSES BY AGE ADJUSTMENT OR NOT

ADJUSTED (OR MATCHED) FOR AGE

Dose Response (Beta)
WEIGHTED on Beta
Weights

	Deviance	(DF)				
Model 1	77.0735	(74)				
	Estimate	**S.E.**	**P**	**RR**	**95%CIl**	**95%CIu**
Constant	0.0150	0.0199	N.S.	1.0151	0.9764	1.0555

NOT ADJUSTED (OR MATCHED) FOR AGE

Dose Response (Beta)
WEIGHTED on Beta
Weights

	Deviance	(DF)				
Model 1	18.3876	(17)				
	Estimate	**S.E.**	**P**	**RR**	**95%CIl**	**95%CIu**
Constant	0.1230	0.0536	+	1.1308	1.0181	1.2561

APPENDIX 15

ETS and Lung Cancer - Meta-Analysis of Dose Response Exposure (or nearest equivalent), 02-NOV-15

Female (Husband's smoking) - Number cigarettes smoked

CORRECTED FOR ALL CONFOUNDERS (FRUIT, VEG, FAT, EDUCATION) AND MISCLASSIFICATION
SEPARATE RANDOM-EFFECTS META-ANALYSES BY STUDY TYPE
Confounder Differences based on Random-effects Regression
Misclassification: Additive, Concordance: 3.0, MissP: US:0.025, EU:0.025, ASIA:0.1

CASE-CONTROL STUDIES

Dose Response (Beta)
WEIGHTED on Beta Weights

	Deviance	(DF)				
Model 1	85.1251	(76)				
	Estimate	**S.E.**	**P**	**RR**	**95%CIl**	**95%CIu**
Constant	0.0336	0.0219	N.S.	1.0342	0.9907	1.0796

PROSPECTIVE STUDIES

Dose Response (Beta)
WEIGHTED on Beta Weights

	Deviance	(DF)				
Model 1	7.8811	(15)				
	Estimate	**S.E.**	**P**	**RR**	**95%CIl**	**95%CIu**
Constant	0.0181	0.0315	N.S.	1.0183	0.9573	1.0831

APPENDIX 15

ETS and Lung Cancer - Meta-Analysis of Dose Response Exposure (or nearest equivalent), 02-NOV-15

Female (Husband's smoking) - Number cigarettes smoked

BASIC DATA USED IN META-ANALYSES

CORRECTED FOR ALL CONFOUNDERS (FRUIT, VEG, FAT, EDUCATION) AND MISCLASSIFICATION

Confounder Differences based on Unweighted Regression

Misclassification: Additive, Concordance: 3.0, MissP: US:0.025, EU:0.025, ASIA:0.1

Study title	Country	RR	RRL	RRU	CA1	CA0	CO1	CO0	NCigs
Akiba	Japan	1.2120	0.5697	2.4311	31.3525	13.3978	96.1413	49.7927	1.0000
Akiba	Japan	1.2915	0.5926	2.8064	21.5037	13.3978	61.8818	49.7927	2.1350
Akiba	Japan	1.6044	0.4119	6.5194	3.5642	13.3978	8.2561	49.7927	3.8390
Al-Zoughool	Canada	0.3675	0.1414	0.9235	5.7867	23.7058	116.6341	175.6089	1.8175
Asomaning	USA	0.6893	0.1988	2.3811	10.0273	4.8490	42.0023	14.0006	2.3157
Boffetta 2	7 countries	0.8649	0.4204	1.6905	22.0451	25.1158	49.3051	48.5831	1.8175
Boffetta	7 countries	0.9076	0.6959	1.1939	278.2421	118.8833	514.3408	199.4482	1.3380
Boffetta	7 countries	0.4725	0.2796	0.7772	23.4656	118.8833	83.3171	199.4482	2.5880
Boffetta	7 countries	0.9807	0.5993	1.6099	31.6160	118.8833	54.0829	199.4482	4.3060
Brenner	Canada	0.3514	0.2174	0.5593	48.6537	36.2042	484.9128	126.8102	1.8175
Brownson 1	USA	1.5674	0.3371	6.9480	3.2907	12.0044	5.6312	32.1978	2.3157
Brownson 2	USA	0.7614	0.5914	0.9411	175.1837	218.5249	546.2635	518.8568	2.3157
Buffler	USA	0.5624	0.2141	1.4914	20.4668	7.1009	110.2741	21.5178	2.3157
Butler	USA	1.8453	0.4264	8.0410	2.5888	5.7092	10972.0868	44651.6844	2.3157
Cardenas	USA	1.0378	0.4603	2.1271	9.4101	21.5869	12732.4398	30311.4506	1.0040
Cardenas	USA	1.0521	0.5807	2.0388	17.7277	21.5869	23659.0285	30311.4506	2.2670
Cardenas	USA	1.4794	0.7007	3.1147	10.1369	21.5869	9621.5198	30311.4506	4.3140
Chan	China	0.5627	0.2949	1.0669	21.6184	42.4871	50.3724	55.7060	1.8175
Choi	Korea	1.4883	0.8299	2.6525	44.2380	25.6703	82.0280	70.8412	1.8175
Correa	USA	1.6473	0.4935	5.4565	7.4080	5.3080	35.2586	41.6158	2.3157
De Waard	Netherlands	2.3607	0.7381	7.5376	16.5270	3.7765	109.5352	59.0869	1.8175
Du	China	0.6224	0.2957	1.3098	12.3918	27.4149	64.0052	88.1309	1.0000
Du	China	1.2145	0.6371	2.3151	22.7670	27.4149	60.2607	88.1309	2.6030
Enstrom	USA	0.8411	0.5844	1.2027	91.0076	43.1701	14056.5982	5608.4800	2.3157
EPIC Adulthood	Western Europe	0.7691	0.2879	2.0853	8.0904	7.5921	12484.5273	9010.9264	1.8175
Fang	China	1.6362	0.9281	2.8765	17.9171	87.2616	70.3646	560.7078	1.8175
Fontham	USA	1.0696	0.8447	1.3544	279.4353	166.0945	524.2384	333.2928	2.3157
Franco-Marina	Mexico	1.6399	0.8542	3.1571	20.0357	37.3659	38.4219	117.5104	1.8175
Gallegos	Mexico	7.7265	0.7727	77.2723	11.9124	0.8225	35.7718	19.0826	1.8175
Gao	China	1.1302	0.7381	1.7173	144.6841	45.9190	213.8513	76.7055	1.8175
Garfinkel 1	USA	1.2016	0.8106	1.7948	37.5002	69.0343	37581.4826	83128.8640	1.0040
Garfinkel 1	USA	0.9450	0.6463	1.3800	43.5015	69.0343	55429.5095	83128.8640	2.7520
Garfinkel 2	USA	0.7951	0.3752	1.6852	10.7987	43.2040	42.2707	134.4749	1.0040
Garfinkel 2	USA	0.9506	0.5518	1.6379	28.1038	43.2040	92.0162	134.4749	2.2670
Garfinkel 2	USA	1.5582	0.8516	2.8511	23.2889	43.2040	46.5196	134.4749	4.3140
GELAC study	Taiwan	1.1828	0.9904	1.4212	422.5565	551.0934	382.9366	590.7135	1.8175
Geng	China	1.3488	0.4572	3.9984	8.0138	12.3164	14.8194	30.7196	0.4850
Geng	China	1.7682	0.5004	6.2412	5.6830	12.3164	8.0162	30.7196	1.2730
Geng	China	2.2350	0.8485	5.9069	14.4423	12.3164	16.1175	30.7196	2.6030
Gorlova	USA	1.0043	0.5332	1.8924	55.3845	28.1050	58.3345	29.7304	2.3157
He	China	1.9051	0.2068	17.2734	4.6238	0.9351	315.0120	121.3605	1.8175
Hill (study 1)	New Zealand	0.8460	0.3858	1.8274	8.0596	29.9531	84122.9467	264499.2800	1.8175
Hill (study 2)	New Zealand	1.2170	0.6641	2.2012	12.9608	61.3098	60845.4640	350272.5310	1.8175
Hirayama	Japan	1.2519	0.8456	1.8617	129.3623	30.4217	58593.2860	17249.5880	0.8600
Hirayama	Japan	1.2653	0.7981	2.0105	43.8793	30.4217	19663.9015	17249.5880	2.6030
Hole	Scotland	1.2758	0.1144	14.4208	2.2631	0.9218	727.5627	378.0528	0.2080
Hole	Scotland	2.1790	0.1603	29.3427	1.4538	0.9218	273.6230	378.0528	2.4090
Humble 1	USA	1.4130	0.3105	6.7688	4.2858	6.3210	6.5295	13.6072	1.5820
Humble 1	USA	0.7141	0.0865	6.4906	1.3562	6.3210	4.0883	13.6072	3.3920
IARC: Kreuzer	Germany	0.6887	0.4224	1.1407	45.0798	45.3549	122.1331	84.6320	1.8175
ILCCO	International	1.0480	0.9199	1.1952	592.2905	600.3839	1753.6632	1862.8832	1.8175
Inoue	Japan	2.4772	0.2933	6.4596	7.0234	3.1618	11.5972	12.9331	1.0000
Inoue	Japan	2.7796	0.7274	14.2692	9.1814	3.1618	13.5109	12.9331	2.6030
Janerich	USA	0.5556	0.3326	0.9305	53.7446	65.2399	71.0605	47.9262	2.3157
Jee	Korea	1.8842	1.0294	3.6988	51.6127	11.4763	75289.0422	31542.4491	1.0000

APPENDIX 15

ETS and Lung Cancer - Meta-Analysis of Dose Response Exposure (or nearest equivalent), 02-NOV-15

Female (Husband's smoking) - Number cigarettes smoked

BASIC DATA USED IN META-ANALYSES

CORRECTED FOR ALL CONFOUNDERS (FRUIT, VEG, FAT, EDUCATION) AND MISCLASSIFICATION

Confounder Differences based on Unweighted Regression

Misclassification: Additive, Concordance: 3.0, MissP: US:0.025, EU:0.025, ASIA:0.1

Study title	Country	RR	RRL	RRU	CA1	CA0	CO1	CO0	NCigs
Jee	Korea	1.2842	0.5890	2.8749	13.0702	11.4763	27972.4262	31542.4491	2.6030
Jiang	China	2.1038	1.0167	4.3542	41.3693	20.4836	30.2943	31.5575	1.8175
Johnson	Canada	0.9317	0.4340	1.9806	24.2650	10.4559	265.5480	106.6057	1.8175
Kabat 1	USA	0.6298	0.1845	2.1101	10.0604	10.6488	12.9433	8.6289	2.3157
Kabat 2	USA	0.6804	0.3310	1.4066	16.1019	25.3708	55.6369	59.6449	1.6540
Kabat 2	USA	0.7031	0.2901	1.7090	8.7493	25.3708	29.2552	59.6449	3.6380
Kalandidi	Greece	1.4616	0.7489	2.8525	32.8951	27.1250	37.2478	44.8921	1.3380
Kalandidi	Greece	1.5743	0.7297	3.3967	20.5842	27.1250	21.6390	44.8921	2.9020
Kalandidi	Greece	1.2690	0.4310	3.7364	7.2280	27.1250	9.4269	44.8921	5.3350
Kiyohara	Japan	0.8767	0.3948	1.9462	27.5877	17.2516	39.5628	21.6890	1.8175
Koo	China	2.2099	0.8542	5.7361	13.8261	18.6248	12.1433	36.1496	0.7080
Koo	China	1.5248	0.6730	3.4660	19.1009	18.6248	24.3145	36.1496	1.7670
Koo	China	0.9381	0.3294	2.6292	7.4384	18.6248	15.3903	36.1496	3.1830
Kurahashi	Japan	0.9652	0.4767	1.9545	11.4234	23.7610	44730.1320	89803.1722	1.0000
Kurahashi	Japan	1.2732	0.7296	2.2275	25.6282	23.7610	76074.5898	89803.1722	2.6030
Lagarde	Sweden	0.9497	0.6695	1.3520	62.5296	107.4240	235.5900	384.3837	1.8175
Lam T	China	2.0676	1.0643	3.9987	21.2269	78.1381	20.9083	159.1369	0.7080
Lam T	China	1.6211	1.0025	2.6159	44.0365	78.1381	55.3229	159.1369	1.7670
Lam T	China	1.6317	0.7857	3.4103	14.8664	78.1381	18.5551	159.1369	3.1830
Lam W	China	1.7696	0.9017	3.4853	28.6174	20.2152	52.0882	65.1102	1.8175
Layard	USA	0.5411	0.1966	1.4893	4.5493	23.4249	313.9666	874.8295	0.8190
Layard	USA	0.4455	0.1739	1.1407	5.4300	23.4249	455.2332	874.8295	2.6640
Lee	England	0.7767	0.2572	2.3518	12.7378	7.6548	28.6721	13.3825	1.8175
Lee C-H	Taiwan	1.7155	1.1803	2.4928	136.4168	60.3549	185.7581	140.9915	1.8175
Liang	China	1.2726	0.8739	1.8531	119.3726	81.8370	132.6574	115.7323	1.8175
Lim	Singapore	0.9640	0.7636	1.2169	163.1158	214.7467	533.9745	677.6687	1.8175
Lin	China	2.3178	1.5364	3.4956	96.5107	80.1277	71.8962	138.3557	1.8175
Liu Q	China	0.6447	0.2023	2.1218	5.8898	12.9779	15.1226	21.4829	1.0000
Liu Q	China	2.3408	0.8591	6.6440	16.2314	12.9779	11.4781	21.4829	2.6030
Liu Z	China	0.6630	0.2509	1.7377	30.5327	6.7972	121.7273	17.9673	1.8175
Lopez-Cima	Spain	0.9010	0.0018	466.8899	4.0663	0.1300	16.4155	0.4728	1.8175
Malats	7 Europe+Brazil	1.3282	0.6659	2.6382	31.7015	44.9012	22.0298	41.4429	1.8175
Masjedi	Iran	1.8381	0.9100	3.7125	19.3829	34.2708	27.3145	88.7723	1.8175
McGhee	China	1.1745	0.7705	1.8029	61.7809	68.3735	109.0743	141.7815	1.8175
Nishino	Japan	1.7136	0.6044	4.6216	8.5887	6.5372	20204.0611	26351.8742	1.8175
Ohno	Japan	0.8748	0.5784	1.3209	120.8956	52.0399	216.4108	81.4942	1.8175
Pershagen	Sweden	1.0455	0.5925	1.8836	30.3393	26.7408	124.7714	114.9813	1.8175
Rapiti	India	1.0446	0.4064	2.7037	10.2490	21.4883	16.2577	35.6069	1.8175
Ren	China	1.0453	0.8557	1.2817	562.8756	235.4321	714.6355	312.4451	1.8175
Rylander	Sweden	1.1032	0.3864	3.1564	5.1675	18.7195	31.1428	124.4566	1.8175
Schoenberg	USA	0.7868	0.4738	1.3054	41.1667	33.8474	195.9362	126.7519	2.3157
Schwartz	USA	0.8765	0.5565	1.3800	97.1738	64.3443	97.7823	56.7489	2.3157
Seki	Japan	1.1652	0.8712	1.5464	168.4648	79.0888	991.8915	542.5941	1.8175
Shen	China	0.6252	0.2009	2.0022	10.7746	14.4852	12.0186	10.1023	0.4850
Shen	China	0.9482	0.2848	3.0969	11.6493	14.4852	8.5680	10.1023	1.2730
Shen	China	0.5683	0.2207	1.4718	27.3773	14.4852	33.5982	10.1023	2.6030
Shimizu	Japan	0.9299	0.5338	1.6178	42.3019	35.9985	79.1659	62.6476	1.8175
Sobue	Japan	0.9744	0.6547	1.4440	63.0828	55.0708	324.1004	275.6918	1.8175
Speize	USA	1.1886	0.1946	6.0981	17.5843	1.3977	190517.0570	17999.9999	2.3157
Stockwell	USA	1.3422	0.6345	2.6617	37.1133	18.1000	48.9810	32.0620	2.3157
Sun	China	1.0042	0.6806	1.4886	123.0355	84.6729	122.8275	84.8840	1.8175
Svensson	Sweden	1.1527	0.4175	3.1826	14.0933	6.4352	68.8429	36.2353	1.8175
Torres-Duran	Spain	0.6321	0.4076	0.9839	46.0589	88.6327	103.8187	126.2757	1.8175
Trichopoulos	Greece	0.5533	0.1190	2.5709	1.9961	25.0397	15.5736	108.0862	0.7080
Trichopoulos	Greece	2.3424	1.1800	4.6498	21.0787	25.0397	38.8438	108.0862	1.7670
Trichopoulos	Greece	3.6170	1.1909	10.9851	6.7552	25.0397	8.0618	108.0862	2.5880
Trichopoulos	Greece	1.5990	0.5927	4.3131	6.6156	25.0397	17.8595	108.0862	4.3060

APPENDIX 15

ETS and Lung Cancer - Meta-Analysis of Dose Response Exposure (or nearest equivalent), 02-NOV-15

Female (Husband's smoking) - Number cigarettes smoked

BASIC DATA USED IN META-ANALYSES

CORRECTED FOR ALL CONFOUNDERS (FRUIT, VEG, FAT, EDUCATION) AND MISCLASSIFICATION

Confounder Differences based on Unweighted Regression

Misclassification: Additive, Concordance: 3.0, MissP: US:0.025, EU:0.025, ASIA:0.1

Study title	Country	RR	RRL	RRU	CA1	CA0	CO1	CO0	NCigs
Wang L	China	0.9796	0.5683	1.6235	119.4210	25.3197	243.9132	50.6609	1.8175
Wang S	China	2.3372	1.1538	4.7526	62.6121	15.1808	56.9236	32.2564	1.8175
Wang T	China	0.3368	0.1052	1.1230	4.1553	43.4015	12.6921	44.6442	0.4850
Wang T	China	1.2201	0.6582	2.2500	41.3447	43.4015	34.8553	44.6442	1.2730
Wang T	China	1.1385	0.5982	2.1592	34.0961	43.4015	30.8069	44.6442	2.6030
Wen	China	0.9629	0.6365	1.4607	55.7937	36.9674	34822.5199	22216.8156	1.8175
WHI-OS	USA	0.6854	0.3706	1.2682	17.0965	24.9451	31814.1780	31814.1790	2.3157
Wu	USA	1.0268	0.3985	3.0316	14.2776	9.2710	27.7537	18.5039	2.3157
Wu-Williams	China	0.5432	0.4519	0.7196	197.3345	297.4448	392.7350	321.5460	1.8175
Yang	USA	1.7235	0.8987	3.2996	53.6435	24.2857	45.3931	35.4199	2.3157
Yu	China	1.2406	0.6331	2.4337	105.1996	15.8509	139.8140	26.1354	1.8175
Zaridze	Russia	1.5844	1.0396	2.4068	64.9435	77.6537	86.8923	164.6113	0.7080
Zaridze	Russia	1.1607	0.7206	1.8785	37.9438	77.6537	69.2958	164.6113	2.2930
Zatloukal	Czech Republic	0.2327	0.0524	1.0262	1.8754	38.1680	73.8896	349.9028	1.8175
Zheng	China	2.2949	0.9487	5.5670	52.0572	6.4580	151.8302	43.2255	1.8175
Zhong	China	1.3508	0.8633	2.1351	98.0335	48.1112	112.1279	74.3312	0.7080
Zhong	China	0.8231	0.5408	1.2991	97.3425	48.1112	182.7155	74.3312	1.7670
Zhong	China	1.1919	0.5806	2.2724	20.3747	48.1112	26.4097	74.3312	3.1830

NOTES: RR,RL,RU RELATIVE RISKS AND LOWER AND UPPER CONFIDENCE INTERVALS

CA1,CA0 NUMBERS (OR PSEUDO-NUMBERS) OF EXPOSED AND UNEXPOSED CASES

CO1,CO0 NUMBERS (OR PSEUDO-NUMBERS) OF EXPOSED AND UNEXPOSED CONTROLS

NCIGS MIDPOINT OF NUMBER OF CIGARETTES SMOKED BY HUSBAND (IN UNITS OF 10)

Study title	Country	Beta	St.Err. Beta	Z	Weight	ETSse	FRU	VEG	FAT	EDU	TEA
Akiba	Japan	0.1114	0.1457	0.7646	47.1065	0.9896	0	0	0	0	0
Al-Zoughool	Canada	-0.5507	0.2634	-2.0907	14.4135	0.8916	0	0	0	1	0
Asomaning	USA	-0.1607	0.2735	-0.5876	13.3686	1.0091	0	0	0	0	0
Boffetta 2	7 countries	-0.0799	0.1953	-0.4091	26.2178	0.9130	0	0	0	0	0
Boffetta	7 countries	-0.0600	0.0545	-1.1009	336.6720	1.1768	0	0	0	0	0
Brenner	Canada	-0.5754	0.1326	-4.3394	56.8739	0.7374	0	0	0	0	0
Brownson 1	USA	0.1941	0.3333	0.5824	9.0018	0.8345	0	0	0	1	0
Brownson 2	USA	-0.1177	0.0512	-2.2988	381.4697	1.1579	0	0	0	0	0
Buffler	USA	-0.2485	0.2138	-1.1623	21.8768	0.8581	0	0	0	0	0
Butler	USA	0.2646	0.3235	0.8179	9.5555	0.9215	0	0	0	0	0
Cardenas	USA	0.0796	0.0841	0.9465	141.3865	1.4556	0	1	1	2	0
Chan	China	-0.3164	0.1805	-1.7529	30.6934	0.9109	0	0	0	0	0
Choi	Korea	0.2188	0.1631	1.3415	37.5917	0.9091	0	0	0	0	0
Correa	USA	0.2155	0.2647	0.8141	14.2722	1.1582	0	0	0	0	0
De Waard	Netherlands	0.4726	0.3261	1.4492	9.4037	0.8696	0	0	0	0	0
Du	China	0.0853	0.1263	0.6754	62.6893	1.0879	0	0	0	0	0
Enstrom	USA	-0.0747	0.0795	-0.9396	158.2216	1.0456	1	0	0	2	0
EPIC Adulthood	Western Europe	-0.1444	0.2779	-0.5196	12.9486	0.8968	1	1	1	2	0
Fang	China	0.2709	0.1588	1.7059	39.6551	0.5724	0	1	0	1	0
Fontham	USA	0.0291	0.0520	0.5596	369.8225	1.1293	1	1	0	2	0
Franco-Marina	Mexico	0.2722	0.1835	1.4834	29.6980	0.7856	0	0	0	0	0
Gallegos	Mexico	1.1250	0.6464	1.7404	2.3933	0.8730	0	0	0	0	0
Gao	China	0.0673	0.1185	0.5679	71.2137	0.8022	0	0	0	2	0
Garfinkel 1	USA	-0.0223	0.0703	-0.3172	202.3435	1.1963	0	0	0	0	0
Garfinkel 2	USA	0.0910	0.0689	1.3208	210.6500	1.5345	0	0	0	0	0

APPENDIX 15

ETS and Lung Cancer - Meta-Analysis of Dose Response Exposure (or nearest equivalent), 02-NOV-15

Female (Husband's smoking) - Number cigarettes smoked

BASIC DATA USED IN META-ANALYSES

CORRECTED FOR ALL CONFOUNDERS (FRUIT, VEG, FAT, EDUCATION) AND MISCLASSIFICATION

Confounder Differences based on Unweighted Regression

Misclassification: Additive, Concordance: 3.0, MissP: US:0.025, EU:0.025, ASIA:0.1

Study title	Country	Beta	St.Err. Beta	Z	Weight	ETSse	FRU	VEG	FAT	EDU	TEA
GELAC study	Taiwan	0.0924	0.0507	1.8225	389.0309	0.8883	0	0	0	2	0
Geng	China	0.2979	0.1829	1.6288	29.8932	1.0478	0	0	0	0	0
Gorlova	USA	0.0019	0.1395	0.0136	51.3868	1.1005	0	0	0	1	0
He	China	0.3546	0.6211	0.5709	2.5923	0.8152	0	0	2	2	0
Hill (study 1)	New Zealand	-0.0920	0.2183	-0.4214	20.9842	0.7776	0	0	0	0	0
Hill (study 2)	New Zealand	0.1080	0.1682	0.6421	35.3466	0.6455	0	0	0	3	0
Hirayama	Japan	0.0573	0.0833	0.6879	144.1153	0.8998	0	0	0	0	0
Hole	Scotland	0.2726	0.4389	0.6211	5.1912	1.0530	0	0	0	0	0
Humble 1	USA	-0.0249	0.3015	-0.0826	11.0008	1.2885	0	0	0	0	0
IARC: Kreuzer	Germany	-0.2052	0.1394	-1.4720	51.4606	0.8957	0	0	0	0	0
ILCCO	International	0.0258	0.0367	0.7030	742.4511	0.9085	0	0	0	0	0
Inoue	Japan	0.3087	0.2726	1.1324	13.4570	1.1196	0	0	0	0	0
Janerich	USA	-0.2538	0.1133	-2.2401	77.9005	1.1397	0	0	0	0	0
Jee	Korea	0.0172	0.1509	0.1140	43.9159	0.9132	0	1	0	3	0
Jiang	China	0.4092	0.2042	2.0039	23.9822	0.9152	1	1	0	0	0
Johnson	Canada	-0.0390	0.2131	-0.1830	22.0208	0.8225	1	1	0	2	0
Kabat 1	USA	-0.1996	0.2685	-0.7434	13.8711	1.1579	0	0	0	0	0
Kabat 2	USA	-0.1147	0.1211	-0.9472	68.1886	1.3646	0	0	0	2	0
Kalandidi	Greece	0.0737	0.0916	0.8046	119.1816	1.5584	0	0	0	0	0
Kiyohara	Japan	-0.0724	0.2239	-0.3234	19.9477	0.8757	0	0	0	0	0
Koo	China	-0.0019	0.1537	-0.0124	42.3304	1.1884	0	0	0	2	0
Kurahashi	Japan	0.0977	0.1086	0.8996	84.7892	1.1771	0	0	0	0	0
Lagarde	Sweden	-0.0284	0.0987	-0.2877	102.6516	0.8828	0	0	0	3	0
Lam T	China	0.1959	0.0983	1.9929	103.4887	1.0055	0	0	0	0	0
Lam W	China	0.3140	0.1898	1.6544	27.7592	0.9063	0	0	0	0	0
Layard	USA	-0.3177	0.1790	-1.7749	31.2100	1.1466	0	0	0	0	0
Lee	England	-0.1391	0.3106	-0.4478	10.3657	0.8544	0	0	0	0	0
Lee C-H	Taiwan	0.2970	0.1049	2.8313	90.8760	0.9015	0	0	0	2	0
Liang	China	0.1326	0.1055	1.2569	89.8452	0.9083	0	0	0	0	0
Lim	Singapore	-0.0202	0.0654	-0.3089	233.8000	0.9027	0	0	0	0	0
Lin	China	0.4625	0.1154	4.0078	75.0911	0.8642	0	0	0	2	0
Liu Q	China	0.3451	0.2000	1.7255	25.0000	1.0561	0	0	0	2	0
Liu Z	China	-0.2261	0.2716	-0.8325	13.5563	0.6106	0	0	0	0	0
Lopez-Cima	Spain	-0.0574	1.7499	-0.0328	0.3266	0.3069	0	0	0	0	0
Malats	7 Europe+Brazil	0.1562	0.1932	0.8085	26.7908	0.8717	0	0	0	0	0
Masjedi	Iran	0.3349	0.1973	1.6974	25.6889	0.7742	0	0	0	0	0
McGhee	China	0.0885	0.1193	0.7418	70.2618	0.9025	0	0	0	2	0
Nishino	Japan	0.2963	0.2855	1.0378	12.2684	0.8950	1	1	1	0	0
Ohno	Japan	-0.0736	0.1159	-0.6350	74.4446	0.8114	0	0	0	0	0
Pershagen	Sweden	0.0245	0.1624	0.1509	37.9165	0.9097	0	0	0	0	0
Rapiti	India	0.0240	0.2660	0.0902	14.1331	0.8504	0	0	0	0	0
Ren	China	0.0244	0.0567	0.4303	311.0526	0.8365	0	0	0	0	0
Rylander	Sweden	0.0540	0.2948	0.1832	11.5065	0.7290	0	0	0	0	0
Schoenberg	USA	-0.1035	0.1116	-0.9274	80.2919	1.1321	0	1	0	2	0
Schwartz	USA	-0.0569	0.1001	-0.5684	99.8003	1.1194	0	0	0	0	0
Seki	Japan	0.0841	0.0805	1.0447	154.3150	0.8692	0	0	0	0	0
Shen	China	-0.1675	0.1626	-1.0301	37.8233	1.0903	0	0	0	0	0
Shimizu	Japan	-0.0400	0.1556	-0.2571	41.3029	0.9053	0	0	0	0	0
Sobue	Japan	-0.0143	0.1110	-0.1288	81.1622	0.9064	0	0	0	2	0
Speize	USA	0.0746	0.3795	0.1966	6.9435	0.6375	0	0	0	0	0
Stockwell	USA	0.1271	0.1580	0.8044	40.0577	1.1381	0	0	0	2	0
Sun	China	0.0023	0.1098	0.0209	82.9460	0.8954	0	0	0	2	0
Svensson	Sweden	0.0782	0.2851	0.2743	12.3028	0.8673	0	0	0	0	0
Torres-Duran	Spain	-0.2524	0.1237	-2.0404	65.3523	0.9064	0	0	0	0	0
Trichopoulos	Greece	0.2247	0.1068	2.1039	87.6713	1.3389	0	0	0	0	0
Wang L	China	-0.0113	0.1473	-0.0767	46.0887	0.6870	0	0	0	1	0
Wang S	China	0.4671	0.1987	2.3508	25.3282	0.8780	0	0	0	0	0

APPENDIX 15

ETS and Lung Cancer - Meta-Analysis of Dose Response Exposure (or nearest equivalent), 02-NOV-15

Female (Husband's smoking) - Number cigarettes smoked

BASIC DATA USED IN META-ANALYSES

CORRECTED FOR ALL CONFOUNDERS (FRUIT, VEG, FAT, EDUCATION) AND MISCLASSIFICATION

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Misclassification: Additive, Concordance: 3.0, MissP: US:0.025, EU:0.025, ASIA:0.1

Study title	Country	Beta	St.Err. Beta	Z	Weight	ETSse	FRU	VEG	FAT	EDU	TEA
Wang T	China	0.0900	0.1241	0.7252	64.9316	1.0379	0	0	0	0	0
Wen	China	-0.0208	0.1166	-0.1784	73.5534	0.8863	1	1	0	2	0
WHI-OS	USA	-0.1631	0.1355	-1.2037	54.4655	1.1579	0	0	0	0	0
Wu	USA	0.0114	0.2235	0.0510	20.0191	1.1449	0	0	0	0	0
Wu-Williams	China	-0.3358	0.0653	-5.1424	234.5166	0.9047	0	0	0	2	0
Yang	USA	0.2351	0.1433	1.6406	48.6976	1.1548	0	0	0	0	0
Yu	China	0.1186	0.1890	0.6275	27.9947	0.6640	1	1	0	2	0
Zaridze	Russia	0.0627	0.1066	0.5882	88.0006	0.8744	0	0	0	2	0
Zatloukal	Czech Republic	-0.8023	0.4175	-1.9217	5.7370	0.6900	0	0	0	2	0
Zheng	China	0.4571	0.2484	1.8402	16.2068	0.7567	0	0	0	0	0
Zhong	China	-0.0887	0.0912	-0.9726	120.2293	0.9343	1	0	0	1	0

NOTES: BETA SLOPE OF LOG RR ON NCIGS

SE BETA STANDARD ERROR OF BETA

Z RATIO OF BETA TO ITS STANDARD ERROR (APPROXIMATE NORMAL STATISTIC)

WEIGHT INVERSE OF THE VARIANCE OF BETA

ETSse STANDARD ERROR OF ETS EXPOSURE OVER THE CONTROL GROUPS

FRU = 1 DOSE-RESPONSE ANALYSIS ADJUSTED FOR FRUIT

VEG = 1 " " " " VEGETABLES

FAT = 1 " " " " FRUIT

EDU = 1 " " " " INCOME

= 2 " " " " EDUCATION

= 3 " " " " SOCIO-ECONOMIC STATUS

TEA = 0 NO ADJUSTMENT (OR MATCHING) FOR TEA

RANDOM-EFFECTS META-ANALYSES

Dose Response (Beta)
WEIGHTED on Beta
Weights

	Deviance	(DF)
Model 1	98.7878	(92)

	Estimate	S.E.	P	RR	95%CIl	95%CIu
Constant	0.0221	0.0190	N.S.	1.0223	0.9849	1.0611

SEPARATE RANDOM-EFFECTS META-ANALYSES BY REGION

NORTH AMERICA, EUROPE AND NEW ZEALAND

APPENDIX 15

ETS and Lung Cancer - Meta-Analysis of Dose Response Exposure (or nearest equivalent), 02-NOV-15

Female (Husband's smoking) - Number cigarettes smoked

CORRECTED FOR ALL CONFOUNDERS (FRUIT, VEG, FAT, EDUCATION) AND MISCLASSIFICATION
SEPARATE RANDOM-EFFECTS META-ANALYSES BY REGION
Confounder Differences based on Unweighted Regression
Misclassification: Additive, Concordance: 3.0, MissP: US:0.025, EU:0.025, ASIA:0.1

Dose Response (Beta)
WEIGHTED on Beta Weights

	Deviance	(DF)				
Model 1	51.1275	(48)				
	Estimate	**S.E.**	**P**	**RR**	**95%Cll**	**95%Clu**
Constant	-0.0348	0.0251	N.S.	0.9658	0.9194	1.0145

ASIA

Dose Response (Beta)
WEIGHTED on Beta Weights

	Deviance	(DF)				
Model 1	42.7885	(43)				
	Estimate	**S.E.**	**P**	**RR**	**95%Cll**	**95%Clu**
Constant	0.0756	0.0270	++	1.0785	1.0229	1.1372

NORTH AMERICA

Dose Response (Beta)
WEIGHTED on Beta Weights

	Deviance	(DF)				
Model 1	31.7349	(28)				
	Estimate	**S.E.**	**P**	**RR**	**95%Cll**	**95%Clu**
Constant	-0.0523	0.0340	N.S.	0.9491	0.8879	1.0145

EUROPE AND NEW ZEALAND

Dose Response (Beta)
WEIGHTED on Beta Weights

	Deviance	(DF)				
Model 1	18.7270	(19)				
	Estimate	**S.E.**	**P**	**RR**	**95%Cll**	**95%Clu**
Constant	-0.0069	0.0350	N.S.	0.9932	0.9274	1.0636

CHINA AND HONG KONG

Dose Response (Beta)
WEIGHTED on Beta Weights

	Deviance	(DF)				
Model 1	24.1917	(26)				
	Estimate	**S.E.**	**P**	**RR**	**95%Cll**	**95%Clu**
Constant	0.0810	0.0433	(+)	1.0844	0.9962	1.1804

REST OF ASIA

Dose Response (Beta)
WEIGHTED on Beta Weights

	Deviance	(DF)				
Model 1	13.6923	(16)				
	Estimate	**S.E.**	**P**	**RR**	**95%Cll**	**95%Clu**
Constant	0.0659	0.0223	++	1.0681	1.0225	1.1157

SEPARATE RANDOM-EFFECTS META-ANALYSES BY YEAR OF PUBLICATION

PUBLISHED IN 1980S

APPENDIX 15

ETS and Lung Cancer - Meta-Analysis of Dose Response Exposure (or nearest equivalent), 02-NOV-15

Female (Husband's smoking) - Number cigarettes smoked

CORRECTED FOR ALL CONFOUNDERS (FRUIT, VEG, FAT, EDUCATION) AND MISCLASSIFICATION
SEPARATE RANDOM-EFFECTS META-ANALYSES BY YEAR OF PUBLICATION
Confounder Differences based on Unweighted Regression
Misclassification: Additive, Concordance: 3.0, MissP: US:0.025, EU:0.025, ASIA:0.1

Dose Response (Beta) WEIGHTED on Beta Weights

	Deviance	(DF)				
Model 1	23.0607	(25)				
	Estimate	**S.E.**	**P**	**RR**	**95%CIl**	**95%CIu**
Constant	0.0630	0.0274	+	1.0650	1.0094	1.1237

PUBLISHED IN 1990S

Dose Response (Beta) WEIGHTED on Beta Weights

	Deviance	(DF)				
Model 1	27.2658	(26)				
	Estimate	**S.E.**	**P**	**RR**	**95%CIl**	**95%CIu**
Constant	-0.0211	0.0331	N.S.	0.9791	0.9175	1.0448

PUBLISHED IN 2000S

Dose Response (Beta) WEIGHTED on Beta Weights

	Deviance	(DF)				
Model 1	24.7267	(25)				
	Estimate	**S.E.**	**P**	**RR**	**95%CIl**	**95%CIu**
Constant	0.0511	0.0328	N.S.	1.0524	0.9869	1.1223

PUBLISHED IN 2010S

Dose Response (Beta) WEIGHTED on Beta Weights

	Deviance	(DF)				
Model 1	24.2973	(13)				
	Estimate	**S.E.**	**P**	**RR**	**95%CIl**	**95%CIu**
Constant	0.0036	0.0546	N.S.	1.0036	0.9018	1.1169

SEPARATE RANDOM-EFFECTS META-ANALYSES BY NUMBER OF LUNG CANCER CASES

<100 CASES

Dose Response (Beta) WEIGHTED on Beta Weights

	Deviance	(DF)				
Model 1	48.6664	(48)				
	Estimate	**S.E.**	**P**	**RR**	**95%CIl**	**95%CIu**
Constant	0.0604	0.0334	(+)	1.0623	0.9950	1.1340

100-199 CASES

Dose Response (Beta) WEIGHTED on Beta Weights

	Deviance	(DF)				
Model 1	23.7093	(21)				
	Estimate	**S.E.**	**P**	**RR**	**95%CIl**	**95%CIu**
Constant	-0.0158	0.0362	N.S.	0.9843	0.9170	1.0566

200-399 CASES

APPENDIX 15
ETS and Lung Cancer - Meta-Analysis of Dose Response Exposure (or nearest equivalent), 02-NOV-15
Female (Husband's smoking) - Number cigarettes smoked

CORRECTED FOR ALL CONFOUNDERS (FRUIT, VEG, FAT, EDUCATION) AND MISCLASSIFICATION
SEPARATE RANDOM-EFFECTS META-ANALYSES BY NUMBER OF LUNG CANCER CASES
Confounder Differences based on Unweighted Regression
Misclassification: Additive, Concordance: 3.0, MissP: US:0.025, EU:0.025, ASIA:0.1

Dose Response (Beta)
WEIGHTED on Beta
Weights

	Deviance	(DF)				
Model 1	12.5834	(12)				
	Estimate	**S.E.**	**P**	**RR**	**95%CIl**	**95%CIu**
Constant	0.0963	0.0405	+	1.1011	1.0172	1.1920

400+ CASES
Dose Response (Beta)
WEIGHTED on Beta
Weights

	Deviance	(DF)				
Model 1	9.0128	(8)				
	Estimate	**S.E.**	**P**	**RR**	**95%CIl**	**95%CIu**
Constant	-0.0447	0.0391	N.S.	0.9563	0.8858	1.0324

SEPARATE RANDOM-EFFECTS META-ANALYSES BY DOSE-RESPONSE OR NOT

RESULTS FOR DOSE-RESPONSE
Dose Response (Beta)
WEIGHTED on Beta
Weights

	Deviance	(DF)				
Model 1	22.8198	(23)				
	Estimate	**S.E.**	**P**	**RR**	**95%CIl**	**95%CIu**
Constant	0.0431	0.0242	(+)	1.0441	0.9956	1.0948

NO RESULTS FOR DOSE-RESPONSE
Dose Response (Beta)
WEIGHTED on Beta
Weights

	Deviance	(DF)				
Model 1	74.3546	(68)				
	Estimate	**S.E.**	**P**	**RR**	**95%CIl**	**95%CIu**
Constant	0.0113	0.0247	N.S.	1.0114	0.9635	1.0616

SEPARATE RANDOM-EFFECTS META-ANALYSES BY AGE ADJUSTMENT OR NOT

ADJUSTED (OR MATCHED) FOR AGE
Dose Response (Beta)
WEIGHTED on Beta
Weights

	Deviance	(DF)				
Model 1	77.2656	(74)				
	Estimate	**S.E.**	**P**	**RR**	**95%CIl**	**95%CIu**
Constant	0.0058	0.0200	N.S.	1.0059	0.9671	1.0461

NOT ADJUSTED (OR MATCHED) FOR AGE
Dose Response (Beta)
WEIGHTED on Beta
Weights

	Deviance	(DF)				
Model 1	18.4306	(17)				
	Estimate	**S.E.**	**P**	**RR**	**95%CIl**	**95%CIu**
Constant	0.1142	0.0540	+	1.1210	1.0083	1.2462

APPENDIX 15

ETS and Lung Cancer - Meta-Analysis of Dose Response Exposure (or nearest equivalent), 02-NOV-15

Female (Husband's smoking) - Number cigarettes smoked

CORRECTED FOR ALL CONFOUNDERS (FRUIT, VEG, FAT, EDUCATION) AND MISCLASSIFICATION
SEPARATE RANDOM-EFFECTS META-ANALYSES BY STUDY TYPE
Confounder Differences based on Unweighted Regression
Misclassification: Additive, Concordance: 3.0, MissP: US:0.025, EU:0.025, ASIA:0.1

CASE-CONTROL STUDIES

Dose Response (Beta)
WEIGHTED on Beta Weights

	Deviance	(DF)				
Model 1	85.3957	(76)				
	Estimate	**S.E.**	**P**	**RR**	**95%CIl**	**95%CIu**
Constant	0.0242	0.0221	N.S.	1.0244	0.9811	1.0698

PROSPECTIVE STUDIES

Dose Response (Beta)
WEIGHTED on Beta Weights

	Deviance	(DF)				
Model 1	7.8954	(15)				
	Estimate	**S.E.**	**P**	**RR**	**95%CIl**	**95%CIu**
Constant	0.0107	0.0315	N.S.	1.0108	0.9503	1.0752

APPENDIX 15

ETS and Lung Cancer - Meta-Analysis of Dose Response Exposure (or nearest equivalent), 02-NOV-15

Female (Husband's smoking) - Number cigarettes smoked

BASIC DATA USED IN META-ANALYSES

CORRECTED FOR ALL CONFOUNDERS (FRUIT, VEG, FAT, EDUCATION) AND MISCLASSIFICATION

Confounder Differences based on Weighted Regression

Misclassification: Additive, Concordance: 3.0, MissP: US:0.025, EU:0.025, ASIA:0.1

Study title	Country	RR	RRL	RRU	CA1	CA0	CO1	CO0	NCigs
Akiba	Japan	1.2528	0.5890	2.5125	32.2856	13.1085	99.8671	50.7972	1.0000
Akiba	Japan	1.3861	0.6362	3.0110	22.1565	13.1085	61.9451	50.7972	2.1350
Akiba	Japan	1.8219	0.4680	7.3985	3.6754	13.1085	7.8174	50.7972	3.8390
Al-Zoughool	Canada	0.3873	0.1489	0.9731	5.8592	22.7805	113.2615	170.5310	1.8175
Asomaning	USA	0.7378	0.2133	2.5431	10.4751	4.7356	42.9293	14.3197	2.3157
Boffetta 2	7 countries	0.9193	0.4472	1.7954	22.7689	24.4080	49.3203	48.6050	1.8175
Boffetta	7 countries	0.9478	0.7268	1.2469	286.6903	115.6333	529.4872	202.4252	1.3380
Boffetta	7 countries	0.5139	0.3041	0.8453	23.7528	115.6333	80.9121	202.4252	2.5880
Boffetta	7 countries	1.1278	0.6892	1.8514	32.9091	115.6333	51.0802	202.4252	4.3060
Brenner	Canada	0.3766	0.2330	0.5991	50.6315	35.1579	490.2385	128.2023	1.8175
Brownson 1	USA	1.6330	0.3524	7.2159	3.3620	11.7670	5.5718	31.8460	2.3157
Brownson 2	USA	0.8155	0.6341	1.0069	182.7416	212.8356	548.8564	521.3195	2.3157
Buffler	USA	0.6020	0.2293	1.5953	21.4057	6.9376	113.3854	22.1217	2.3157
Butler	USA	1.9401	0.4484	8.4527	2.5984	5.6676	10617.3341	44931.4800	2.3157
Cardenas	USA	1.0438	0.4629	2.1395	9.4439	21.4085	12812.7576	30316.9677	1.0040
Cardenas	USA	1.0660	0.5883	2.0657	17.8462	21.4085	23708.6119	30316.9677	2.2670
Cardenas	USA	1.5166	0.7183	3.1932	10.1738	21.4085	9499.9952	30316.9677	4.3140
Chan	China	0.6070	0.3196	1.1457	22.6957	41.3581	50.3274	55.6684	1.8175
Choi	Korea	1.5650	0.8729	2.7885	45.5268	25.1257	82.8990	71.6005	1.8175
Correa	USA	1.7496	0.5248	5.7884	7.6799	5.1811	35.6602	42.0910	2.3157
De Waard	Netherlands	2.4680	0.7710	7.8865	17.0666	3.7337	112.1727	60.5647	1.8175
Du	China	0.6413	0.3048	1.3491	12.5439	26.6162	64.9551	88.3878	1.0000
Du	China	1.3130	0.6895	2.5004	23.5992	26.6162	59.6866	88.3878	2.6030
Enstrom	USA	0.8855	0.6153	1.2659	94.3639	42.5201	14340.1062	5721.6047	2.3157
EPIC Adulthood	Western Europe	0.7794	0.2919	2.1122	8.1522	7.5495	12499.9630	9022.0100	1.8175
Fang	China	1.7050	0.9687	2.9927	18.2417	85.2573	69.2409	551.7536	1.8175
Fontham	USA	1.1262	0.8895	1.4259	287.6847	162.4081	529.6097	336.7234	2.3157
Franco-Marina	Mexico	1.7251	0.8987	3.3204	20.5045	36.3527	38.0575	116.3960	1.8175
Gallegos	Mexico	7.9164	0.7921	79.1377	12.1799	0.8204	36.5651	19.4976	1.8175
Gao	China	1.1962	0.7812	1.8179	149.3380	44.7786	217.7881	78.1175	1.8175
Garfinkel 1	USA	1.2367	0.8344	1.8471	38.2703	66.6257	38500.4089	82888.9382	1.0040
Garfinkel 1	USA	1.0226	0.6995	1.4931	44.5788	66.6257	54232.0804	82888.9382	2.7520
Garfinkel 2	USA	0.8119	0.3832	1.7206	10.8459	41.8579	42.9508	134.5856	1.0040
Garfinkel 2	USA	0.9965	0.5786	1.7165	28.6968	41.8579	92.5902	134.5856	2.2670
Garfinkel 2	USA	1.7045	0.9319	3.1173	24.0732	41.8579	45.4117	134.5856	4.3140
GELAC study	Taiwan	1.2484	1.0454	1.5000	434.2426	536.5737	381.8220	588.9942	1.8175
Geng	China	1.3676	0.4635	4.0550	8.0446	11.9843	15.1544	30.8747	0.4850
Geng	China	1.8337	0.5186	6.4758	5.7253	11.9843	8.0439	30.8747	1.2730
Geng	China	2.4074	0.9130	6.3698	14.9078	11.9843	15.9534	30.8747	2.6030
Gorlova	USA	1.0494	0.5572	1.9771	56.6384	27.5078	58.7935	29.9642	2.3157
He	China	1.9982	0.2173	18.0909	4.8199	0.9292	325.7967	125.5082	1.8175
Hill (study 1)	New Zealand	0.8939	0.4039	1.9486	7.3308	40.3497	75380.0179	370892.5590	1.8175
Hill (study 2)	New Zealand	1.2856	0.6996	2.3320	11.9910	91.2838	53390.3099	522538.4340	1.8175
Hirayama	Japan	1.2959	0.8752	1.9275	135.7583	30.0600	62054.3555	17805.8931	0.8600
Hirayama	Japan	1.4048	0.8857	2.2334	44.4132	30.0600	18726.6499	17805.8931	2.6030
Hole	Scotland	1.2851	0.1152	14.5239	2.2997	0.9162	765.1727	391.7378	0.2080
Hole	Scotland	2.3711	0.1747	31.8679	1.4736	0.9162	265.7294	391.7378	2.4090
Humble 1	USA	1.4875	0.3286	7.0885	4.4345	6.0864	6.6468	13.5704	1.5820
Humble 1	USA	0.7973	0.0976	7.1656	1.4098	6.0864	3.9423	13.5704	3.3920
IARC: Kreuzer	Germany	0.7348	0.4509	1.2162	46.6931	44.0299	122.5232	84.8971	1.8175
ILCCO	International	1.1102	0.9747	1.2660	611.1056	584.7142	1758.2883	1867.7961	1.8175
Inoue	Japan	2.5342	0.3001	6.6073	7.1227	3.1067	11.9198	13.1756	1.0000
Inoue	Japan	2.9494	0.7721	15.1341	9.5026	3.1067	13.6643	13.1756	2.6030
Janerich	USA	0.5982	0.3588	0.9999	56.1958	63.3564	71.3992	48.1547	2.3157
Jee	Korea	1.9533	1.0670	3.8351	54.2837	11.3460	80009.6175	32665.7680	1.0000

APPENDIX 15

ETS and Lung Cancer - Meta-Analysis of Dose Response Exposure (or nearest equivalent), 02-NOV-15

Female (Husband's smoking) - Number cigarettes smoked

BASIC DATA USED IN META-ANALYSES

CORRECTED FOR ALL CONFOUNDERS (FRUIT, VEG, FAT, EDUCATION) AND MISCLASSIFICATION

Confounder Differences based on Weighted Regression

Misclassification: Additive, Concordance: 3.0, MissP: US:0.025, EU:0.025, ASIA:0.1

Study title	Country	RR	RRL	RRU	CA1	CA0	CO1	CO0	NCigs
Jee	Korea	1.4106	0.6467	3.1590	13.2156	11.3460	26973.2212	32665.7680	2.6030
Jiang	China	2.1885	1.0578	4.5288	42.2279	20.1005	30.5276	31.8012	1.8175
Johnson	Canada	0.9840	0.4585	2.0911	25.1910	10.2782	271.2646	108.9052	1.8175
Kabat 1	USA	0.6740	0.1978	2.2535	10.4416	10.3284	12.9812	8.6543	2.3157
Kabat 2	USA	0.7136	0.3477	1.4730	16.5747	24.4923	56.4816	59.5621	1.6540
Kabat 2	USA	0.7809	0.3234	1.8915	9.0852	24.4923	28.2927	59.5621	3.6380
Kalandidi	Greece	1.5056	0.7715	2.9384	33.3966	26.2972	38.0744	45.1396	1.3380
Kalandidi	Greece	1.6790	0.7782	3.6225	21.0994	26.2972	21.5710	45.1396	2.9020
Kalandidi	Greece	1.4283	0.4851	4.2056	7.5276	26.2972	9.0463	45.1396	5.3350
Kiyohara	Japan	0.9316	0.4198	2.0667	28.5136	16.7803	39.9624	21.9086	1.8175
Koo	China	2.2575	0.8726	5.8597	13.8744	17.9642	12.3935	36.2261	0.7080
Koo	China	1.6081	0.7097	3.6554	19.6292	17.9642	24.6157	36.2261	1.7670
Koo	China	1.0324	0.3626	2.8937	7.6553	17.9642	14.9526	36.2261	3.1830
Kurahashi	Japan	0.9895	0.4887	2.0032	11.5744	23.1817	45620.6895	90408.7414	1.0000
Kurahashi	Japan	1.3582	0.7787	2.3747	26.4666	23.1817	75998.5706	90408.7414	2.6030
Lagarde	Sweden	1.0109	0.7136	1.4372	64.7159	104.4521	234.4966	382.6048	1.8175
Lam T	China	2.1110	1.0868	4.0819	21.2736	75.7360	21.0781	158.4088	0.7080
Lam T	China	1.7073	1.0562	2.7539	45.1221	75.7360	55.2792	158.4088	1.7670
Lam T	China	1.7913	0.8631	3.7411	15.4115	75.7360	17.9954	158.4088	3.1830
Lam W	China	1.8603	0.9478	3.6645	29.3900	19.7467	52.4103	65.5080	1.8175
Layard	USA	0.5592	0.2037	1.5353	4.6218	22.2888	315.8965	851.8688	0.8190
Layard	USA	0.4956	0.1950	1.2593	5.6168	22.2888	433.1196	851.8688	2.6640
Lee	England	0.8297	0.2753	2.5075	13.2480	7.4530	29.1047	13.5855	1.8175
Lee C-H	Taiwan	1.7994	1.2380	2.6145	140.1527	59.1150	188.1146	142.7706	1.8175
Liang	China	1.3437	0.9229	1.9564	122.8683	79.7730	133.6010	116.5586	1.8175
Lim	Singapore	1.0236	0.8112	1.2916	168.4196	208.8236	533.0995	676.5582	1.8175
Lin	China	2.4207	1.6046	3.6508	98.6393	78.4145	72.0657	138.6808	1.8175
Liu Q	China	0.6611	0.2073	2.1768	5.9207	12.6297	15.3002	21.5775	1.0000
Liu Q	China	2.4992	0.9161	7.1015	16.7063	12.6297	11.4207	21.5775	2.6030
Liu Z	China	0.7043	0.2664	1.8461	31.7268	6.6563	125.1122	18.4857	1.8175
Lopez-Cima	Spain	0.9918	0.0020	516.1995	4.4400	0.1300	17.8800	0.5100	1.8175
Malats	7 Europe+Brazil	1.4022	0.7034	2.7835	32.6453	43.7982	21.9848	41.3581	1.8175
Masjedi	Iran	1.9309	0.9561	3.8992	19.8421	33.3962	27.1042	88.0832	1.8175
McGhee	China	1.2443	0.8169	1.9084	63.8214	66.6709	109.3506	142.1398	1.8175
Nishino	Japan	1.7298	0.6103	4.6642	8.6393	6.5136	20241.2868	26398.5474	1.8175
Ohno	Japan	0.9284	0.6139	1.4017	124.9576	50.6833	219.7985	82.7676	1.8175
Pershagen	Sweden	1.1076	0.6280	1.9942	31.3318	26.0688	125.4718	115.6268	1.8175
Rapiti	India	1.1069	0.4313	2.8608	10.5587	20.8923	16.1098	35.2841	1.8175
Ren	China	1.1072	0.9064	1.3576	580.4094	229.1781	724.7294	316.8378	1.8175
Rylander	Sweden	1.1761	0.4149	3.3406	5.3415	18.1506	30.6283	122.3997	1.8175
Schoenberg	USA	0.8404	0.5071	1.3917	42.9631	33.0703	198.5988	128.4743	2.3157
Schwartz	USA	0.9338	0.5931	1.4698	100.4485	62.4264	98.6025	57.2250	2.3157
Seki	Japan	1.2316	0.9209	1.6343	174.6891	77.5912	1010.8307	552.9544	1.8175
Shen	China	0.6354	0.2042	2.0346	10.7143	13.9520	12.3375	10.2081	0.4850
Shen	China	0.9892	0.2972	3.2305	11.7074	13.9520	8.6593	10.2081	1.2730
Shen	China	0.6196	0.2407	1.6045	28.5869	13.9520	33.7557	10.2081	2.6030
Shimizu	Japan	0.9867	0.5666	1.7159	43.6692	35.0211	79.5636	62.9565	1.8175
Sobue	Japan	1.0345	0.6956	1.5319	65.3655	53.7477	326.7321	277.9309	1.8175
Speize	USA	1.2646	0.2056	6.5340	19.2947	1.3757	137632.8440	12409.5628	2.3157
Stockwell	USA	1.4198	0.6711	2.8159	38.2456	17.6337	49.5711	32.4495	2.3157
Sun	China	1.0648	0.7219	1.5781	126.8409	82.3265	123.6877	85.4809	1.8175
Svensson	Sweden	1.2208	0.4423	3.3697	14.6214	6.3036	70.1786	36.9351	1.8175
Torres-Duran	Spain	0.6746	0.4351	1.0498	47.4919	85.6367	102.6084	124.8138	1.8175
Trichopoulos	Greece	0.5613	0.1208	2.6082	1.9972	24.3310	15.7953	108.0081	0.7080
Trichopoulos	Greece	2.4281	1.2232	4.8198	21.4820	24.3310	39.2740	108.0081	1.7670
Trichopoulos	Greece	3.8124	1.2553	11.5785	6.8617	24.3310	7.9897	108.0081	2.5880
Trichopoulos	Greece	1.7453	0.6470	4.7077	6.7639	24.3310	17.2039	108.0081	4.3060

APPENDIX 15

ETS and Lung Cancer - Meta-Analysis of Dose Response Exposure (or nearest equivalent), 02-NOV-15

Female (Husband's smoking) - Number cigarettes smoked

BASIC DATA USED IN META-ANALYSES

CORRECTED FOR ALL CONFOUNDERS (FRUIT, VEG, FAT, EDUCATION) AND MISCLASSIFICATION

Confounder Differences based on Weighted Regression

Misclassification: Additive, Concordance: 3.0, MissP: US:0.025, EU:0.025, ASIA:0.1

Study title	Country	RR	RRL	RRU	CA1	CA0	CO1	CO0	NCigs
Wang L	China	1.0213	0.5925	1.6925	122.5411	24.9211	248.4811	51.6102	1.8175
Wang S	China	2.4409	1.2050	4.9636	64.2053	14.9059	57.8892	32.8045	1.8175
Wang T	China	0.3421	0.1069	1.1406	4.1427	42.0109	12.9266	44.8421	0.4850
Wang T	China	1.2712	0.6859	2.3439	41.9957	42.0109	35.2616	44.8421	1.2730
Wang T	China	1.2381	0.6507	2.3475	35.3872	42.0109	30.5088	44.8421	2.6030
Wen	China	1.0128	0.6698	1.5357	57.6583	36.3195	35279.2270	22508.2146	1.8175
WHI-OS	USA	0.7350	0.3990	1.3547	17.8277	24.2563	31846.2589	31846.2595	2.3157
Wu	USA	1.0891	0.4231	3.2121	14.7707	9.0399	28.0677	18.7083	2.3157
Wu-Williams	China	0.5850	0.4873	0.7741	206.6647	289.2149	393.6097	322.2617	1.8175
Yang	USA	1.8158	0.9463	3.4780	55.0165	23.6429	45.8177	35.7520	2.3157
Yu	China	1.3002	0.6634	2.5511	108.0875	15.5386	142.8033	26.6924	1.8175
Zaridze	Russia	1.6287	1.0687	2.4741	65.9166	75.1854	88.4773	164.3640	0.7080
Zaridze	Russia	1.2692	0.7880	2.0541	39.1741	75.1854	67.4727	164.3640	2.2930
Zatloukal	Czech Republic	0.2626	0.0630	1.0876	2.0635	37.2152	72.4794	343.2225	1.8175
Zheng	China	2.4094	0.9953	5.8488	53.9580	6.3796	156.5338	44.5923	1.8175
Zhong	China	1.3743	0.8783	2.1724	98.9116	47.1654	114.4888	75.0261	0.7080
Zhong	China	0.8593	0.5645	1.3565	99.3889	47.1654	183.9873	75.0261	1.7670
Zhong	China	1.2880	0.6271	2.4563	20.8555	47.1654	25.7570	75.0261	3.1830

NOTES: RR,RL,RU RELATIVE RISKS AND LOWER AND UPPER CONFIDENCE INTERVALS

CA1,CA0 NUMBERS (OR PSEUDO-NUMBERS) OF EXPOSED AND UNEXPOSED CASES

CO1,CO0 NUMBERS (OR PSEUDO-NUMBERS) OF EXPOSED AND UNEXPOSED CONTROLS

NCIGS MIDPOINT OF NUMBER OF CIGARETTES SMOKED BY HUSBAND (IN UNITS OF 10)

Study title	Country	Beta	St.Err. Beta	Z	Weight	ETSse	FRU	VEG	FAT	EDU	TEA
Akiba	Japan	0.1441	0.1454	0.9911	47.3011	0.9896	0	0	0	0	0
Al-Zoughool	Canada	-0.5220	0.2634	-1.9818	14.4135	0.8916	0	0	0	1	0
Asomaning	USA	-0.1313	0.2730	-0.4810	13.4176	1.0091	0	0	0	0	0
Boffetta 2	7 countries	-0.0463	0.1951	-0.2373	26.2715	0.9130	0	0	0	0	0
Boffetta	7 countries	-0.0274	0.0546	-0.5018	335.4399	1.1768	0	0	0	0	0
Brenner	Canada	-0.5373	0.1325	-4.0551	56.9598	0.7374	0	0	0	0	0
Brownson 1	USA	0.2118	0.3326	0.6368	9.0397	0.8345	0	0	0	1	0
Brownson 2	USA	-0.0881	0.0509	-1.7308	385.9797	1.1579	0	0	0	0	0
Buffler	USA	-0.2192	0.2137	-1.0257	21.8973	0.8581	0	0	0	0	0
Butler	USA	0.2862	0.3235	0.8847	9.5555	0.9215	0	0	0	0	0
Cardenas	USA	0.0855	0.0842	1.0154	141.0509	1.4556	0	1	1	2	0
Chan	China	-0.2747	0.1792	-1.5329	31.1404	0.9109	0	0	0	0	0
Choi	Korea	0.2464	0.1630	1.5117	37.6378	0.9091	0	0	0	0	0
Correa	USA	0.2416	0.2645	0.9134	14.2938	1.1582	0	0	0	0	0
De Waard	Netherlands	0.4971	0.3264	1.5230	9.3864	0.8696	0	0	0	0	0
Du	China	0.1173	0.1260	0.9310	62.9882	1.0879	0	0	0	0	0
Enstrom	USA	-0.0525	0.0795	-0.6604	158.2216	1.0456	1	0	0	2	0
EPIC Adulthood	Western Europe	-0.1371	0.2778	-0.4935	12.9579	0.8968	1	1	1	2	0
Fang	China	0.2936	0.1583	1.8547	39.9060	0.5724	0	1	0	1	0
Fontham	USA	0.0513	0.0520	0.9865	369.8225	1.1293	1	1	0	2	0
Franco-Marina	Mexico	0.3000	0.1834	1.6358	29.7304	0.7856	0	0	0	0	0
Gallegos	Mexico	1.1383	0.6463	1.7613	2.3940	0.8730	0	0	0	0	0
Gao	China	0.0986	0.1185	0.8321	71.2137	0.8022	0	0	0	2	0
Garfinkel 1	USA	0.0052	0.0702	0.0741	202.9204	1.1963	0	0	0	0	0
Garfinkel 2	USA	0.1127	0.0689	1.6357	210.6500	1.5345	0	0	0	0	0

APPENDIX 15

ETS and Lung Cancer - Meta-Analysis of Dose Response Exposure (or nearest equivalent), 02-NOV-15

Female (Husband's smoking) - Number cigarettes smoked

BASIC DATA USED IN META-ANALYSES

CORRECTED FOR ALL CONFOUNDERS (FRUIT, VEG, FAT, EDUCATION) AND MISCLASSIFICATION

Confounder Differences based on Weighted Regression

Misclassification: Additive, Concordance: 3.0, MissP: US:0.025, EU:0.025, ASIA:0.1

Study title	Country	Beta	St.Err. Beta	Z	Weight	ETSse	FRU	VEG	FAT	EDU	TEA
GELAC study	Taiwan	0.1221	0.0507	2.4083	389.0309	0.8883	0	0	0	2	0
Geng	China	0.3258	0.1828	1.7823	29.9259	1.0478	0	0	0	0	0
Gorlova	USA	0.0208	0.1395	0.1491	51.3868	1.1005	0	0	0	1	0
He	China	0.3809	0.6207	0.6137	2.5956	0.8152	0	0	2	2	0
Hill (study 1)	New Zealand	-0.0617	0.2209	-0.2793	20.4931	0.7776	0	0	0	0	0
Hill (study 2)	New Zealand	0.1382	0.1690	0.8178	35.0128	0.6455	0	0	0	3	0
Hirayama	Japan	0.0964	0.0829	1.1628	145.5094	0.8998	0	0	0	0	0
Hole	Scotland	0.3072	0.4364	0.7039	5.2509	1.0530	0	0	0	0	0
Humble 1	USA	0.0063	0.3010	0.0209	11.0374	1.2885	0	0	0	0	0
IARC: Kreuzer	Germany	-0.1695	0.1393	-1.2168	51.5345	0.8957	0	0	0	0	0
ILCCO	International	0.0575	0.0367	1.5668	742.4511	0.9085	0	0	0	0	0
Inoue	Japan	0.3287	0.2713	1.2116	13.5863	1.1196	0	0	0	0	0
Janerich	USA	-0.2219	0.1129	-1.9655	78.4535	1.1397	0	0	0	0	0
Jee	Korea	0.0493	0.1506	0.3274	44.0910	0.9132	0	1	0	3	0
Jiang	China	0.4309	0.2041	2.1112	24.0057	0.9152	1	1	0	0	0
Johnson	Canada	-0.0089	0.2130	-0.0418	22.0415	0.8225	1	1	0	2	0
Kabat 1	USA	-0.1704	0.2680	-0.6358	13.9229	1.1579	0	0	0	0	0
Kabat 2	USA	-0.0851	0.1209	-0.7039	68.4144	1.3646	0	0	0	2	0
Kalandidi	Greece	0.0953	0.0916	1.0404	119.1816	1.5584	0	0	0	0	0
Kiyohara	Japan	-0.0390	0.2237	-0.1743	19.9833	0.8757	0	0	0	0	0
Koo	China	0.0254	0.1539	0.1650	42.2204	1.1884	0	0	0	2	0
Kurahashi	Japan	0.1231	0.1084	1.1356	85.1023	1.1771	0	0	0	0	0
Lagarde	Sweden	0.0060	0.0983	0.0610	103.4887	0.8828	0	0	0	3	0
Lam T	China	0.2243	0.0984	2.2795	103.2785	1.0055	0	0	0	0	0
Lam W	China	0.3415	0.1898	1.7993	27.7592	0.9063	0	0	0	0	0
Layard	USA	-0.2760	0.1778	-1.5523	31.6327	1.1466	0	0	0	0	0
Lee	England	-0.1027	0.3101	-0.3312	10.3991	0.8544	0	0	0	0	0
Lee C-H	Taiwan	0.3232	0.1049	3.0810	90.8760	0.9015	0	0	0	2	0
Liang	China	0.1626	0.1055	1.5412	89.8452	0.9083	0	0	0	0	0
Lim	Singapore	0.0128	0.0653	0.1960	234.5166	0.9027	0	0	0	0	0
Lin	China	0.4864	0.1154	4.2149	75.0911	0.8642	0	0	0	2	0
Liu Q	China	0.3719	0.2002	1.8576	24.9501	1.0561	0	0	0	2	0
Liu Z	China	-0.1929	0.2717	-0.7100	13.5463	0.6106	0	0	0	0	0
Lopez-Cima	Spain	-0.0039	1.7473	-0.0022	0.3275	0.3069	0	0	0	0	0
Malats	7 Europe+Brazil	0.1860	0.1931	0.9632	26.8186	0.8717	0	0	0	0	0
Masjedi	Iran	0.3620	0.1973	1.8348	25.6889	0.7742	0	0	0	0	0
McGhee	China	0.1203	0.1191	1.0101	70.4979	0.9025	0	0	0	2	0
Nishino	Japan	0.3015	0.2855	1.0560	12.2684	0.8950	1	1	1	0	0
Ohno	Japan	-0.0409	0.1159	-0.3529	74.4446	0.8114	0	0	0	0	0
Pershagen	Sweden	0.0562	0.1622	0.3465	38.0100	0.9097	0	0	0	0	0
Rapiti	India	0.0559	0.2656	0.2105	14.1757	0.8504	0	0	0	0	0
Ren	China	0.0560	0.0567	0.9877	311.0526	0.8365	0	0	0	0	0
Rylander	Sweden	0.0892	0.2928	0.3046	11.6643	0.7290	0	0	0	0	0
Schoenberg	USA	-0.0751	0.1112	-0.6754	80.8706	1.1321	0	1	0	2	0
Schwartz	USA	-0.0296	0.1000	-0.2960	100.0000	1.1194	0	0	0	0	0
Seki	Japan	0.1146	0.0805	1.4236	154.3150	0.8692	0	0	0	0	0
Shen	China	-0.1340	0.1618	-0.8282	38.1982	1.0903	0	0	0	0	0
Shimizu	Japan	-0.0074	0.1555	-0.0476	41.3561	0.9053	0	0	0	0	0
Sobue	Japan	0.0187	0.1108	0.1688	81.4555	0.9064	0	0	0	2	0
Speize	USA	0.1014	0.3811	0.2661	6.8853	0.6375	0	0	0	0	0
Stockwell	USA	0.1514	0.1580	0.9582	40.0577	1.1381	0	0	0	2	0
Sun	China	0.0345	0.1098	0.3142	82.9460	0.8954	0	0	0	2	0
Svensson	Sweden	0.1098	0.2850	0.3853	12.3115	0.8673	0	0	0	0	0
Torres-Duran	Spain	-0.2166	0.1236	-1.7524	65.4580	0.9064	0	0	0	0	0
Trichopoulos	Greece	0.2442	0.1071	2.2801	87.1808	1.3389	0	0	0	0	0
Wang L	China	0.0116	0.1473	0.0788	46.0887	0.6870	0	0	0	1	0
Wang S	China	0.4910	0.1987	2.4711	25.3282	0.8780	0	0	0	0	0

APPENDIX 15

ETS and Lung Cancer - Meta-Analysis of Dose Response Exposure (or nearest equivalent), 02-NOV-15

Female (Husband's smoking) - Number cigarettes smoked

BASIC DATA USED IN META-ANALYSES

CORRECTED FOR ALL CONFOUNDERS (FRUIT, VEG, FAT, EDUCATION) AND MISCLASSIFICATION

Confounder Differences based on Weighted Regression

Misclassification: Additive, Concordance: 3.0, MissP: US:0.025, EU:0.025, ASIA:0.1

Study title	Country	Beta	St.Err. Beta	Z	Weight	ETSse	FRU	VEG	FAT	EDU	TEA
Wang T	China	0.1225	0.1241	0.9871	64.9316	1.0379	0	0	0	0	0
Wen	China	0.0070	0.1165	0.0601	73.6798	0.8863	1	1	0	2	0
WHI-OS	USA	-0.1330	0.1347	-0.9874	55.1144	1.1579	0	0	0	0	0
Wu	USA	0.0369	0.2233	0.1652	20.0550	1.1449	0	0	0	0	0
Wu-Williams	China	-0.2949	0.0650	-4.5369	236.6864	0.9047	0	0	0	2	0
Yang	USA	0.2576	0.1434	1.7964	48.6297	1.1548	0	0	0	0	0
Yu	China	0.1444	0.1891	0.7636	27.9651	0.6640	1	1	0	2	0
Zaridze	Russia	0.0997	0.1066	0.9353	88.0006	0.8744	0	0	0	2	0
Zatloukal	Czech Republic	-0.7358	0.3999	-1.8400	6.2531	0.6900	0	0	0	2	0
Zheng	China	0.4838	0.2486	1.9461	16.1807	0.7567	0	0	0	0	0
Zhong	China	-0.0661	0.0911	-0.7256	120.4934	0.9343	1	0	0	1	0

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NOTES: BETA       SLOPE OF LOG RR ON NCIGS

       SE BETA    STANDARD ERROR OF BETA

       Z          RATIO OF BETA TO ITS STANDARD ERROR (APPROXIMATE NORMAL STATISTIC)

       WEIGHT     INVERSE OF THE VARIANCE OF BETA

       ETSse      STANDARD ERROR OF ETS EXPOSURE OVER THE CONTROL GROUPS

       FRU = 1    DOSE-RESPONSE ANALYSIS ADJUSTED FOR FRUIT

       VEG = 1           "         "        "      " VEGETABLES

       FAT = 1           "         "        "      " FRUIT

       EDU = 1           "         "        "      " INCOME

           = 2           "         "        "      " EDUCATION

           = 3           "         "        "      " SOCIO-ECONOMIC STATUS

       TEA = 0    NO ADJUSTMENT (OR MATCHING) FOR TEA
```

RANDOM-EFFECTS META-ANALYSES

Dose Response (Beta)
WEIGHTED on Beta
Weights

	Deviance	(DF)				
Model 1	98.2585	(92)				
	Estimate	**S.E.**	**P**	**RR**	**95%CIl**	**95%CIu**
Constant	0.0504	0.0187	++	1.0517	1.0138	1.0909

SEPARATE RANDOM-EFFECTS META-ANALYSES BY REGION

NORTH AMERICA, EUROPE AND NEW ZEALAND

APPENDIX 15

ETS and Lung Cancer - Meta-Analysis of Dose Response Exposure (or nearest equivalent), 02-NOV-15

Female (Husband's smoking) - Number cigarettes smoked

CORRECTED FOR ALL CONFOUNDERS (FRUIT, VEG, FAT, EDUCATION) AND MISCLASSIFICATION
SEPARATE RANDOM-EFFECTS META-ANALYSES BY REGION
Confounder Differences based on Weighted Regression
Misclassification: Additive, Concordance: 3.0, MissP: US:0.025, EU:0.025, ASIA:0.1

Dose Response (Beta)
WEIGHTED on Beta Weights

	Deviance	(DF)				
Model 1	50.9073	(48)				
	Estimate	**S.E.**	**P**	**RR**	**95%CIl**	**95%CIu**
Constant	-0.0076	0.0244	N.S.	0.9924	0.9461	1.0410

ASIA

Dose Response (Beta)
WEIGHTED on Beta Weights

	Deviance	(DF)				
Model 1	42.5446	(43)				
	Estimate	**S.E.**	**P**	**RR**	**95%CIl**	**95%CIu**
Constant	0.1047	0.0265	+++	1.1104	1.0541	1.1697

NORTH AMERICA

Dose Response (Beta)
WEIGHTED on Beta Weights

	Deviance	(DF)				
Model 1	31.5170	(28)				
	Estimate	**S.E.**	**P**	**RR**	**95%CIl**	**95%CIu**
Constant	-0.0264	0.0330	N.S.	0.9739	0.9130	1.0390

EUROPE AND NEW ZEALAND

Dose Response (Beta)
WEIGHTED on Beta Weights

	Deviance	(DF)				
Model 1	18.8277	(19)				
	Estimate	**S.E.**	**P**	**RR**	**95%CIl**	**95%CIu**
Constant	0.0222	0.0333	N.S.	1.0225	0.9578	1.0915

CHINA AND HONG KONG

Dose Response (Beta)
WEIGHTED on Beta Weights

	Deviance	(DF)				
Model 1	24.1608	(26)				
	Estimate	**S.E.**	**P**	**RR**	**95%CIl**	**95%CIu**
Constant	0.1097	0.0425	+	1.1160	1.0267	1.2130

REST OF ASIA

Dose Response (Beta)
WEIGHTED on Beta Weights

	Deviance	(DF)				
Model 1	13.0103	(16)				
	Estimate	**S.E.**	**P**	**RR**	**95%CIl**	**95%CIu**
Constant	0.0969	0.0223	+++	1.1017	1.0547	1.1509

SEPARATE RANDOM-EFFECTS META-ANALYSES BY YEAR OF PUBLICATION

PUBLISHED IN 1980S

APPENDIX 15

ETS and Lung Cancer - Meta-Analysis of Dose Response Exposure (or nearest equivalent), 02-NOV-15

Female (Husband's smoking) - Number cigarettes smoked

CORRECTED FOR ALL CONFOUNDERS (FRUIT, VEG, FAT, EDUCATION) AND MISCLASSIFICATION

SEPARATE RANDOM-EFFECTS META-ANALYSES BY YEAR OF PUBLICATION

Confounder Differences based on Weighted Regression

Misclassification: Additive, Concordance: 3.0, MissP: US:0.025, EU:0.025, ASIA:0.1

Dose Response (Beta) WEIGHTED on Beta Weights

	Deviance	(DF)				
Model 1	22.3647	(25)				
	Estimate	**S.E.**	**P**	**RR**	**95%CIl**	**95%CIu**
Constant	0.0912	0.0273	++	1.0954	1.0383	1.1557

PUBLISHED IN 1990S

Dose Response (Beta) WEIGHTED on Beta Weights

	Deviance	(DF)				
Model 1	27.2989	(26)				
	Estimate	**S.E.**	**P**	**RR**	**95%CIl**	**95%CIu**
Constant	0.0062	0.0322	N.S.	1.0063	0.9447	1.0718

PUBLISHED IN 2000S

Dose Response (Beta) WEIGHTED on Beta Weights

	Deviance	(DF)				
Model 1	24.6642	(25)				
	Estimate	**S.E.**	**P**	**RR**	**95%CIl**	**95%CIu**
Constant	0.0780	0.0324	+	1.0811	1.0145	1.1520

PUBLISHED IN 2010S

Dose Response (Beta) WEIGHTED on Beta Weights

	Deviance	(DF)				
Model 1	24.1462	(13)				
	Estimate	**S.E.**	**P**	**RR**	**95%CIl**	**95%CIu**
Constant	0.0345	0.0539	N.S.	1.0351	0.9313	1.1505

SEPARATE RANDOM-EFFECTS META-ANALYSES BY NUMBER OF LUNG CANCER CASES

<100 CASES

Dose Response (Beta) WEIGHTED on Beta Weights

	Deviance	(DF)				
Model 1	48.5695	(48)				
	Estimate	**S.E.**	**P**	**RR**	**95%CIl**	**95%CIu**
Constant	0.0884	0.0327	++	1.0924	1.0245	1.1648

100-199 CASES

Dose Response (Beta) WEIGHTED on Beta Weights

	Deviance	(DF)				
Model 1	23.6160	(21)				
	Estimate	**S.E.**	**P**	**RR**	**95%CIl**	**95%CIu**
Constant	0.0130	0.0356	N.S.	1.0131	0.9448	1.0864

200-399 CASES

APPENDIX 15
ETS and Lung Cancer - Meta-Analysis of Dose Response Exposure (or nearest equivalent), 02-NOV-15
Female (Husband's smoking) - Number cigarettes smoked

CORRECTED FOR ALL CONFOUNDERS (FRUIT, VEG, FAT, EDUCATION) AND MISCLASSIFICATION
SEPARATE RANDOM-EFFECTS META-ANALYSES BY NUMBER OF LUNG CANCER CASES
Confounder Differences based on Weighted Regression
Misclassification: Additive, Concordance: 3.0, MissP: US:0.025, EU:0.025, ASIA:0.1

Dose Response (Beta)
WEIGHTED on Beta
Weights

	Deviance	(DF)				
Model 1	12.5715	(12)				
	Estimate	**S.E.**	**P**	**RR**	**95%CIl**	**95%CIu**
Constant	0.1237	0.0400	++	1.1317	1.0464	1.2240

400+ CASES
Dose Response (Beta)
WEIGHTED on Beta
Weights

	Deviance	(DF)				
Model 1	8.9344	(8)				
	Estimate	**S.E.**	**P**	**RR**	**95%CIl**	**95%CIu**
Constant	-0.0140	0.0383	N.S.	0.9861	0.9148	1.0629

SEPARATE RANDOM-EFFECTS META-ANALYSES BY DOSE-RESPONSE OR NOT

RESULTS FOR DOSE-RESPONSE
Dose Response (Beta)
WEIGHTED on Beta
Weights

	Deviance	(DF)				
Model 1	22.8627	(23)				
	Estimate	**S.E.**	**P**	**RR**	**95%CIl**	**95%CIu**
Constant	0.0693	0.0235	++	1.0718	1.0234	1.1224

NO RESULTS FOR DOSE-RESPONSE
Dose Response (Beta)
WEIGHTED on Beta
Weights

	Deviance	(DF)				
Model 1	73.8981	(68)				
	Estimate	**S.E.**	**P**	**RR**	**95%CIl**	**95%CIu**
Constant	0.0401	0.0244	N.S.	1.0409	0.9923	1.0918

SEPARATE RANDOM-EFFECTS META-ANALYSES BY AGE ADJUSTMENT OR NOT

ADJUSTED (OR MATCHED) FOR AGE
Dose Response (Beta)
WEIGHTED on Beta
Weights

	Deviance	(DF)				
Model 1	76.8904	(74)				
	Estimate	**S.E.**	**P**	**RR**	**95%CIl**	**95%CIu**
Constant	0.0343	0.0197	(+)	1.0349	0.9957	1.0756

NOT ADJUSTED (OR MATCHED) FOR AGE
Dose Response (Beta)
WEIGHTED on Beta
Weights

	Deviance	(DF)				
Model 1	18.3461	(17)				
	Estimate	**S.E.**	**P**	**RR**	**95%CIl**	**95%CIu**
Constant	0.1420	0.0530	+	1.1526	1.0388	1.2788

APPENDIX 15

ETS and Lung Cancer - Meta-Analysis of Dose Response Exposure (or nearest equivalent), 02-NOV-15

Female (Husband's smoking) - Number cigarettes smoked

CORRECTED FOR ALL CONFOUNDERS (FRUIT, VEG, FAT, EDUCATION) AND MISCLASSIFICATION
SEPARATE RANDOM-EFFECTS META-ANALYSES BY STUDY TYPE
Confounder Differences based on Weighted Regression
Misclassification: Additive, Concordance: 3.0, MissP: US:0.025, EU:0.025, ASIA:0.1

CASE-CONTROL STUDIES

Dose Response (Beta)
WEIGHTED on Beta Weights

	Deviance	(DF)				
Model 1	84.8883	(76)				
	Estimate	**S.E.**	**P**	**RR**	**95%CIl**	**95%CIu**
Constant	0.0532	0.0217	+	1.0546	1.0106	1.1005

PROSPECTIVE STUDIES

Dose Response (Beta)
WEIGHTED on Beta Weights

	Deviance	(DF)				
Model 1	7.7346	(15)				
	Estimate	**S.E.**	**P**	**RR**	**95%CIl**	**95%CIu**
Constant	0.0358	0.0315	N.S.	1.0365	0.9745	1.1024

Appendix 16

Fuller details of the analyses relating lung cancer risk to the number of cigarettes smoked by the husband – adjusted for different confounders and corrected for misclassification

APPENDIX 16

ETS and Lung Cancer - Meta-Analysis of Dose Response Exposure (or nearest equivalent), 05-NOV-15

Female (Husband's smoking) - Number cigarettes smoked

CORRECTED FOR NO CONFOUNDERS (BACK CORRECTED FOR FRUIT, VEG, FAT, EDUCATION) AND MISCLASSIFICATION
RANDOM-EFFECTS META-ANALYSES
Confounder Differences based on Weighted Regression
Misclassification: Additive, Concordance: 3.0, MissP: US:0.025, EU:0.025, ASIA:0.1

Dose Response (Beta)
WEIGHTED on Beta
Weights

	Deviance	(DF)
Model 1	98.2585	(92)

	Estimate	S.E.	P(+)	RR	95%Cll	95%Clu
Constant	0.0504	0.0187	0.0042 ++	1.0517	1.0138	1.0909

SEPARATE RANDOM-EFFECTS META-ANALYSES BY REGION

NORTH AMERICA, EUROPE AND NEW ZEALAND

Dose Response (Beta)
WEIGHTED on Beta
Weights

	Deviance	(DF)
Model 1	50.9073	(48)

	Estimate	S.E.	P(+)	RR	95%Cll	95%Clu
Constant	-0.0076	0.0244	0.6216	0.9924	0.9461	1.0410

ASIA

Dose Response (Beta)
WEIGHTED on Beta
Weights

	Deviance	(DF)
Model 1	42.5446	(43)

	Estimate	S.E.	P(+)	RR	95%Cll	95%Clu
Constant	0.1047	0.0265	0.0001 +++	1.1104	1.0541	1.1697

CORRECTED FOR FRUIT AND MISCLASSIFICATION
RANDOM-EFFECTS META-ANALYSES

	Deviance	(DF)
Model 1	98.0243	(92)

	Estimate	S.E.	P(+)	RR	95%Cll	95%Clu
Constant	0.0658	0.0186	0.0003 +++	1.0680	1.0298	1.1077

SEPARATE RANDOM-EFFECTS META-ANALYSES BY REGION

NORTH AMERICA, EUROPE AND NEW ZEALAND

Dose Response (Beta)
WEIGHTED on Beta
Weights

	Deviance	(DF)
Model 1	50.7550	(48)

	Estimate	S.E.	P(+)	RR	95%Cll	95%Clu
Constant	0.0072	0.0242	0.3835	1.0072	0.9606	1.0562

ASIA

Dose Response (Beta)
WEIGHTED on Beta
Weights

	Deviance	(DF)
Model 1	42.4775	(43)

	Estimate	S.E.	P(+)	RR	95%Cll	95%Clu
Constant	0.1206	0.0264	0.0000 +++	1.1282	1.0713	1.1880

APPENDIX 16

ETS and Lung Cancer - Meta-Analysis of Dose Response Exposure (or nearest equivalent), 05-NOV-15

Female (Husband's smoking) - Number cigarettes smoked

CORRECTED FOR VEGETABLES AND MISCLASSIFICATION
RANDOM-EFFECTS META-ANALYSES
Confounder Differences based on Weighted Regression
Misclassification: Additive, Concordance: 3.0, MissP: US:0.025, EU:0.025, ASIA:0.1

Dose Response (Beta)
WEIGHTED on Beta
Weights

	Deviance	(DF)
Model 1	98.0114	(92)

	Estimate	S.E.	P(+)	RR	95%CIl	95%CIu
Constant	0.0677	0.0186	0.0002 +++	1.0700	1.0317	1.1097

SEPARATE RANDOM-EFFECTS META-ANALYSES BY REGION

NORTH AMERICA, EUROPE AND NEW ZEALAND

Dose Response (Beta)
WEIGHTED on Beta
Weights

	Deviance	(DF)
Model 1	50.7373	(48)

	Estimate	S.E.	P(+)	RR	95%CIl	95%CIu
Constant	0.0090	0.0242	0.3561	1.0090	0.9623	1.0580

ASIA

Dose Response (Beta)
WEIGHTED on Beta
Weights

	Deviance	(DF)
Model 1	42.4798	(43)

	Estimate	S.E.	P(+)	RR	95%CIl	95%CIu
Constant	0.1226	0.0264	0.0000 +++	1.1304	1.0735	1.1903

CORRECTED FOR DIETARY FAT AND MISCLASSIFICATION
RANDOM-EFFECTS META-ANALYSES

	Deviance	(DF)
Model 1	98.1176	(92)

	Estimate	S.E.	P(+)	RR	95%CIl	95%CIu
Constant	0.0578	0.0187	0.0013 ++	1.0595	1.0215	1.0990

SEPARATE RANDOM-EFFECTS META-ANALYSES BY REGION

NORTH AMERICA, EUROPE AND NEW ZEALAND

Dose Response (Beta)
WEIGHTED on Beta
Weights

	Deviance	(DF)
Model 1	50.8074	(48)

	Estimate	S.E.	P(+)	RR	95%CIl	95%CIu
Constant	-0.0004	0.0243	0.5064	0.9996	0.9531	1.0484

ASIA

Dose Response (Beta)
WEIGHTED on Beta
Weights

	Deviance	(DF)
Model 1	42.5149	(43)

	Estimate	S.E.	P(+)	RR	95%CIl	95%CIu
Constant	0.1124	0.0265	0.0001 +++	1.1189	1.0624	1.1785

APPENDIX 16

ETS and Lung Cancer - Meta-Analysis of Dose Response Exposure (or nearest equivalent), 05-NOV-15

Female (Husband's smoking) - Number cigarettes smoked

CORRECTED FOR YEARS OF EDUCATION AND MISCLASSIFICATION
RANDOM-EFFECTS META-ANALYSES
Confounder Differences based on Weighted Regression
Misclassification: Additive, Concordance: 3.0, MissP: US:0.025, EU:0.025, ASIA:0.1

Dose Response (Beta)
WEIGHTED on Beta
Weights

	Deviance	**(DF)**				
Model 1	98.3984	(92)				
	Estimate	**S.E.**	**P(+)**	**RR**	**95%CIl**	**95%CIu**
Constant	0.0458	0.0188	0.0084 ++	1.0469	1.0090	1.0862

SEPARATE RANDOM-EFFECTS META-ANALYSES BY REGION

NORTH AMERICA, EUROPE AND NEW ZEALAND

Dose Response (Beta)
WEIGHTED on Beta
Weights

	Deviance	**(DF)**				
Model 1	50.9634	(48)				
	Estimate	**S.E.**	**P(+)**	**RR**	**95%CIl**	**95%CIu**
Constant	-0.0121	0.0246	0.6874	0.9880	0.9414	1.0368

ASIA

Dose Response (Beta)
WEIGHTED on Beta
Weights

	Deviance	**(DF)**				
Model 1	42.6166	(43)				
	Estimate	**S.E.**	**P(+)**	**RR**	**95%CIl**	**95%CIu**
Constant	0.1001	0.0267	0.0003 +++	1.1053	1.0490	1.1647

Appendix 17

Fuller details of the analyses relating lung cancer risk to whether or not the husband smoked – unadjusted for confounding and uncorrected for misclassification

APPENDIX 17

ETS and Lung Cancer - Meta-Analysis of exposed/unexposed Risks, 02-NOV-15

Female (Husband's smoking)

BASIC DATA USED IN META-ANALYSES

UNCORRECTED FOR CONFOUNDERS OR MISCLASSIFICATION

Study title	Country	RR	RRL	RRU	CA1	CA0	CO1	CO0	Expos
Akiba	Japan	1.5000	0.9300	2.7600	74.2100	21.5800	191.5700	83.5600	1.0000
Al-Zoughool	Canada	0.3900	0.1500	0.9800	5.8691	22.6601	112.8202	169.8787	1.0000
Asomaning	USA	0.9300	0.3100	2.7800	15.4332	5.5313	59.1915	19.7294	1.0000
Boffetta 2	7 countries	1.0000	0.5000	1.9000	25.7383	25.3652	53.4266	52.6522	1.0000
Boffetta	7 countries	1.1100	0.8800	1.3900	313.8738	168.2298	599.7825	356.8326	1.0000
Brenner	Canada	0.4000	0.2500	0.6300	54.6755	35.7517	516.7407	135.1564	1.0000
Brownson 1	USA	1.6800	0.3900	6.9000	3.7600	12.7800	6.0900	34.8200	1.0000
Brownson 2	USA	1.0000	0.8000	1.2000	262.8000	249.6100	710.9600	675.2900	1.0000
Buffler	USA	0.8000	0.3400	1.9000	33.0000	8.0000	164.0000	32.0000	1.0000
Butler	USA	2.0200	0.4800	8.5600	2.7700	5.5800	11040.8400	44931.4800	1.0000
Cardenas	USA	1.2000	0.8000	1.6000	84.8172	51.2828	107432.5248	77947.9981	1.0000
Chan	China	0.7500	0.4300	1.3000	34.0000	50.0000	66.0000	73.0000	1.0000
Choi	Korea	1.6300	0.9200	2.8700	49.0000	26.0000	88.0000	76.0000	1.0000
Correa	USA	2.0700	0.8100	5.2500	14.0000	8.0000	61.0000	72.0000	1.0000
De Waard	Netherlands	2.5700	0.8400	7.8500	19.0000	4.0000	124.0000	67.0000	1.0000
Du	China	1.0900	0.6400	1.8500	47.0000	28.0000	154.0000	100.0000	1.0000
Enstrom	USA	0.9400	0.6600	1.3300	105.7649	44.8930	15783.0932	6297.3389	1.0000
EPIC Adulthood	Western Europe	0.8400	0.3300	2.1700	9.3664	8.0480	13863.3285	10006.0387	1.0000
Fang	China	1.7700	1.0700	2.9200	23.2928	104.9022	85.7355	683.4344	1.0000
Fontham	USA	1.2900	1.0400	1.6000	372.1100	183.3900	653.6300	415.5600	1.0000
Franco-Marina	Mexico	1.8000	0.9500	3.4200	21.7539	36.9675	39.3017	120.2171	1.0000
Gallegos	Mexico	8.0000	0.8500	75.3100	12.9595	0.8640	38.8786	20.7349	1.0000
Gao	China	1.3041	0.8700	1.9400	191.5800	52.8600	274.2500	98.3700	1.0000
Garfinkel 1	USA	1.1700	0.8500	1.6100	88.0000	65.0000	94880.0000	81859.0000	1.0000
Garfinkel 2	USA	1.2300	0.8100	1.8700	91.0000	43.0000	254.0000	148.0000	1.0000
GELAC study	Taiwan	1.3000	1.0900	1.5600	449.4704	533.2445	386.5457	596.1692	1.0000
Geng	China	2.1600	1.0800	4.2900	34.0000	20.0000	41.0000	52.0000	1.0000
Gorlova	USA	1.1500	0.6300	2.1000	66.8200	29.5300	67.3200	34.3100	1.0000
He	China	2.0700	0.2300	18.3400	5.0641	0.9426	340.3803	131.1465	1.0000
Hill (study 1)	New Zealand	1.0000	0.4900	2.0100	10.1641	31.9638	93216.1758	293144.8122	1.0000
Hill (study 2)	New Zealand	1.3800	0.7800	2.4100	14.9666	62.4129	63410.9424	364916.1456	1.0000
Hirayama	Japan	1.4500	1.0200	2.0800	169.5500	36.7600	71842.2400	22585.7700	1.0000
Hole	Scotland	1.8900	0.2200	16.1200	5.0000	1.0000	1295.0000	489.0000	1.0000
Humble 1	USA	2.2000	0.7600	6.5600	13.8600	4.9100	85.4200	66.6400	1.0000
IARC: Kreuzer	Germany	0.8000	0.5000	1.3000	52.5746	45.5399	132.5006	91.8170	1.0000
ILCCO	International	1.2000	1.0600	1.3600	700.2118	619.7408	1941.0050	2061.5249	1.0000
Inoue	Japan	2.2500	0.7700	8.8500	16.9800	4.2800	28.9900	16.4300	1.0000
Janerich	USA	0.7500	0.4700	1.2000	76.0000	68.0000	86.0000	58.0000	1.0000
Jee	Korea	1.7200	0.9300	3.1800	69.0583	11.9253	124439.5435	36960.6697	1.0000
Jiang	China	2.2670	1.1340	4.5330	47.3649	21.7629	33.8586	35.2680	1.0000
Johnson	Canada	1.2000	0.6200	2.3000	38.7236	12.9554	395.2353	158.6764	1.0000
Kabat 1	USA	0.7900	0.2500	2.4500	13.0000	11.0000	15.0000	10.0000	1.0000
Kabat 2	USA	1.0800	0.6000	1.9400	39.3300	25.3500	98.4700	68.5400	1.0000
Kalandidi	Greece	2.1100	1.0900	4.0800	58.9500	18.3600	60.1300	39.5100	1.0000
Kiyohara	Japan	1.0050	0.4660	2.1670	31.9057	17.4021	43.5062	23.8479	1.0000
Koo	China	1.6400	0.8700	3.0900	39.0600	25.2600	49.3700	52.3600	1.0000
Kurahashi	Japan	1.2600	0.7800	2.0300	77.6450	21.4241	254803.8943	88585.9487	1.0000
Lagarde	Sweden	1.1500	0.8400	1.5800	84.1500	119.3890	282.1461	460.3436	1.0000
Lam T	China	1.6500	1.1600	2.3500	115.0000	84.0000	152.0000	183.0000	1.0000
Lam W	China	2.0100	1.0900	3.7200	37.0000	23.0000	64.0000	80.0000	1.0000
Layard	USA	0.5800	0.3000	1.1300	14.0200	24.3700	946.0900	953.9600	1.0000
Lee	England	1.0000	0.3700	2.7100	18.0900	8.4400	37.3000	17.4100	1.0000
Lee C-H	Taiwan	1.8700	1.2900	2.7100	145.3012	58.9669	192.8351	146.3413	1.0000
Liang	China	1.4473	1.0123	2.0692	141.0000	85.0000	149.0000	130.0000	1.0000
Lim	Singapore	1.1231	0.9029	1.3970	200.0000	226.0000	602.0000	764.0000	1.0000
Lin	China	2.5030	1.6600	3.7730	100.5614	77.2974	72.4017	139.2977	1.0000
Liu Q	China	1.7200	0.7700	3.8700	26.3000	13.2300	38.4900	33.2900	1.0000

APPENDIX 17

ETS and Lung Cancer - Meta-Analysis of exposed/unexposed Risks, 02-NOV-15

Female (Husband's smoking)

BASIC DATA USED IN META-ANALYSES

UNCORRECTED FOR CONFOUNDERS OR MISCLASSIFICATION

Study title	Country	RR	RRL	RRU	CA1	CA0	CO1	CO0	Expos
Liu Z	China	0.7700	0.3000	1.9600	35.8200	6.8700	139.1500	20.5600	1.0000
Lopez-Cima	Spain	0.9930	0.0020	509.8740	4.4400	0.1300	17.8800	0.5100	1.0000
Malats	7 Europe+Brazil	1.5000	0.7700	2.9100	36.1634	45.3493	23.4436	44.0978	1.0000
Masjedi	Iran	2.0074	1.0074	3.9998	21.0000	34.0000	28.0000	91.0000	1.0000
McGhee	China	1.3800	0.9400	2.0400	80.5883	75.9186	131.1497	170.4993	1.0000
Nishino	Japan	1.8000	0.6700	4.6000	9.3962	7.4053	21398.0642	30355.3445	1.0000
Ohno	Japan	1.0000	0.6700	1.4900	138.9793	52.3348	239.3942	90.1475	1.0000
Pershagen	Sweden	1.2000	0.7000	2.1000	36.1800	27.7800	139.8100	128.8400	1.0000
Rapiti	India	1.2000	0.5000	2.9000	12.7016	23.1855	18.3812	40.2637	1.0000
Ren	China	1.2000	0.9900	1.4600	655.3649	238.7315	800.4530	349.8997	1.0000
Rylander	Sweden	1.3700	0.5700	3.3000	7.9200	23.0900	40.4300	161.5700	1.0000
Schoenberg	USA	1.0710	0.6980	1.6420	68.5216	41.3858	287.0856	185.7055	1.0000
Schwartz	USA	1.1000	0.7200	1.6800	125.0000	65.9500	115.6000	67.0900	1.0000
Seki	Japan	1.3100	0.9900	1.7200	196.0403	81.8593	1113.5021	609.0952	1.0000
Shen	China	0.7500	0.3100	1.7800	56.0000	14.0000	59.0000	11.0000	1.0000
Shimizu	Japan	1.0800	0.6400	1.8200	52.0000	38.0000	91.0000	72.0000	1.0000
Sobue	Japan	1.1300	0.7800	1.6300	78.6600	59.2200	378.2100	321.7200	1.0000
Speize	USA	1.5000	0.3000	6.3000	29.2793	1.7574	199924.6090	18000.0001	1.0000
Stockwell	USA	1.6000	0.8000	3.0000	48.0800	19.6700	60.1000	39.3400	1.0000
Sun	China	1.1600	0.8000	1.6900	144.8200	86.2900	136.6600	94.4500	1.0000
Svensson	Sweden	1.3600	0.5300	3.4900	18.2000	7.0400	84.6400	44.5500	1.0000
Torres-Duran	Spain	0.7100	0.4600	1.1000	49.6338	85.0138	103.7945	126.2249	1.0000
Trichopoulos	Greece	2.0800	1.2000	3.5900	53.0000	24.0000	116.0000	109.0000	1.0000
Wang L	China	1.0300	0.6000	1.7000	125.1000	25.2300	253.2979	52.6138	1.0000
Wang S	China	2.5300	1.2600	5.1000	67.0000	15.0000	60.0000	34.0000	1.0000
Wang T	China	1.1100	0.6700	1.8400	92.0000	43.0000	89.0000	46.0000	1.0000
Wen	China	1.0900	0.7400	1.6100	68.7718	40.2469	40928.3228	26107.9401	1.0000
WHI-OS	USA	0.8800	0.5200	1.4900	26.0505	29.6029	42114.6908	42114.6908	1.0000
Wu	USA	1.2000	0.5000	3.3000	17.9700	9.9800	32.9400	21.9600	1.0000
Wu-Williams	China	0.7000	0.6000	0.9000	293.9500	343.8000	506.2200	414.4600	1.0000
Yang	USA	2.0000	1.1000	3.6300	68.7786	26.8357	55.6941	43.4609	1.0000
Yu	China	1.3500	0.6950	2.6250	113.5206	15.7243	149.2588	27.9107	1.0000
Zaridze	Russia	1.5300	1.0600	2.2100	98.8742	77.3100	151.9500	181.7800	1.0000
Zatloukal	Czech Republic	0.4800	0.2100	1.0900	6.5824	64.9388	131.9736	624.9586	1.0000
Zheng	China	2.5200	1.0882	5.8521	62.0000	7.0000	179.0000	51.0000	1.0000
Zhong	China	1.1000	0.8000	1.5000	201.4400	108.8077	232.0702	137.8878	1.0000

NOTES: RR,RL,RU RELATIVE RISKS AND LOWER AND UPPER CONFIDENCE INTERVALS

CA1,CA0 NUMBERS (OR PSEUDO-NUMBERS) OF EXPOSED AND UNEXPOSED CASES

CO1,CO0 NUMBERS (OR PSEUDO-NUMBERS) OF EXPOSED AND UNEXPOSED CONTROLS

EXPOS ASSIGNED EXPOSURE FOR SMOKING BY HUSBAND

APPENDIX 17
ETS and Lung Cancer - Meta-Analysis of exposed/unexposed Risks, 02-NOV-15
Female (Husband's smoking)
BASIC DATA USED IN META-ANALYSES
UNCORRECTED FOR CONFOUNDERS OR MISCLASSIFICATION

Study title	Country	Beta	St.Err. Beta	Z	Weight	FRU	VEG	FAT	EDU
Akiba	Japan	0.4055	0.2775	1.4611	12.9854	0	0	0	0
Al-Zoughool	Canada	-0.9416	0.4788	-1.9665	4.3618	0	0	0	1
Asomaning	USA	-0.0726	0.5596	-0.1297	3.1932	0	0	0	0
Boffetta 2	7 countries	0.0000	0.3406	0.0000	8.6217	0	0	0	0
Boffetta	7 countries	0.1044	0.1166	0.8949	73.5297	0	0	0	0
Brenner	Canada	-0.9163	0.2358	-3.8861	17.9874	0	0	0	0
Brownson 1	USA	0.5188	0.7330	0.7078	1.8614	0	0	0	1
Brownson 2	USA	0.0000	0.1034	0.0000	93.4649	0	0	0	0
Buffler	USA	-0.2231	0.4390	-0.5084	5.1900	0	0	0	0
Butler	USA	0.7031	0.7350	0.9566	1.8512	0	0	0	0
Cardenas	USA	0.1823	0.1768	1.0311	31.9819	0	1	1	2
Chan	China	-0.2877	0.2822	-1.0193	12.5540	0	0	0	0
Choi	Korea	0.4886	0.2902	1.6834	11.8715	0	0	0	0
Correa	USA	0.7275	0.4768	1.5260	4.3991	0	0	0	0
De Waard	Netherlands	0.9439	0.5701	1.6556	3.0765	0	0	0	0
Du	China	0.0862	0.2708	0.3182	13.6376	0	0	0	0
Enstrom	USA	-0.0619	0.1788	-0.3462	31.2967	1	0	0	2
EPIC Adulthood	Western Europe	-0.1744	0.4805	-0.3629	4.3319	1	1	1	2
Fang	China	0.5710	0.2561	2.2294	15.2459	0	1	0	1
Fontham	USA	0.2546	0.1099	2.3171	82.8016	1	1	0	2
Franco-Marina	Mexico	0.5878	0.3268	1.7988	9.3649	0	0	0	0
Gallegos	Mexico	2.0794	1.1439	1.8178	0.7642	0	0	0	0
Gao	China	0.2655	0.2046	1.2977	23.8925	0	0	0	2
Garfinkel 1	USA	0.1570	0.1630	0.9635	37.6608	0	0	0	0
Garfinkel 2	USA	0.2070	0.2134	0.9699	21.9512	0	0	0	0
GELAC study	Taiwan	0.2624	0.0915	2.8687	119.5522	0	0	0	2
Geng	China	0.7701	0.3519	2.1886	8.0765	0	0	0	0
Gorlova	USA	0.1398	0.3071	0.4550	10.6004	0	0	0	1
He	China	0.7275	1.1171	0.6513	0.8014	0	0	2	2
Hill (study 1)	New Zealand	0.0000	0.3601	0.0000	7.7126	0	0	0	0
Hill (study 2)	New Zealand	0.3221	0.2878	1.1192	12.0745	0	0	0	3
Hirayama	Japan	0.3716	0.1818	2.0440	30.2626	0	0	0	0
Hole	Scotland	0.6366	1.0955	0.5811	0.8333	0	0	0	0
Humble 1	USA	0.7885	0.5499	1.4339	3.3074	0	0	0	0
IARC: Kreuzer	Germany	-0.2231	0.2438	-0.9154	16.8300	0	0	0	0
ILCCO	International	0.1823	0.0636	2.8677	247.4028	0	0	0	0
Inoue	Japan	0.8109	0.6229	1.3018	2.5772	0	0	0	0
Janerich	USA	-0.2877	0.2391	-1.2031	17.4887	0	0	0	0
Jee	Korea	0.5423	0.3136	1.7291	10.1656	0	1	0	3
Jiang	China	0.8185	0.3535	2.3154	8.0031	1	1	0	0
Johnson	Canada	0.1823	0.3344	0.5452	8.9410	1	1	0	2
Kabat 1	USA	-0.2357	0.5823	-0.4048	2.9497	0	0	0	0
Kabat 2	USA	0.0770	0.2994	0.2571	11.1578	0	0	0	2
Kalandidi	Greece	0.7467	0.3367	2.2175	8.8198	1	0	0	2
Kiyohara	Japan	0.0050	0.3921	0.0127	6.5051	0	0	0	0
Koo	China	0.4947	0.3233	1.5300	9.5655	0	0	0	2
Kurahashi	Japan	0.2311	0.2440	0.9471	16.7953	0	0	0	0
Lagarde	Sweden	0.1398	0.1612	0.8672	38.4970	0	0	0	3
Lam T	China	0.5008	0.1801	2.7805	30.8285	0	0	0	0
Lam W	China	0.6981	0.3132	2.2294	10.1972	0	0	0	0
Layard	USA	-0.5447	0.3383	-1.6101	8.7366	0	0	0	0
Lee	England	0.0000	0.5080	0.0000	3.8755	0	0	0	0
Lee C-H	Taiwan	0.6259	0.1894	3.3054	27.8862	0	0	0	2
Liang	China	0.3697	0.1824	2.0271	30.0656	0	0	0	0
Lim	Singapore	0.1161	0.1113	1.0428	80.6789	0	0	0	0
Lin	China	0.9175	0.2095	4.3803	22.7936	0	0	0	2
Liu Q	China	0.5423	0.4119	1.3166	5.8941	0	0	0	2
Liu Z	China	-0.2614	0.4788	-0.5459	4.3618	0	0	0	0
Lopez-Cima	Spain	-0.0070	3.1758	-0.0022	0.0992	0	0	0	0

APPENDIX 17
ETS and Lung Cancer - Meta-Analysis of exposed/unexposed Risks, 02-NOV-15
Female (Husband's smoking)
BASIC DATA USED IN META-ANALYSES
UNCORRECTED FOR CONFOUNDERS OR MISCLASSIFICATION

Study title	Country	Beta	St.Err. Beta	Z	Weight	FRU	VEG	FAT	EDU
Malats	7 Europe+Brazil	0.4055	0.3392	1.1955	8.6930	0	0	0	0
Masjedi	Iran	0.6968	0.3518	1.9810	8.0818	0	0	0	0
McGhee	China	0.3221	0.1977	1.6295	25.5946	0	0	0	2
Nishino	Japan	0.5878	0.4915	1.1960	4.1400	1	1	1	0
Ohno	Japan	0.0000	0.2039	0.0000	24.0539	0	0	0	0
Pershagen	Sweden	0.1823	0.2803	0.6505	12.7311	0	0	0	0
Rapiti	India	0.1823	0.4484	0.4066	4.9727	0	0	0	0
Ren	China	0.1823	0.0991	1.8397	101.8130	0	0	0	0
Rylander	Sweden	0.3148	0.4480	0.7027	4.9829	0	0	0	0
Schoenberg	USA	0.0686	0.2182	0.3143	20.9974	0	1	0	2
Schwartz	USA	0.0953	0.2162	0.4409	21.4034	0	0	0	0
Seki	Japan	0.2700	0.1409	1.9162	50.3603	0	0	0	0
Shen	China	-0.2877	0.4459	-0.6452	5.0301	0	0	0	0
Shimizu	Japan	0.0770	0.2666	0.2887	14.0676	0	0	0	0
Sobue	Japan	0.1222	0.1880	0.6500	28.2860	0	0	0	2
Speize	USA	0.4055	0.7767	0.5221	1.6577	0	0	0	0
Stockwell	USA	0.4700	0.3372	1.3939	8.7954	0	0	0	2
Sun	China	0.1484	0.1908	0.7779	27.4727	0	0	0	2
Svensson	Sweden	0.3075	0.4808	0.6395	4.3255	0	0	0	0
Torres-Duran	Spain	-0.3425	0.2224	-1.5399	20.2154	0	0	0	0
Trichopoulos	Greece	0.7324	0.2796	2.6198	12.7958	0	0	0	0
Wang L	China	0.0296	0.2657	0.1113	14.1669	0	0	0	1
Wang S	China	0.9282	0.3567	2.6024	7.8607	0	0	0	0
Wang T	China	0.1044	0.2577	0.4049	15.0558	0	0	0	0
Wen	China	0.0862	0.1983	0.4346	25.4293	1	1	0	2
WHI-OS	USA	-0.1278	0.2686	-0.4760	13.8658	0	0	0	0
Wu	USA	0.1823	0.4814	0.3787	4.3150	0	0	0	0
Wu-Williams	China	-0.3567	0.1034	-3.4482	93.4649	0	0	0	2
Yang	USA	0.6931	0.3046	2.2758	10.7796	0	0	0	0
Yu	China	0.3001	0.3390	0.8852	8.7007	1	1	0	2
Zaridze	Russia	0.4253	0.1874	2.2689	28.4648	0	0	0	2
Zatloukal	Czech Republic	-0.7340	0.4201	-1.7471	5.6658	0	0	0	2
Zheng	China	0.9243	0.4292	2.1536	5.4295	0	0	0	0
Zhong	China	0.0953	0.1604	0.5943	38.8862	1	0	0	1

NOTES: BETA SLOPE OF LOG RR ON NCIGS

SE BETA STANDARD ERROR OF BETA

Z RATIO OF BETA TO ITS STANDARD ERROR (APPROXIMATE NORMAL STATISTIC)

WEIGHT INVERSE OF THE VARIANCE OF BETA

FRU = 1 ANALYSIS ADJUSTED FOR FRUIT

VEG = 1 " " " VEGETABLES

FAT = 1 " " " FRUIT

EDU = 1 " " " INCOME

= 2 " " " EDUCATION

= 3 " " " SOCIO-ECONOMIC STATUS

APPENDIX 17

ETS and Lung Cancer - Meta-Analysis of exposed/unexposed Risks, 02-NOV-15

Female (Husband's smoking)

UNCORRECTED FOR CONFOUNDERS OR MISCLASSIFICATION

RANDOM-EFFECTS META-ANALYSES

Log RR (Beta)
WEIGHTED on Beta
Weights

	Deviance	(DF)				
Model 1	97.7981	(92)				
	Estimate	**S.E.**	**P**	**RR**	**95%Cll**	**95%Clu**
Constant	0.1981	0.0349	+++	1.2190	1.1384	1.3054

SEPARATE RANDOM-EFFECTS META-ANALYSES BY REGION

NORTH AMERICA, EUROPE AND NEW ZEALAND

Log RR (Beta)
WEIGHTED on Beta
Weights

	Deviance	(DF)				
Model 1	51.9534	(48)				
	Estimate	**S.E.**	**P**	**RR**	**95%Cll**	**95%Clu**
Constant	0.1059	0.0521	+	1.1117	1.0038	1.2312

ASIA

Log RR (Beta)
WEIGHTED on Beta
Weights

	Deviance	(DF)				
Model 1	41.0490	(43)				
	Estimate	**S.E.**	**P**	**RR**	**95%Cll**	**95%Clu**
Constant	0.2728	0.0464	+++	1.3136	1.1994	1.4387

NORTH AMERICA

Log RR (Beta)
WEIGHTED on Beta
Weights

	Deviance	(DF)				
Model 1	31.5468	(28)				
	Estimate	**S.E.**	**P**	**RR**	**95%Cll**	**95%Clu**
Constant	0.0716	0.0700	N.S.	1.0742	0.9366	1.2321

EUROPE AND NEW ZEALAND

Log RR (Beta)
WEIGHTED on Beta
Weights

	Deviance	(DF)				
Model 1	19.2695	(19)				
	Estimate	**S.E.**	**P**	**RR**	**95%Cll**	**95%Clu**
Constant	0.1602	0.0783	(+)	1.1737	1.0067	1.3685

CHINA AND HONG KONG

Log RR (Beta)
WEIGHTED on Beta
Weights

	Deviance	(DF)				
Model 1	23.5645	(26)				
	Estimate	**S.E.**	**P**	**RR**	**95%Cll**	**95%Clu**
Constant	0.2780	0.0731	+++	1.3205	1.1442	1.5240

REST OF ASIA

APPENDIX 17
ETS and Lung Cancer - Meta-Analysis of exposed/unexposed Risks, 02-NOV-15
Female (Husband's smoking)

UNCORRECTED FOR CONFOUNDERS OR MISCLASSIFICATION
SEPARATE RANDOM-EFFECTS META-ANALYSES BY REGION

Log RR (Beta)
WEIGHTED on Beta
Weights

	Deviance	(DF)
Model 1	13.1208	(16)

	Estimate	S.E.	P	RR	95%CIl	95%CIu
Constant	0.2498	0.0402	+++	1.2838	1.1866	1.3889

SEPARATE RANDOM-EFFECTS META-ANALYSES BY YEAR OF PUBLICATION

PUBLISHED IN 1980S
Log RR (Beta)
WEIGHTED on Beta
Weights

	Deviance	(DF)
Model 1	20.8521	(25)

	Estimate	S.E.	P	RR	95%CIl	95%CIu
Constant	0.3079	0.0572	+++	1.3605	1.2163	1.5218

PUBLISHED IN 1990S
Log RR (Beta)
WEIGHTED on Beta
Weights

	Deviance	(DF)
Model 1	25.6280	(26)

	Estimate	S.E.	P	RR	95%CIl	95%CIu
Constant	0.1411	0.0637	+	1.1515	1.0163	1.3047

PUBLISHED IN 2000S
Log RR (Beta)
WEIGHTED on Beta
Weights

	Deviance	(DF)
Model 1	24.8531	(25)

	Estimate	S.E.	P	RR	95%CIl	95%CIu
Constant	0.2153	0.0589	++	1.2402	1.1049	1.3920

PUBLISHED IN 2010S
Log RR (Beta)
WEIGHTED on Beta
Weights

	Deviance	(DF)
Model 1	24.9198	(13)

	Estimate	S.E.	P	RR	95%CIl	95%CIu
Constant	0.1298	0.0950	N.S.	1.1387	0.9452	1.3717

SEPARATE RANDOM-EFFECTS META-ANALYSES BY NUMBER OF LUNG CANCER CASES

<100 CASES
Log RR (Beta)
WEIGHTED on Beta
Weights

	Deviance	(DF)
Model 1	47.4712	(48)

	Estimate	S.E.	P	RR	95%CIl	95%CIu
Constant	0.2915	0.0651	+++	1.3385	1.1782	1.5205

100-199 CASES

APPENDIX 17
ETS and Lung Cancer - Meta-Analysis of exposed/unexposed Risks, 02-NOV-15
Female (Husband's smoking)

UNCORRECTED FOR CONFOUNDERS OR MISCLASSIFICATION
SEPARATE RANDOM-EFFECTS META-ANALYSES BY NUMBER OF LUNG CANCER CASES

Log RR (Beta)
WEIGHTED on Beta
Weights

	Deviance	(DF)				
Model 1	22.1286	(21)				
	Estimate	**S.E.**	**P**	**RR**	**95%Cll**	**95%Clu**
Constant	0.1109	0.0708	N.S.	1.1173	0.9726	1.2835

200-399 CASES
Log RR (Beta)
WEIGHTED on Beta
Weights

	Deviance	(DF)				
Model 1	12.3710	(12)				
	Estimate	**S.E.**	**P**	**RR**	**95%Cll**	**95%Clu**
Constant	0.3097	0.0692	+++	1.3630	1.1903	1.5609

400+ CASES
Log RR (Beta)
WEIGHTED on Beta
Weights

	Deviance	(DF)				
Model 1	8.0294	(8)				
	Estimate	**S.E.**	**P**	**RR**	**95%Cll**	**95%Clu**
Constant	0.0964	0.0633	N.S.	1.1012	0.9727	1.2466

SEPARATE RANDOM-EFFECTS META-ANALYSES BY DOSE-RESPONSE OR NOT

RESULTS FOR DOSE-RESPONSE
Log RR (Beta)
WEIGHTED on Beta
Weights

	Deviance	(DF)				
Model 1	23.2090	(23)				
	Estimate	**S.E.**	**P**	**RR**	**95%Cll**	**95%Clu**
Constant	0.2686	0.0523	+++	1.3081	1.1807	1.4493

NO RESULTS FOR DOSE-RESPONSE
Log RR (Beta)
WEIGHTED on Beta
Weights

	Deviance	(DF)				
Model 1	73.6920	(68)				
	Estimate	**S.E.**	**P**	**RR**	**95%Cll**	**95%Clu**
Constant	0.1676	0.0427	+++	1.1824	1.0876	1.2855

SEPARATE RANDOM-EFFECTS META-ANALYSES BY AGE ADJUSTMENT OR NOT

ADJUSTED (OR MATCHED) FOR AGE
Log RR (Beta)
WEIGHTED on Beta
Weights

	Deviance	(DF)				
Model 1	77.4031	(74)				
	Estimate	**S.E.**	**P**	**RR**	**95%Cll**	**95%Clu**
Constant	0.1687	0.0373	+++	1.1838	1.1004	1.2736

NOT ADJUSTED (OR MATCHED) FOR AGE

APPENDIX 17

ETS and Lung Cancer - Meta-Analysis of exposed/unexposed Risks, 02-NOV-15

Female (Husband's smoking)

UNCORRECTED FOR CONFOUNDERS OR MISCLASSIFICATION

SEPARATE RANDOM-EFFECTS META-ANALYSES BY AGE ADJUSTMENT OR NOT

Log RR (Beta)
WEIGHTED on Beta
Weights

	Deviance	**(DF)**				
Model 1	17.3756	(17)				
	Estimate	**S.E.**	**P**	**RR**	**95%CIl**	**95%CIu**
Constant	0.3623	0.0943	++	1.4366	1.1943	1.7282

SEPARATE RANDOM-EFFECTS META-ANALYSES BY STUDY TYPE

CASE-CONTROL STUDIES

Log RR (Beta)
WEIGHTED on Beta
Weights

	Deviance	**(DF)**				
Model 1	85.0115	(76)				
	Estimate	**S.E.**	**P**	**RR**	**95%CIl**	**95%CIu**
Constant	0.2034	0.0400	+++	1.2255	1.1331	1.3255

PROSPECTIVE STUDIES

Log RR (Beta)
WEIGHTED on Beta
Weights

	Deviance	**(DF)**				
Model 1	8.5907	(15)				
	Estimate	**S.E.**	**P**	**RR**	**95%CIl**	**95%CIu**
Constant	0.1712	0.0658	+	1.1867	1.0431	1.3501

Appendix 18

Fuller details of the analyses relating lung cancer risk to whether or not the husband smoked – adjusted for confounding

APPENDIX 18

ETS and Lung Cancer - Meta-Analysis of exposed/unexposed Risks, 02-NOV-15

Female (Husband's smoking)

BASIC DATA USED IN META-ANALYSES

CORRECTED FOR ALL CONFOUNDERS (FRUIT, VEG, FAT, EDUCATION)

Confounder Differences based on Random-effects Regression

Study title	Country	RR	RRL	RRU	CA1	CA0	CO1	CO0	Expos
Akiba	Japan	1.3968	0.8660	2.5701	70.8567	22.1279	185.9701	81.1206	1.0000
Al-Zoughool	Canada	0.3781	0.1454	0.9500	5.8254	23.1997	114.7862	172.8264	1.0000
Asomaning	USA	0.8605	0.2868	2.5722	14.6969	5.6933	57.5721	19.1908	1.0000
Boffetta 2	7 countries	0.9258	0.4629	1.7590	24.7709	26.3647	53.4627	52.6801	1.0000
Boffetta	7 countries	1.0294	0.8161	1.2890	301.1645	174.0608	591.2301	351.7413	1.0000
Brenner	Canada	0.3669	0.2293	0.5778	52.0867	37.1284	509.8162	133.3215	1.0000
Brownson 1	USA	1.6368	0.3800	6.7227	3.7163	12.9813	6.1480	35.1516	1.0000
Brownson 2	USA	0.9258	0.7406	1.1110	252.8222	259.3830	710.6758	675.0201	1.0000
Buffler	USA	0.7396	0.3143	1.7565	31.1557	8.2177	157.5105	30.7264	1.0000
Butler	USA	1.8846	0.4478	7.9861	2.7079	5.8475	11312.3600	46036.4488	1.0000
Cardenas	USA	1.1493	0.7662	1.5324	82.5822	52.1353	106341.2310	77156.1926	1.0000
Chan	China	0.6911	0.3962	1.1979	32.0984	51.3674	65.5857	72.5338	1.0000
Choi	Korea	1.5212	0.8586	2.6784	46.7077	26.5177	85.9209	74.2033	1.0000
Correa	USA	1.9393	0.7589	4.9186	13.4489	8.1852	59.9862	70.8026	1.0000
De Waard	Netherlands	2.4134	0.7888	7.3716	18.1476	4.0628	119.7458	64.6975	1.0000
Du	China	1.0105	0.5933	1.7151	45.1313	29.0003	152.2174	98.8421	1.0000
Enstrom	USA	0.8792	0.6173	1.2440	99.5425	45.1721	15160.4539	6048.9107	1.0000
EPIC Adulthood	Western Europe	0.8050	0.3163	2.0797	9.1566	8.2096	13824.9587	9978.3448	1.0000
Fang	China	1.7289	1.0452	2.8522	23.1266	106.5903	86.7806	691.5207	1.0000
Fontham	USA	1.2153	0.9798	1.5073	359.9457	188.3055	645.1047	410.1370	1.0000
Franco-Marina	Mexico	1.6789	0.8861	3.1900	21.0855	38.4105	39.8232	121.7972	1.0000
Gallegos	Mexico	7.6428	0.8120	71.9471	12.4466	0.8685	37.4502	19.9711	1.0000
Gao	China	1.2117	0.8084	1.8026	166.8486	49.3888	242.6102	87.0217	1.0000
Garfinkel 1	USA	1.0860	0.7889	1.4944	84.9916	67.5230	94579.0065	81599.3044	1.0000
Garfinkel 2	USA	1.1424	0.7523	1.7369	85.8170	43.7718	245.6449	143.1391	1.0000
GELAC study	Taiwan	1.2085	1.0133	1.4503	433.3118	553.0779	387.9471	598.4427	1.0000
Geng	China	2.0250	1.0125	4.0218	32.6684	20.4620	40.3391	51.1644	1.0000
Gorlova	USA	1.1196	0.6133	2.0445	64.7692	29.4836	65.8549	33.5632	1.0000
He	China	1.9352	0.2150	17.1461	4.7848	0.9525	325.1242	125.2528	1.0000
Hill (study 1)	New Zealand	0.9261	0.4538	1.8615	9.9833	33.8940	97100.6098	305305.5620	1.0000
Hill (study 2)	New Zealand	1.2818	0.7245	2.2385	14.7598	66.2900	66399.2839	382244.5260	1.0000
Hirayama	Japan	1.3488	0.9488	1.9348	159.8030	37.2477	68617.6258	21572.2705	1.0000
Hole	Scotland	1.7647	0.2054	15.0515	4.7160	1.0091	1235.6573	466.5959	1.0000
Humble 1	USA	2.0630	0.7127	6.1514	13.2570	5.0132	83.1473	64.8643	1.0000
IARC: Kreuzer	Germany	0.7381	0.4613	1.1993	50.4570	47.3752	132.1228	91.5577	1.0000
ILCCO	International	1.1143	0.9843	1.2628	674.1443	642.6864	1936.2181	2056.8075	1.0000
Inoue	Japan	2.1094	0.7219	8.2970	16.2893	4.3758	28.1813	15.9691	1.0000
Janerich	USA	0.6912	0.4332	1.1060	72.2144	70.4551	85.2073	57.4626	1.0000
Jee	Korea	1.6139	0.8726	2.9839	65.2105	12.0377	121200.2980	36109.0000	1.0000
Jiang	China	2.1540	1.0775	4.3071	46.1397	22.3122	33.5278	34.9242	1.0000
Johnson	Canada	1.1291	0.5834	2.1641	37.0982	13.1905	384.6107	154.4047	1.0000
Kabat 1	USA	0.7286	0.2306	2.2595	12.3347	11.2864	14.7632	9.8420	1.0000
Kabat 2	USA	1.0011	0.5562	1.7983	37.7377	26.2409	97.3980	67.8019	1.0000
Kalandidi	Greece	1.9962	1.0312	3.8600	57.1286	18.8052	59.0603	38.8085	1.0000
Kiyohara	Japan	0.9306	0.4315	2.0065	30.6501	18.0564	42.9740	23.5592	1.0000
Koo	China	1.5307	0.8120	2.8841	37.6725	26.1030	48.9518	51.9201	1.0000
Kurahashi	Japan	1.1702	0.7244	1.8854	73.3006	21.7800	244536.6940	85027.8861	1.0000
Lagarde	Sweden	1.0670	0.7794	1.4660	81.3850	124.4428	285.3189	465.5203	1.0000
Lam T	China	1.5401	1.0827	2.1934	111.7389	87.3425	152.0643	183.0575	1.0000
Lam W	China	1.8821	1.0206	3.4833	35.8879	23.8383	63.7075	79.6455	1.0000
Layard	USA	0.5322	0.2753	1.0369	13.5920	25.7510	969.5946	977.6443	1.0000
Lee	England	0.9259	0.3426	2.5093	17.3225	8.7320	36.6331	17.0985	1.0000
Lee C-H	Taiwan	1.7488	1.2064	2.5343	139.8913	60.7066	189.3708	143.7132	1.0000
Liang	China	1.3480	0.9429	1.9273	135.9199	87.9697	147.6092	128.7839	1.0000
Lim	Singapore	1.0417	0.8375	1.2958	192.8699	234.9655	604.5937	767.2917	1.0000
Lin	China	2.3492	1.5580	3.5411	97.4054	79.7760	72.1274	138.7715	1.0000
Liu Q	China	1.6067	0.7193	3.6150	25.3277	13.6345	37.9371	32.8119	1.0000

APPENDIX 18

ETS and Lung Cancer - Meta-Analysis of exposed/unexposed Risks, 02-NOV-15

Female (Husband's smoking)

BASIC DATA USED IN META-ANALYSES

CORRECTED FOR ALL CONFOUNDERS (FRUIT, VEG, FAT, EDUCATION)

Confounder Differences based on Random-effects Regression

Study title	Country	RR	RRL	RRU	CA1	CA0	CO1	CO0	Expos
Liu Z	China	0.7120	0.2774	1.8124	33.9915	7.0534	133.7822	19.7653	1.0000
Lopez-Cima	Spain	0.9203	0.0019	472.5566	4.4400	0.1300	17.8800	0.5100	1.0000
Malats	7 Europe+Brazil	1.3973	0.7173	2.7108	34.8823	46.9569	23.5375	44.2744	1.0000
Masjedi	Iran	1.8745	0.9407	3.7349	20.3366	35.2603	28.3039	91.9876	1.0000
McGhee	China	1.2843	0.8748	1.8985	77.7329	78.6866	131.0764	170.4041	1.0000
Nishino	Japan	1.7389	0.6473	4.4439	9.6569	7.2427	22574.7167	29441.7083	1.0000
Ohno	Japan	0.9260	0.6204	1.3798	133.1635	54.1497	234.3878	88.2622	1.0000
Pershagen	Sweden	1.1143	0.6500	1.9500	34.7721	28.7573	138.8688	127.9726	1.0000
Rapiti	India	1.1140	0.4642	2.6922	12.2688	24.1237	18.6400	40.8307	1.0000
Ren	China	1.1140	0.9190	1.3553	629.7285	247.1442	784.9891	343.1922	1.0000
Rylander	Sweden	1.2731	0.5297	3.0666	7.7248	24.2485	41.6857	166.5886	1.0000
Schoenberg	USA	0.9997	0.6516	1.5328	65.8730	42.6241	283.3936	183.3284	1.0000
Schwartz	USA	1.0199	0.6676	1.5577	120.3786	68.4961	114.3430	66.3598	1.0000
Seki	Japan	1.2178	0.9203	1.5990	187.0032	83.9988	1085.8439	593.9888	1.0000
Shen	China	0.6930	0.2864	1.6448	53.6542	14.4339	57.3915	10.6996	1.0000
Shimizu	Japan	1.0011	0.5933	1.6871	49.4599	39.0905	89.5322	70.8413	1.0000
Sobue	Japan	1.0482	0.7236	1.5121	75.5276	61.2897	375.2953	319.2404	1.0000
Speize	USA	1.3927	0.2785	5.8492	27.2133	1.7651	199267.7580	17999.9996	1.0000
Stockwell	USA	1.4924	0.7462	2.7982	46.2689	20.2940	59.0479	38.6510	1.0000
Sun	China	1.0765	0.7424	1.5684	139.5002	89.5604	135.4456	93.6097	1.0000
Svensson	Sweden	1.2650	0.4930	3.2462	17.3624	7.2243	82.4503	43.3979	1.0000
Torres-Duran	Spain	0.6537	0.4235	1.0127	47.7852	88.9152	105.3666	128.1587	1.0000
Trichopoulos	Greece	1.9489	1.1244	3.3638	51.1635	24.6689	114.2425	107.3527	1.0000
Wang L	China	1.0025	0.5840	1.6546	123.0301	25.4928	250.2653	51.9849	1.0000
Wang S	China	2.3758	1.1832	4.7892	64.7972	15.4553	58.7229	33.2772	1.0000
Wang T	China	1.0294	0.6213	1.7063	89.6597	45.0194	88.7887	45.8906	1.0000
Wen	China	1.0244	0.6955	1.5132	66.5320	41.0532	40157.9203	25385.0005	1.0000
WHI-OS	USA	0.8130	0.4804	1.3766	25.1223	30.9005	42394.2660	42394.2661	1.0000
Wu	USA	1.1142	0.4643	3.0641	17.2537	10.3231	32.5009	21.6670	1.0000
Wu-Williams	China	0.6443	0.5523	0.8284	282.2160	358.6011	508.6545	416.4532	1.0000
Yang	USA	1.8726	1.0299	3.3988	66.4524	27.6907	54.8368	42.7897	1.0000
Yu	China	1.2708	0.6542	2.4710	109.5921	16.1126	145.2120	27.1308	1.0000
Zaridze	Russia	1.4263	0.9882	2.0602	95.3557	79.9776	151.2212	180.9048	1.0000
Zatloukal	Czech Republic	0.4416	0.1932	1.0028	6.5113	69.8279	140.8617	667.0539	1.0000
Zheng	China	2.3584	1.0184	5.4767	58.8147	7.1024	171.0208	48.7057	1.0000
Zhong	China	1.0760	0.7825	1.4673	199.1634	109.9796	231.2444	137.3991	1.0000

NOTES: RR,RL,RU   RELATIVE RISKS AND LOWER AND UPPER CONFIDENCE INTERVALS

CA1,CA0   NUMBERS (OR PSEUDO-NUMBERS) OF EXPOSED AND UNEXPOSED CASES

CO1,CO0   NUMBERS (OR PSEUDO-NUMBERS) OF EXPOSED AND UNEXPOSED CONTROLS

EXPOS   ASSIGNED EXPOSURE FOR SMOKING BY HUSBAND

APPENDIX 18
ETS and Lung Cancer - Meta-Analysis of exposed/unexposed Risks, 02-NOV-15
Female (Husband's smoking)
BASIC DATA USED IN META-ANALYSES
CORRECTED FOR ALL CONFOUNDERS (FRUIT, VEG, FAT, EDUCATION)

Confounder Differences based on Random-effects Regression

Study title	Country	Beta	St.Err. Beta	Z	Weight	ETSse	FRU	VEG	FAT	EDU	TEA
Akiba	Japan	0.3342	0.2775	1.2043	12.9854	0.4607	0	0	0	0	0
Al-Zoughool	Canada	-0.9727	0.4788	-2.0315	4.3618	0.4906	0	0	0	1	0
Asomaning	USA	-0.1503	0.5596	-0.2686	3.1932	0.4358	0	0	0	0	0
Boffetta 2	7 countries	-0.0771	0.3406	-0.2264	8.6217	0.5024	0	0	0	0	0
Boffetta	7 countries	0.0289	0.1166	0.2478	73.5297	0.4839	0	0	0	0	0
Brenner	Canada	-1.0028	0.2358	-4.2530	17.9874	0.4057	0	0	0	0	0
Brownson 1	USA	0.4928	0.7330	0.6723	1.8614	0.3604	0	0	0	1	0
Brownson 2	USA	-0.0771	0.1034	-0.7454	93.4649	0.5000	0	0	0	0	0
Buffler	USA	-0.3017	0.4390	-0.6873	5.1900	0.3706	0	0	0	0	0
Butler	USA	0.6337	0.7350	0.8622	1.8512	0.3979	0	0	0	0	0
Cardenas	USA	0.1391	0.1768	0.7866	31.9819	0.4936	0	1	1	2	0
Chan	China	-0.3695	0.2822	-1.3092	12.5540	0.5012	0	0	0	0	0
Choi	Korea	0.4195	0.2902	1.4454	11.8715	0.5002	0	0	0	0	0
Correa	USA	0.6623	0.4768	1.3891	4.3991	0.5002	0	0	0	0	0
De Waard	Netherlands	0.8810	0.5701	1.5453	3.0765	0.4785	0	0	0	0	0
Du	China	0.0105	0.2708	0.0388	13.6376	0.4895	0	0	0	0	0
Enstrom	USA	-0.1287	0.1788	-0.7200	31.2967	0.4515	1	0	0	2	0
EPIC Adulthood	Western Europe	-0.2169	0.4805	-0.4514	4.3319	0.4934	1	1	1	2	0
Fang	China	0.5475	0.2561	2.1378	15.2459	0.3149	0	1	0	1	0
Fontham	USA	0.1950	0.1099	1.7744	82.8016	0.4877	1	1	0	2	0
Franco-Marina	Mexico	0.5182	0.3268	1.5858	9.3649	0.4323	0	0	0	0	0
Gallegos	Mexico	2.0338	1.1439	1.7779	0.7642	0.4803	0	0	0	0	0
Gao	China	0.1921	0.2046	0.9390	23.8925	0.4414	0	0	0	2	0
Garfinkel 1	USA	0.0825	0.1630	0.5063	37.6608	0.4986	0	0	0	0	0
Garfinkel 2	USA	0.1332	0.2134	0.6241	21.9512	0.4829	0	0	0	0	0
GELAC study	Taiwan	0.1894	0.0915	2.0709	119.5522	0.4887	0	0	0	2	0
Geng	China	0.7056	0.3519	2.0053	8.0765	0.4992	0	0	0	0	0
Gorlova	USA	0.1130	0.3071	0.3679	10.6004	0.4752	0	0	0	1	0
He	China	0.6602	1.1171	0.5910	0.8014	0.4486	0	0	2	2	0
Hill (study 1)	New Zealand	-0.0768	0.3601	-0.2133	7.7126	0.4279	0	0	0	0	0
Hill (study 2)	New Zealand	0.2482	0.2878	0.8625	12.0745	0.3551	0	0	0	3	0
Hirayama	Japan	0.2992	0.1818	1.6459	30.2626	0.4266	0	0	0	0	0
Hole	Scotland	0.5680	1.0955	0.5185	0.8333	0.4462	0	0	0	0	0
Humble 1	USA	0.7241	0.5499	1.3169	3.3074	0.4978	0	0	0	0	0
IARC: Kreuzer	Germany	-0.3037	0.2438	-1.2459	16.8300	0.4928	0	0	0	0	0
ILCCO	International	0.1082	0.0636	1.7019	247.4028	0.4998	0	0	0	0	0
Inoue	Japan	0.7464	0.6229	1.1982	2.5772	0.4859	0	0	0	0	0
Janerich	USA	-0.3693	0.2391	-1.5444	17.4887	0.4922	0	0	0	0	0
Jee	Korea	0.4787	0.3136	1.5263	10.1656	0.4202	0	1	0	3	0
Jiang	China	0.7673	0.3535	2.1707	8.0031	0.5036	1	1	0	0	0
Johnson	Canada	0.1214	0.3344	0.3630	8.9410	0.4525	1	1	0	2	0
Kabat 1	USA	-0.3167	0.5823	-0.5439	2.9497	0.5000	0	0	0	0	0
Kabat 2	USA	0.0011	0.2994	0.0037	11.1578	0.4934	0	0	0	2	0
Kalandidi	Greece	0.6913	0.3367	2.0530	8.8198	0.4917	1	0	0	2	0
Kiyohara	Japan	-0.0719	0.3921	-0.1834	6.5051	0.4818	0	0	0	0	0
Koo	China	0.4257	0.3233	1.3166	9.5655	0.5023	0	0	0	2	0
Kurahashi	Japan	0.1572	0.2440	0.6442	16.7953	0.4375	0	0	0	0	0
Lagarde	Sweden	0.0649	0.1612	0.4027	38.4970	0.4857	0	0	0	3	0
Lam T	China	0.4318	0.1801	2.3975	30.8285	0.4986	0	0	0	0	0
Lam W	China	0.6324	0.3132	2.0194	10.1972	0.4986	0	0	0	0	0
Layard	USA	-0.6307	0.3383	-1.8642	8.7366	0.5001	0	0	0	0	0
Lee	England	-0.0769	0.5080	-0.1514	3.8755	0.4701	0	0	0	0	0
Lee C-H	Taiwan	0.5589	0.1894	2.9514	27.8862	0.4960	0	0	0	2	0
Liang	China	0.2986	0.1824	1.6373	30.0656	0.4997	0	0	0	0	0
Lim	Singapore	0.0409	0.1113	0.3674	80.6789	0.4967	0	0	0	0	0
Lin	China	0.8541	0.2095	4.0777	22.7936	0.4755	0	0	0	2	0
Liu Q	China	0.4742	0.4119	1.1512	5.8941	0.5022	0	0	0	2	0
Liu Z	China	-0.3397	0.4788	-0.7095	4.3618	0.3360	0	0	0	0	0
Lopez-Cima	Spain	-0.0070	3.1758	-0.0022	0.0992	0.1689	0	0	0	0	0

APPENDIX 18

ETS and Lung Cancer - Meta-Analysis of exposed/unexposed Risks, 02-NOV-15

Female (Husband's smoking)

BASIC DATA USED IN META-ANALYSES

CORRECTED FOR ALL CONFOUNDERS (FRUIT, VEG, FAT, EDUCATION)

Confounder Differences based on Random-effects Regression

Study title	Country	Beta	St.Err. Beta	Z	Weight	ETSse	FRU	VEG	FAT	EDU	TEA
Malats	7 Europe+Brazil	0.3346	0.3392	0.9865	8.6930	0.4796	0	0	0	0	0
Masjedi	Iran	0.6283	0.3518	1.7862	8.0818	0.4260	0	0	0	0	0
McGhee	China	0.2502	0.1977	1.2658	25.5946	0.4966	0	0	0	2	0
Nishino	Japan	0.5533	0.4915	1.1258	4.1400	0.4925	1	1	1	0	0
Ohno	Japan	-0.0768	0.2039	-0.3767	24.0539	0.4465	0	0	0	0	0
Pershagen	Sweden	0.1082	0.2803	0.3861	12.7311	0.5005	0	0	0	0	0
Rapiti	India	0.1080	0.4484	0.2408	4.9727	0.4679	0	0	0	0	0
Ren	China	0.1079	0.0991	1.0887	101.8130	0.4603	0	0	0	0	0
Rylander	Sweden	0.2415	0.4480	0.5391	4.9829	0.4011	0	0	0	0	0
Schoenberg	USA	-0.0002	0.2182	-0.0009	20.9974	0.4889	0	1	0	2	0
Schwartz	USA	0.0198	0.2162	0.0916	21.4034	0.4834	0	0	0	0	0
Seki	Japan	0.1971	0.1409	1.3987	50.3603	0.4782	0	0	0	0	0
Shen	China	-0.3667	0.4459	-0.8224	5.0301	0.3666	0	0	0	0	0
Shimizu	Japan	0.0011	0.2666	0.0041	14.0676	0.4981	0	0	0	0	0
Sobue	Japan	0.0471	0.1880	0.2505	28.2860	0.4987	0	0	0	2	0
Speize	USA	0.3312	0.7767	0.4264	1.6577	0.2753	0	0	0	0	0
Stockwell	USA	0.4004	0.3372	1.1875	8.7954	0.4915	0	0	0	2	0
Sun	China	0.0737	0.1908	0.3863	27.4727	0.4927	0	0	0	2	0
Svensson	Sweden	0.2351	0.4808	0.4890	4.3255	0.4772	0	0	0	0	0
Torres-Duran	Spain	-0.4251	0.2224	-1.9113	20.2154	0.4987	0	0	0	0	0
Trichopoulos	Greece	0.6673	0.2796	2.3870	12.7958	0.5009	0	0	0	0	0
Wang L	China	0.0025	0.2657	0.0094	14.1669	0.3780	0	0	0	1	0
Wang S	China	0.8654	0.3567	2.4263	7.8607	0.4831	0	0	0	0	0
Wang T	China	0.0289	0.2577	0.1121	15.0558	0.4757	0	0	0	0	0
Wen	China	0.0242	0.1983	0.1220	25.4293	0.4876	1	1	0	2	0
WHI-OS	USA	-0.2070	0.2686	-0.7708	13.8658	0.5000	0	0	0	0	0
Wu	USA	0.1082	0.4814	0.2248	4.3150	0.4944	0	0	0	0	0
Wu-Williams	China	-0.4395	0.1034	-4.2490	93.4649	0.4978	0	0	0	2	0
Yang	USA	0.6273	0.3046	2.0596	10.7796	0.4987	0	0	0	0	0
Yu	China	0.2396	0.3390	0.7067	8.7007	0.3653	1	1	0	2	0
Zaridze	Russia	0.3551	0.1874	1.8945	28.4648	0.4987	0	0	0	2	0
Zatloukal	Czech Republic	-0.8174	0.4201	-1.9457	5.6658	0.3797	0	0	0	2	0
Zheng	China	0.8580	0.4292	1.9992	5.4295	0.4163	0	0	0	0	0
Zhong	China	0.0732	0.1604	0.4565	38.8862	0.4842	1	0	0	1	0

NOTES: BETA   SLOPE OF LOG RR ON NCIGS

SE BETA   STANDARD ERROR OF BETA

Z   RATIO OF BETA TO ITS STANDARD ERROR (APPROXIMATE NORMAL STATISTIC)

WEIGHT   INVERSE OF THE VARIANCE OF BETA

ETSse   STANDARD ERROR OF ETS EXPOSURE OVER THE CONTROL GROUPS

FRU = 1   ANALYSIS ADJUSTED FOR FRUIT

VEG = 1   "   "   " VEGETABLES

FAT = 1   "   "   " FRUIT

EDU = 1   "   "   " INCOME

= 2   "   "   " EDUCATION

= 3   "   "   " SOCIO-ECONOMIC STATUS

APPENDIX 18
ETS and Lung Cancer - Meta-Analysis of exposed/unexposed Risks, 02-NOV-15
Female (Husband's smoking)
BASIC DATA USED IN META-ANALYSES
CORRECTED FOR ALL CONFOUNDERS (FRUIT, VEG, FAT, EDUCATION)

Confounder Differences based on Random-effects Regression

TEA = 0 NO ADJUSTMENT (OR MATCHING) FOR TEA

RANDOM-EFFECTS META-ANALYSES

Log RR (Beta) WEIGHTED on Beta Weights

	Deviance	(DF)				
Model 1	98.1573	(92)				
	Estimate	**S.E.**	**P**	**RR**	**95%Cll**	**95%Clu**
Constant	0.1299	0.0355	+++	1.1387	1.0623	1.2207

SEPARATE RANDOM-EFFECTS META-ANALYSES BY REGION

NORTH AMERICA, EUROPE AND NEW ZEALAND

Log RR (Beta) WEIGHTED on Beta Weights

	Deviance	(DF)				
Model 1	52.0334	(48)				
	Estimate	**S.E.**	**P**	**RR**	**95%Cll**	**95%Clu**
Constant	0.0362	0.0529	N.S.	1.0369	0.9347	1.1502

ASIA

Log RR (Beta) WEIGHTED on Beta Weights

	Deviance	(DF)				
Model 1	41.1236	(43)				
	Estimate	**S.E.**	**P**	**RR**	**95%Cll**	**95%Clu**
Constant	0.2062	0.0471	+++	1.2291	1.1206	1.3480

NORTH AMERICA

Log RR (Beta) WEIGHTED on Beta Weights

	Deviance	(DF)				
Model 1	31.5604	(28)				
	Estimate	**S.E.**	**P**	**RR**	**95%Cll**	**95%Clu**
Constant	0.0038	0.0712	N.S.	1.0038	0.8731	1.1540

EUROPE AND NEW ZEALAND

Log RR (Beta) WEIGHTED on Beta Weights

	Deviance	(DF)				
Model 1	19.3074	(19)				
	Estimate	**S.E.**	**P**	**RR**	**95%Cll**	**95%Clu**
Constant	0.0876	0.0798	N.S.	1.0916	0.9335	1.2765

CHINA AND HONG KONG

Log RR (Beta) WEIGHTED on Beta Weights

	Deviance	(DF)				
Model 1	23.4852	(26)				
	Estimate	**S.E.**	**P**	**RR**	**95%Cll**	**95%Clu**
Constant	0.2143	0.0743	++	1.2390	1.0711	1.4331

REST OF ASIA

APPENDIX 18
ETS and Lung Cancer - Meta-Analysis of exposed/unexposed Risks, 02-NOV-15
Female (Husband's smoking)

CORRECTED FOR ALL CONFOUNDERS (FRUIT, VEG, FAT, EDUCATION)
SEPARATE RANDOM-EFFECTS META-ANALYSES BY REGION
Confounder Differences based on Random-effects Regression

Log RR (Beta)
WEIGHTED on Beta
Weights

	Deviance	(DF)				
Model 1	13.6362	(16)				
	Estimate	**S.E.**	**P**	**RR**	**95%Cll**	**95%Clu**
Constant	0.1769	0.0402	+++	1.1935	1.1032	1.2912

SEPARATE RANDOM-EFFECTS META-ANALYSES BY YEAR OF PUBLICATION

PUBLISHED IN 1980S
Log RR (Beta)
WEIGHTED on Beta
Weights

	Deviance	(DF)				
Model 1	21.4770	(25)				
	Estimate	**S.E.**	**P**	**RR**	**95%Cll**	**95%Clu**
Constant	0.2363	0.0572	+++	1.2666	1.1323	1.4168

PUBLISHED IN 1990S
Log RR (Beta)
WEIGHTED on Beta
Weights

	Deviance	(DF)				
Model 1	25.6393	(26)				
	Estimate	**S.E.**	**P**	**RR**	**95%Cll**	**95%Clu**
Constant	0.0745	0.0653	N.S.	1.0774	0.9479	1.2245

PUBLISHED IN 2000S
Log RR (Beta)
WEIGHTED on Beta
Weights

	Deviance	(DF)				
Model 1	24.8942	(25)				
	Estimate	**S.E.**	**P**	**RR**	**95%Cll**	**95%Clu**
Constant	0.1508	0.0600	+	1.1628	1.0339	1.3078

PUBLISHED IN 2010S
Log RR (Beta)
WEIGHTED on Beta
Weights

	Deviance	(DF)				
Model 1	24.9589	(13)				
	Estimate	**S.E.**	**P**	**RR**	**95%Cll**	**95%Clu**
Constant	0.0571	0.0958	N.S.	1.0587	0.8774	1.2774

SEPARATE RANDOM-EFFECTS META-ANALYSES BY NUMBER OF LUNG CANCER CASES

<100 CASES
Log RR (Beta)
WEIGHTED on Beta
Weights

	Deviance	(DF)				
Model 1	47.4135	(48)				
	Estimate	**S.E.**	**P**	**RR**	**95%Cll**	**95%Clu**
Constant	0.2226	0.0659	++	1.2493	1.0979	1.4215

100-199 CASES

APPENDIX 18
ETS and Lung Cancer - Meta-Analysis of exposed/unexposed Risks, 02-NOV-15
Female (Husband's smoking)

CORRECTED FOR ALL CONFOUNDERS (FRUIT, VEG, FAT, EDUCATION)
SEPARATE RANDOM-EFFECTS META-ANALYSES BY NUMBER OF LUNG CANCER CASES
Confounder Differences based on Random-effects Regression

Log RR (Beta)
WEIGHTED on Beta
Weights

	Deviance	**(DF)**				
Model 1	22.2407	(21)				
	Estimate	**S.E.**	**P**	**RR**	**95%Cll**	**95%Clu**
Constant	0.0409	0.0722	N.S.	1.0418	0.9044	1.2000

200-399 CASES
Log RR (Beta)
WEIGHTED on Beta
Weights

	Deviance	**(DF)**				
Model 1	12.3493	(12)				
	Estimate	**S.E.**	**P**	**RR**	**95%Cll**	**95%Clu**
Constant	0.2433	0.0691	++	1.2754	1.1140	1.4603

400+ CASES
Log RR (Beta)
WEIGHTED on Beta
Weights

	Deviance	**(DF)**				
Model 1	8.0908	(8)				
	Estimate	**S.E.**	**P**	**RR**	**95%Cll**	**95%Clu**
Constant	0.0264	0.0647	N.S.	1.0267	0.9045	1.1655

SEPARATE RANDOM-EFFECTS META-ANALYSES BY DOSE-RESPONSE OR NOT

RESULTS FOR DOSE-RESPONSE
Log RR (Beta)
WEIGHTED on Beta
Weights

	Deviance	**(DF)**				
Model 1	23.2683	(23)				
	Estimate	**S.E.**	**P**	**RR**	**95%Cll**	**95%Clu**
Constant	0.2033	0.0526	+++	1.2255	1.1054	1.3585

NO RESULTS FOR DOSE-RESPONSE
Log RR (Beta)
WEIGHTED on Beta
Weights

	Deviance	**(DF)**				
Model 1	73.9813	(68)				
	Estimate	**S.E.**	**P**	**RR**	**95%Cll**	**95%Clu**
Constant	0.0985	0.0433	+	1.1035	1.0137	1.2012

SEPARATE RANDOM-EFFECTS META-ANALYSES BY AGE ADJUSTMENT OR NOT

ADJUSTED (OR MATCHED) FOR AGE
Log RR (Beta)
WEIGHTED on Beta
Weights

	Deviance	**(DF)**				
Model 1	77.6687	(74)				
	Estimate	**S.E.**	**P**	**RR**	**95%Cll**	**95%Clu**
Constant	0.1007	0.0379	++	1.1060	1.0268	1.1912

NOT ADJUSTED (OR MATCHED) FOR AGE

APPENDIX 18
ETS and Lung Cancer - Meta-Analysis of exposed/unexposed Risks, 02-NOV-15
Female (Husband's smoking)

CORRECTED FOR ALL CONFOUNDERS (FRUIT, VEG, FAT, EDUCATION)
SEPARATE RANDOM-EFFECTS META-ANALYSES BY AGE ADJUSTMENT OR NOT
Confounder Differences based on Random-effects Regression

Log RR (Beta)
WEIGHTED on Beta
Weights

	Deviance	**(DF)**				
Model 1	17.4768	(17)				
	Estimate	**S.E.**	**P**	**RR**	**95%CIl**	**95%CIu**
Constant	0.2928	0.0959	++	1.3402	1.1104	1.6175

SEPARATE RANDOM-EFFECTS META-ANALYSES BY STUDY TYPE

CASE-CONTROL STUDIES
Log RR (Beta)
WEIGHTED on Beta
Weights

	Deviance	**(DF)**				
Model 1	85.3713	(76)				
	Estimate	**S.E.**	**P**	**RR**	**95%CIl**	**95%CIu**
Constant	0.1347	0.0406	++	1.1442	1.0566	1.2390

PROSPECTIVE STUDIES
Log RR (Beta)
WEIGHTED on Beta
Weights

	Deviance	**(DF)**				
Model 1	8.6994	(15)				
	Estimate	**S.E.**	**P**	**RR**	**95%CIl**	**95%CIu**
Constant	0.1053	0.0658	N.S.	1.1111	0.9766	1.2640

Appendix 19

Fuller details of the analyses relating lung cancer risk to whether or not the husband smoked – adjusted for confounding and corrected for misclassification

APPENDIX 19
ETS and Lung Cancer - Meta-Analysis of exposed/unexposed Risks, 02-NOV-15
Female (Husband's smoking)
BASIC DATA USED IN META-ANALYSES
CORRECTED FOR ALL CONFOUNDERS (FRUIT, VEG, FAT, EDUCATION) AND MISCLASSIFICATION

Confounder Differences based on Random-effects Regression
Misclassification: Additive, Concordance: 3.0, MissP: US:0.025, EU:0.025, ASIA:0.1

Study title	Country	RR	RRL	RRU	CA1	CA0	CO1	CO0	Expos
Akiba	Japan	1.3627	0.8268	2.5622	64.5199	20.6526	170.3456	74.3053	1.0000
Al-Zoughool	Canada	0.3781	0.1454	0.9500	5.8254	23.1997	114.7862	172.8264	1.0000
Asomaning	USA	0.7052	0.2036	2.4340	10.1767	4.8105	42.3161	14.1053	1.0000
Boffetta 2	7 countries	0.8827	0.4291	1.7249	22.2843	24.8758	49.3062	48.5844	1.0000
Boffetta	7 countries	0.9909	0.7801	1.2497	277.6384	166.6853	552.7852	328.8692	1.0000
Brenner	Canada	0.3600	0.2227	0.5729	49.3372	35.8372	486.7258	127.2832	1.0000
Brownson 1	USA	1.5973	0.3437	7.0771	3.3188	11.8804	5.5959	31.9960	1.0000
Brownson 2	USA	0.7791	0.6054	0.9626	177.6702	216.6047	547.0494	519.6031	1.0000
Buffler	USA	0.5757	0.2193	1.5260	20.7987	7.0473	111.3957	21.7308	1.0000
Butler	USA	1.8748	0.4333	8.1692	2.5564	5.8749	10684.6191	46036.4488	1.0000
Cardenas	USA	1.0284	0.6555	1.4342	60.5495	42.7173	81515.1715	59143.5717	1.0000
Chan	China	0.5770	0.3028	1.0926	21.9501	42.0751	50.3097	55.6394	1.0000
Choi	Korea	1.5123	0.8433	2.6950	44.6429	25.4949	82.2979	71.0744	1.0000
Correa	USA	1.6775	0.5025	5.5573	7.4822	5.2646	35.3437	41.7168	1.0000
De Waard	Netherlands	2.3925	0.7481	7.6383	16.6986	3.7656	110.3946	59.5596	1.0000
Du	China	0.9592	0.5461	1.6790	39.1627	26.5114	134.8512	87.5654	1.0000
Enstrom	USA	0.8498	0.5904	1.2150	91.6779	43.0465	14113.8819	5631.3359	1.0000
EPIC Adulthood	Western Europe	0.7663	0.2868	2.0778	8.0734	7.6040	12480.4194	9007.9639	1.0000
Fang	China	1.6667	0.9462	2.9279	18.0655	86.3718	69.8685	556.7551	1.0000
Fontham	USA	1.0807	0.8534	1.3683	281.0839	165.3566	525.2898	333.9426	1.0000
Franco-Marina	Mexico	1.6665	0.8681	3.2081	20.1830	37.0399	38.3021	117.1444	1.0000
Gallegos	Mexico	7.7639	0.7766	77.6351	11.9694	0.8220	35.9781	19.1835	1.0000
Gao	China	1.1514	0.7520	1.7496	146.2061	45.5462	215.1445	77.1721	1.0000
Garfinkel 1	USA	1.0678	0.7698	1.4805	80.3302	64.9082	90066.8018	77706.3389	1.0000
Garfinkel 2	USA	1.0809	0.6970	1.6780	75.3732	40.6346	219.9013	128.1381	1.0000
GELAC study	Taiwan	1.2038	1.0080	1.4464	426.3319	546.3181	382.5433	590.1069	1.0000
Geng	China	1.9128	0.8472	4.2891	22.9230	15.1998	28.9443	36.7121	1.0000
Gorlova	USA	1.0258	0.5446	1.9329	55.9792	27.8119	58.5454	29.8377	1.0000
He	China	1.9335	0.2100	17.5216	4.6842	0.9333	318.3378	122.6386	1.0000
Hill (study 1)	New Zealand	0.8640	0.3944	1.8639	8.1210	29.5542	83376.4846	262151.7920	1.0000
Hill (study 2)	New Zealand	1.2403	0.6773	2.2417	13.0362	60.5078	60250.2047	346845.7680	1.0000
Hirayama	Japan	1.3096	0.9077	1.9064	143.8894	34.5435	62134.4795	19534.0747	1.0000
Hole	Scotland	1.7028	0.1687	17.0638	3.9619	0.8786	1044.7374	394.5093	1.0000
Humble 1	USA	1.8238	0.4699	7.2910	7.5401	3.2253	48.9932	38.2202	1.0000
IARC: Kreuzer	Germany	0.7041	0.4319	1.1658	45.6189	44.8997	122.2457	84.7131	1.0000
ILCCO	International	1.0680	0.9376	1.2180	598.3979	595.1750	1754.9845	1864.2864	1.0000
Inoue	Japan	2.1000	0.7017	8.4600	15.6248	4.2161	27.0572	15.3323	1.0000
Janerich	USA	0.5698	0.3414	0.9537	54.5763	64.5944	71.1726	48.0000	1.0000
Jee	Korea	1.6056	0.8596	2.9979	62.6143	11.6795	120569.3440	36108.9993	1.0000
Jiang	China	2.1188	1.0240	4.3851	41.5224	20.4142	30.3356	31.6003	1.0000
Johnson	Canada	0.9418	0.4387	2.0021	24.4416	10.4187	266.6130	107.0339	1.0000
Kabat 1	USA	0.6449	0.1891	2.1585	10.1964	10.5406	12.9607	8.6404	1.0000
Kabat 2	USA	0.8714	0.4543	1.6682	28.5273	22.7885	78.1251	54.3855	1.0000
Kalandidi	Greece	1.9876	1.0200	3.8690	55.8582	18.4677	57.8091	37.9887	1.0000
Kiyohara	Japan	0.8946	0.4030	1.9856	27.8929	17.0927	39.6918	21.7600	1.0000
Koo	China	1.4408	0.7139	2.9066	29.7504	21.8983	39.6439	42.0441	1.0000
Kurahashi	Japan	1.1361	0.6898	1.8660	64.3112	20.4453	235420.7140	85027.8860	1.0000
Lagarde	Sweden	0.9696	0.6838	1.3796	63.2568	106.4450	235.2410	383.8143	1.0000
Lam T	China	1.4383	0.9752	2.1241	88.7200	74.2613	124.4875	149.8684	1.0000
Lam W	China	1.7958	0.9144	3.5394	28.7838	20.0385	52.0768	65.1050	1.0000
Layard	USA	0.4652	0.2200	0.9912	10.0817	21.8529	787.0181	793.5516	1.0000
Lee	England	0.7937	0.2629	2.4021	12.8975	7.5852	28.7986	13.4422	1.0000
Lee C-H	Taiwan	1.7413	1.1980	2.5302	137.5716	59.9638	186.4757	141.5308	1.0000
Liang	China	1.2947	0.8891	1.8854	120.4261	81.1490	132.8977	115.9459	1.0000
Lim	Singapore	0.9835	0.7792	1.2413	164.9149	212.8087	533.7783	677.4197	1.0000
Lin	China	2.3484	1.5567	3.5417	97.1473	79.6071	71.9436	138.4466	1.0000
Liu Q	China	1.4895	0.6107	3.6591	19.7680	11.4773	30.4244	26.3115	1.0000

APPENDIX 19

ETS and Lung Cancer - Meta-Analysis of exposed/unexposed Risks, 02-NOV-15

Female (Husband's smoking)

BASIC DATA USED IN META-ANALYSES

CORRECTED FOR ALL CONFOUNDERS (FRUIT, VEG, FAT, EDUCATION) AND MISCLASSIFICATION

Confounder Differences based on Random-effects Regression

Misclassification: Additive, Concordance: 3.0, MissP: US:0.025, EU:0.025, ASIA:0.1

Study title	Country	RR	RRL	RRU	CA1	CA0	CO1	CO0	Expos
Liu Z	China	0.6771	0.2563	1.7741	30.9482	6.7524	122.8862	18.1539	1.0000
Lopez-Cima	Spain	0.9918	0.0020	516.1995	4.4400	0.1300	17.8800	0.5100	1.0000
Malats	7 Europe+Brazil	1.3514	0.6777	2.6839	31.9973	44.5412	22.0121	41.4100	1.0000
Masjedi	Iran	1.8668	0.9243	3.7703	19.5258	33.9928	27.2456	88.5485	1.0000
McGhee	China	1.1967	0.7852	1.8364	62.4297	67.8189	109.1511	141.8961	1.0000
Nishino	Japan	1.7095	0.6029	4.6109	8.5766	6.5430	20197.0210	26340.7395	1.0000
Ohno	Japan	0.8921	0.5898	1.3470	122.1938	51.5800	217.4490	81.8878	1.0000
Pershagen	Sweden	1.0657	0.6040	1.9194	30.6690	26.5211	125.0118	115.2029	1.0000
Rapiti	India	1.0647	0.4144	2.7543	10.3492	21.2928	16.2061	35.4998	1.0000
Ren	China	1.0652	0.8720	1.3061	568.5659	233.3501	717.8939	313.8535	1.0000
Rylander	Sweden	1.1265	0.3955	3.2152	5.2239	18.5324	30.9725	123.7757	1.0000
Schoenberg	USA	0.8030	0.4839	1.3315	41.7109	33.6023	196.7179	127.2573	1.0000
Schwartz	USA	0.8950	0.5683	1.4090	98.2425	63.7044	98.0406	56.8992	1.0000
Seki	Japan	1.1863	0.8870	1.5744	170.4144	78.5819	997.6721	545.7563	1.0000
Shen	China	0.6563	0.2652	1.5930	49.7150	14.1226	53.8120	10.0320	1.0000
Shimizu	Japan	0.9488	0.5448	1.6502	42.7844	35.6814	79.3350	62.7761	1.0000
Sobue	Japan	0.9939	0.6679	1.4725	63.8257	54.6273	324.9211	276.3902	1.0000
Speize	USA	1.2129	0.1982	6.2355	17.9257	1.3921	191085.9830	17999.9996	1.0000
Stockwell	USA	1.3665	0.6460	2.7099	37.4768	17.9517	49.1718	32.1870	1.0000
Sun	China	1.0239	0.6941	1.5177	124.3069	83.9004	123.1175	85.0866	1.0000
Svensson	Sweden	1.1740	0.4252	3.2419	14.2522	6.3896	69.2226	36.4344	1.0000
Torres-Duran	Spain	0.6463	0.4168	1.0060	46.5362	87.5828	103.3773	125.7388	1.0000
Trichopoulos	Greece	1.9453	1.1188	3.3679	50.5293	24.4119	112.8957	106.1013	1.0000
Wang L	China	0.9999	0.5801	1.6571	120.9278	25.1222	246.1163	51.1247	1.0000
Wang S	China	2.3678	1.1689	4.8149	63.0826	15.0977	57.2065	32.4180	1.0000
Wang T	China	0.9798	0.5794	1.6578	80.7883	42.6157	81.3556	42.0487	1.0000
Wen	China	0.9733	0.6436	1.4760	56.5661	36.7369	34826.8481	22015.0716	1.0000
WHI-OS	USA	0.7019	0.3801	1.2969	17.3473	24.7147	31829.6922	31829.6919	1.0000
Wu	USA	1.0462	0.4060	3.0890	14.4214	9.1902	27.8285	18.5533	1.0000
Wu-Williams	China	0.5572	0.4637	0.7378	200.4972	294.6015	392.9891	321.7539	1.0000
Yang	USA	1.7515	0.9131	3.3536	54.0619	24.0846	45.5198	35.5184	1.0000
Yu	China	1.2523	0.6391	2.4567	105.8333	15.7878	140.4982	26.2477	1.0000
Zaridze	Russia	1.4250	0.9859	2.0613	94.5701	79.3987	150.0452	179.5190	1.0000
Zatloukal	Czech Republic	0.2425	0.0558	1.0467	1.9370	37.8274	73.3735	347.4617	1.0000
Zheng	China	2.3300	0.9633	5.6515	52.6772	6.4382	153.3766	43.6780	1.0000
Zhong	China	1.0249	0.7349	1.4175	177.8872	103.1284	210.2016	124.8968	1.0000

NOTES: RR,RL,RU RELATIVE RISKS AND LOWER AND UPPER CONFIDENCE INTERVALS

CA1,CA0 NUMBERS (OR PSEUDO-NUMBERS) OF EXPOSED AND UNEXPOSED CASES

CO1,CO0 NUMBERS (OR PSEUDO-NUMBERS) OF EXPOSED AND UNEXPOSED CONTROLS

EXPOS ASSIGNED EXPOSURE FOR SMOKING BY HUSBAND

APPENDIX 19

ETS and Lung Cancer - Meta-Analysis of exposed/unexposed Risks, 02-NOV-15

Female (Husband's smoking)

BASIC DATA USED IN META-ANALYSES

CORRECTED FOR ALL CONFOUNDERS (FRUIT, VEG, FAT, EDUCATION) AND MISCLASSIFICATION

Confounder Differences based on Random-effects Regression

Misclassification: Additive, Concordance: 3.0, MissP: US:0.025, EU:0.025, ASIA:0.1

Study title	Country	Beta	St.Err. Beta	Z	Weight	ETSse	FRU	VEG	FAT	EDU	TEA
Akiba	Japan	0.3095	0.2885	1.0728	12.0146	0.4607	0	0	0	0	0
Al-Zoughool	Canada	-0.9727	0.4788	-2.0315	4.3618	0.4906	0	0	0	1	0
Asomaning	USA	-0.3493	0.6330	-0.5518	2.4957	0.4358	0	0	0	0	0
Boffetta 2	7 countries	-0.1248	0.3549	-0.3516	7.9394	0.5024	0	0	0	0	0
Boffetta	7 countries	-0.0091	0.1202	-0.0757	69.2135	0.4839	0	0	0	0	0
Brenner	Canada	-1.0216	0.2410	-4.2390	17.2173	0.4057	0	0	0	0	0
Brownson 1	USA	0.4683	0.7716	0.6069	1.6796	0.3604	0	0	0	1	0
Brownson 2	USA	-0.2496	0.1183	-2.1099	71.4547	0.5000	0	0	0	0	0
Buffler	USA	-0.5521	0.4949	-1.1156	4.0829	0.3706	0	0	0	0	0
Butler	USA	0.6285	0.7492	0.8389	1.7816	0.3979	0	0	0	0	0
Cardenas	USA	0.0280	0.1997	0.1402	25.0752	0.4936	0	1	1	2	0
Chan	China	-0.5500	0.3274	-1.6799	9.3292	0.5012	0	0	0	0	0
Choi	Korea	0.4136	0.2964	1.3954	11.3827	0.5002	0	0	0	0	0
Correa	USA	0.5173	0.6131	0.8437	2.6603	0.5002	0	0	0	0	0
De Waard	Netherlands	0.8723	0.5927	1.4717	2.8466	0.4785	0	0	0	0	0
Du	China	-0.0416	0.2865	-0.1452	12.1829	0.4895	0	0	0	0	0
Enstrom	USA	-0.1628	0.1841	-0.8843	29.5048	0.4515	1	0	0	2	0
EPIC Adulthood	Western Europe	-0.2662	0.5052	-0.5269	3.9181	0.4934	1	1	1	2	0
Fang	China	0.5109	0.2882	1.7727	12.0396	0.3149	0	1	0	1	0
Fontham	USA	0.0776	0.1204	0.6445	68.9838	0.4877	1	1	0	2	0
Franco-Marina	Mexico	0.5107	0.3335	1.5313	8.9910	0.4323	0	0	0	0	0
Gallegos	Mexico	2.0495	1.1747	1.7447	0.7247	0.4803	0	0	0	0	0
Gao	China	0.1410	0.2154	0.6546	21.5530	0.4414	0	0	0	2	0
Garfinkel 1	USA	0.0656	0.1668	0.3933	35.9425	0.4986	0	0	0	0	0
Garfinkel 2	USA	0.0778	0.2241	0.3472	19.9121	0.4829	0	0	0	0	0
GELAC study	Taiwan	0.1855	0.0921	2.0141	117.8910	0.4887	0	0	0	2	0
Geng	China	0.6486	0.4138	1.5674	5.8401	0.4992	0	0	0	0	0
Gorlova	USA	0.0255	0.3231	0.0789	9.5791	0.4752	0	0	0	1	0
He	China	0.6593	1.1286	0.5842	0.7851	0.4486	0	0	2	2	0
Hill (study 1)	New Zealand	-0.1462	0.3962	-0.3690	6.3705	0.4279	0	0	0	0	0
Hill (study 2)	New Zealand	0.2153	0.3053	0.7052	10.7287	0.3551	0	0	0	3	0
Hirayama	Japan	0.2697	0.1893	1.4247	27.9061	0.4266	0	0	0	0	0
Hole	Scotland	0.5323	1.1777	0.4520	0.7210	0.4462	0	0	0	0	0
Humble 1	USA	0.6009	0.6995	0.8590	2.0437	0.4978	0	0	0	0	0
IARC: Kreuzer	Germany	-0.3509	0.2533	-1.3853	15.5858	0.4928	0	0	0	0	0
ILCCO	International	0.0658	0.0668	0.9850	224.1027	0.4998	0	0	0	0	0
Inoue	Japan	0.7420	0.6351	1.1683	2.4792	0.4859	0	0	0	0	0
Janerich	USA	-0.5624	0.2621	-2.1457	14.5568	0.4922	0	0	0	0	0
Jee	Korea	0.4735	0.3187	1.4857	9.8455	0.4202	0	1	0	3	0
Jiang	China	0.7508	0.3711	2.0232	7.2614	0.5036	1	1	0	0	0
Johnson	Canada	-0.0600	0.3873	-0.1549	6.6666	0.4525	1	1	0	2	0
Kabat 1	USA	-0.4387	0.6212	-0.7062	2.5914	0.5000	0	0	0	0	0
Kabat 2	USA	-0.1376	0.3318	-0.4147	9.0834	0.4934	0	0	0	2	0
Kalandidi	Greece	0.6869	0.3401	2.0197	8.6454	0.4917	1	0	0	2	0
Kiyohara	Japan	-0.1114	0.4068	-0.2738	6.0428	0.4818	0	0	0	0	0
Koo	China	0.3652	0.3582	1.0195	7.7938	0.5023	0	0	0	2	0
Kurahashi	Japan	0.1276	0.2539	0.5026	15.5122	0.4375	0	0	0	0	0
Lagarde	Sweden	-0.0309	0.1791	-0.1725	31.1752	0.4857	0	0	0	3	0
Lam T	China	0.3634	0.1986	1.8298	25.3537	0.4986	0	0	0	0	0
Lam W	China	0.5854	0.3453	1.6953	8.3870	0.4986	0	0	0	0	0
Layard	USA	-0.7653	0.3840	-1.9930	6.7817	0.5001	0	0	0	0	0
Lee	England	-0.2311	0.5643	-0.4095	3.1404	0.4701	0	0	0	0	0
Lee C-H	Taiwan	0.5546	0.1907	2.9082	27.4978	0.4960	0	0	0	2	0
Liang	China	0.2583	0.1918	1.3467	27.1833	0.4997	0	0	0	0	0
Lim	Singapore	-0.0167	0.1188	-0.1406	70.8544	0.4967	0	0	0	0	0
Lin	China	0.8537	0.2097	4.0711	22.7407	0.4755	0	0	0	2	0
Liu Q	China	0.3985	0.4567	0.8726	4.7944	0.5022	0	0	0	2	0
Liu Z	China	-0.3900	0.4936	-0.7901	4.1044	0.3360	0	0	0	0	0
Lopez-Cima	Spain	-0.0070	3.1758	-0.0022	0.0992	0.1689	0	0	0	0	0

APPENDIX 19

ETS and Lung Cancer - Meta-Analysis of exposed/unexposed Risks, 02-NOV-15

Female (Husband's smoking)

BASIC DATA USED IN META-ANALYSES

CORRECTED FOR ALL CONFOUNDERS (FRUIT, VEG, FAT, EDUCATION) AND MISCLASSIFICATION

Confounder Differences based on Random-effects Regression

Misclassification: Additive, Concordance: 3.0, MissP: US:0.025, EU:0.025, ASIA:0.1

Study title	Country	Beta	St.Err. Beta	Z	Weight	ETSse	FRU	VEG	FAT	EDU	TEA
Malats	7 Europe+Brazil	0.3012	0.3511	0.8579	8.1122	0.4796	0	0	0	0	0
Masjedi	Iran	0.6242	0.3586	1.7407	7.7764	0.4260	0	0	0	0	0
McGhee	China	0.1796	0.2167	0.8288	21.2952	0.4966	0	0	0	2	0
Nishino	Japan	0.5362	0.5190	1.0331	3.7125	0.4925	1	1	1	0	0
Ohno	Japan	-0.1141	0.2107	-0.5415	22.5253	0.4465	0	0	0	0	0
Pershagen	Sweden	0.0636	0.2949	0.2157	11.4987	0.5005	0	0	0	0	0
Rapiti	India	0.0627	0.4832	0.1298	4.2830	0.4679	0	0	0	0	0
Ren	China	0.0632	0.1031	0.6130	94.0768	0.4603	0	0	0	0	0
Rylander	Sweden	0.1191	0.5346	0.2228	3.4990	0.4011	0	0	0	0	0
Schoenberg	USA	-0.2194	0.2582	-0.8497	14.9999	0.4889	0	1	0	2	0
Schwartz	USA	-0.1109	0.2316	-0.4788	18.6433	0.4834	0	0	0	0	0
Seki	Japan	0.1708	0.1464	1.1667	46.6571	0.4782	0	0	0	0	0
Shen	China	-0.4212	0.4574	-0.9209	4.7798	0.3666	0	0	0	0	0
Shimizu	Japan	-0.0526	0.2827	-0.1861	12.5126	0.4981	0	0	0	0	0
Sobue	Japan	-0.0061	0.2017	-0.0302	24.5804	0.4987	0	0	0	2	0
Speize	USA	0.1931	0.8798	0.2195	1.2919	0.2753	0	0	0	0	0
Stockwell	USA	0.3123	0.3658	0.8537	7.4733	0.4915	0	0	0	2	0
Sun	China	0.0237	0.1996	0.1187	25.1003	0.4927	0	0	0	2	0
Svensson	Sweden	0.1604	0.5182	0.3095	3.7240	0.4772	0	0	0	0	0
Torres-Duran	Spain	-0.4365	0.2248	-1.9417	19.7882	0.4987	0	0	0	0	0
Trichopoulos	Greece	0.6654	0.2811	2.3671	12.6555	0.5009	0	0	0	0	0
Wang L	China	-0.0001	0.2678	-0.0004	13.9437	0.3780	0	0	0	1	0
Wang S	China	0.8619	0.3611	2.3869	7.6691	0.4831	0	0	0	0	0
Wang T	China	-0.0204	0.2682	-0.0761	13.9022	0.4757	0	0	0	0	0
Wen	China	-0.0270	0.2117	-0.1275	22.3130	0.4876	1	1	0	2	0
WHI-OS	USA	-0.3540	0.3131	-1.1306	10.2008	0.5000	0	0	0	0	0
Wu	USA	0.0452	0.5177	0.0873	3.7312	0.4944	0	0	0	0	0
Wu-Williams	China	-0.5848	0.1185	-4.9350	71.2137	0.4978	0	0	0	2	0
Yang	USA	0.5605	0.3319	1.6888	9.0779	0.4987	0	0	0	0	0
Yu	China	0.2250	0.3435	0.6550	8.4751	0.3653	1	1	0	2	0
Zaridze	Russia	0.3542	0.1882	1.8820	28.2332	0.4987	0	0	0	2	0
Zatloukal	Czech Republic	-1.4168	0.7478	-1.8946	1.7883	0.3797	0	0	0	2	0
Zheng	China	0.8459	0.4514	1.8739	4.9077	0.4163	0	0	0	0	0
Zhong	China	0.0246	0.1676	0.1468	35.6002	0.4842	1	0	0	1	0

NOTES: BETA SLOPE OF LOG RR ON NCIGS

BETA	SLOPE OF LOG RR ON NCIGS	
SE BETA	STANDARD ERROR OF BETA	
Z	RATIO OF BETA TO ITS STANDARD ERROR (APPROXIMATE NORMAL STATISTIC)	
WEIGHT	INVERSE OF THE VARIANCE OF BETA	
ETSse	STANDARD ERROR OF ETS EXPOSURE OVER THE CONTROL GROUPS	
FRU = 1	ANALYSIS ADJUSTED FOR FRUIT	
VEG = 1	" " "	VEGETABLES
FAT = 1	" " "	FRUIT
EDU = 1	" " "	INCOME
= 2	" " "	EDUCATION
= 3	" " "	SOCIO-ECONOMIC STATUS

APPENDIX 19
ETS and Lung Cancer - Meta-Analysis of exposed/unexposed Risks, 02-NOV-15
Female (Husband's smoking)
BASIC DATA USED IN META-ANALYSES
CORRECTED FOR ALL CONFOUNDERS (FRUIT, VEG, FAT, EDUCATION) AND MISCLASSIFICATION

Confounder Differences based on Random-effects Regression
Misclassification: Additive, Concordance: 3.0, MissP: US:0.025, EU:0.025, ASIA:0.1

TEA = 0 NO ADJUSTMENT (OR MATCHING) FOR TEA

RANDOM-EFFECTS META-ANALYSES

Log RR (Beta)
WEIGHTED on Beta
Weights

	Deviance	(DF)				
Model 1	96.8974	(92)				
	Estimate	**S.E.**	**P**	**RR**	**95%Cll**	**95%Clu**
Constant	0.0744	0.0385	(+)	1.0772	0.9989	1.1617

SEPARATE RANDOM-EFFECTS META-ANALYSES BY REGION

NORTH AMERICA, EUROPE AND NEW ZEALAND
Log RR (Beta)
WEIGHTED on Beta
Weights

	Deviance	(DF)				
Model 1	50.6199	(48)				
	Estimate	**S.E.**	**P**	**RR**	**95%Cll**	**95%Clu**
Constant	-0.0417	0.0569	N.S.	0.9591	0.8580	1.0722

ASIA
Log RR (Beta)
WEIGHTED on Beta
Weights

	Deviance	(DF)				
Model 1	41.5245	(43)				
	Estimate	**S.E.**	**P**	**RR**	**95%Cll**	**95%Clu**
Constant	0.1664	0.0506	++	1.1810	1.0696	1.3040

NORTH AMERICA
Log RR (Beta)
WEIGHTED on Beta
Weights

	Deviance	(DF)				
Model 1	30.1147	(28)				
	Estimate	**S.E.**	**P**	**RR**	**95%Cll**	**95%Clu**
Constant	-0.1082	0.0747	N.S.	0.8975	0.7753	1.0389

EUROPE AND NEW ZEALAND
Log RR (Beta)
WEIGHTED on Beta
Weights

	Deviance	(DF)				
Model 1	19.1257	(19)				
	Estimate	**S.E.**	**P**	**RR**	**95%Cll**	**95%Clu**
Constant	0.0599	0.0848	N.S.	1.0617	0.8991	1.2537

CHINA AND HONG KONG
Log RR (Beta)
WEIGHTED on Beta
Weights

	Deviance	(DF)				
Model 1	23.5008	(26)				
	Estimate	**S.E.**	**P**	**RR**	**95%Cll**	**95%Clu**
Constant	0.1615	0.0798	(+)	1.1753	1.0052	1.3742

REST OF ASIA

APPENDIX 19
ETS and Lung Cancer - Meta-Analysis of exposed/unexposed Risks, 02-NOV-15
Female (Husband's smoking)

CORRECTED FOR ALL CONFOUNDERS (FRUIT, VEG, FAT, EDUCATION) AND MISCLASSIFICATION
SEPARATE RANDOM-EFFECTS META-ANALYSES BY REGION
Confounder Differences based on Random-effects Regression
Misclassification: Additive, Concordance: 3.0, MissP: US:0.025, EU:0.025, ASIA:0.1

Log RR (Beta)
WEIGHTED on Beta
Weights

	Deviance	**(DF)**				
Model 1	15.0928	(16)				
	Estimate	**S.E.**	**P**	**RR**	**95%Cll**	**95%Clu**
Constant	0.1514	0.0416	++	1.1635	1.0723	1.2624

SEPARATE RANDOM-EFFECTS META-ANALYSES BY YEAR OF PUBLICATION

PUBLISHED IN 1980S
Log RR (Beta)
WEIGHTED on Beta
Weights

	Deviance	**(DF)**				
Model 1	22.5316	(25)				
	Estimate	**S.E.**	**P**	**RR**	**95%Cll**	**95%Clu**
Constant	0.1773	0.0613	++	1.1940	1.0587	1.3465

PUBLISHED IN 1990S
Log RR (Beta)
WEIGHTED on Beta
Weights

	Deviance	**(DF)**				
Model 1	26.2005	(26)				
	Estimate	**S.E.**	**P**	**RR**	**95%Cll**	**95%Clu**
Constant	0.0051	0.0732	N.S.	1.0052	0.8707	1.1603

PUBLISHED IN 2000S
Log RR (Beta)
WEIGHTED on Beta
Weights

	Deviance	**(DF)**				
Model 1	24.7229	(25)				
	Estimate	**S.E.**	**P**	**RR**	**95%Cll**	**95%Clu**
Constant	0.1088	0.0622	(+)	1.1150	0.9870	1.2595

PUBLISHED IN 2010S
Log RR (Beta)
WEIGHTED on Beta
Weights

	Deviance	**(DF)**				
Model 1	24.1921	(13)				
	Estimate	**S.E.**	**P**	**RR**	**95%Cll**	**95%Clu**
Constant	0.0255	0.0997	N.S.	1.0258	0.8437	1.2471

SEPARATE RANDOM-EFFECTS META-ANALYSES BY NUMBER OF LUNG CANCER CASES

<100 CASES
Log RR (Beta)
WEIGHTED on Beta
Weights

	Deviance	**(DF)**				
Model 1	47.5519	(48)				
	Estimate	**S.E.**	**P**	**RR**	**95%Cll**	**95%Clu**
Constant	0.1759	0.0710	+	1.1924	1.0375	1.3704

100-199 CASES

APPENDIX 19
ETS and Lung Cancer - Meta-Analysis of exposed/unexposed Risks, 02-NOV-15
Female (Husband's smoking)

CORRECTED FOR ALL CONFOUNDERS (FRUIT, VEG, FAT, EDUCATION) AND MISCLASSIFICATION
SEPARATE RANDOM-EFFECTS META-ANALYSES BY NUMBER OF LUNG CANCER CASES
Confounder Differences based on Random-effects Regression
Misclassification: Additive, Concordance: 3.0, MissP: US:0.025, EU:0.025, ASIA:0.1

Log RR (Beta)
WEIGHTED on Beta
Weights

	Deviance	(DF)				
Model 1	21.9219	(21)				
	Estimate	**S.E.**	**P**	**RR**	**95%Cll**	**95%Clu**
Constant	-0.0225	0.0742	N.S.	0.9778	0.8455	1.1308

200-399 CASES
Log RR (Beta)
WEIGHTED on Beta
Weights

	Deviance	(DF)				
Model 1	12.1954	(12)				
	Estimate	**S.E.**	**P**	**RR**	**95%Cll**	**95%Clu**
Constant	0.2036	0.0784	+	1.2258	1.0512	1.4293

400+ CASES
Log RR (Beta)
WEIGHTED on Beta
Weights

	Deviance	(DF)				
Model 1	8.5336	(8)				
	Estimate	**S.E.**	**P**	**RR**	**95%Cll**	**95%Clu**
Constant	-0.0444	0.0750	N.S.	0.9566	0.8258	1.1081

SEPARATE RANDOM-EFFECTS META-ANALYSES BY DOSE-RESPONSE OR NOT

RESULTS FOR DOSE-RESPONSE
Log RR (Beta)
WEIGHTED on Beta
Weights

	Deviance	(DF)				
Model 1	23.2128	(23)				
	Estimate	**S.E.**	**P**	**RR**	**95%Cll**	**95%Clu**
Constant	0.1571	0.0545	++	1.1701	1.0515	1.3020

NO RESULTS FOR DOSE-RESPONSE
Log RR (Beta)
WEIGHTED on Beta
Weights

	Deviance	(DF)				
Model 1	72.6233	(68)				
	Estimate	**S.E.**	**P**	**RR**	**95%Cll**	**95%Clu**
Constant	0.0389	0.0474	N.S.	1.0397	0.9475	1.1409

SEPARATE RANDOM-EFFECTS META-ANALYSES BY AGE ADJUSTMENT OR NOT

ADJUSTED (OR MATCHED) FOR AGE
Log RR (Beta)
WEIGHTED on Beta
Weights

	Deviance	(DF)				
Model 1	76.0266	(74)				
	Estimate	**S.E.**	**P**	**RR**	**95%Cll**	**95%Clu**
Constant	0.0464	0.0412	N.S.	1.0475	0.9663	1.1356

NOT ADJUSTED (OR MATCHED) FOR AGE

APPENDIX 19

ETS and Lung Cancer - Meta-Analysis of exposed/unexposed Risks, 02-NOV-15

Female (Husband's smoking)

CORRECTED FOR ALL CONFOUNDERS (FRUIT, VEG, FAT, EDUCATION) AND MISCLASSIFICATION

SEPARATE RANDOM-EFFECTS META-ANALYSES BY AGE ADJUSTMENT OR NOT

Confounder Differences based on Random-effects Regression

Misclassification: Additive, Concordance: 3.0, MissP: US:0.025, EU:0.025, ASIA:0.1

Log RR (Beta)
WEIGHTED on Beta
Weights

	Deviance	(DF)
Model 1	18.0380	(17)

	Estimate	S.E.	P	RR	95%Cll	95%Clu
Constant	0.2339	0.1062	+	1.2635	1.0262	1.5557

SEPARATE RANDOM-EFFECTS META-ANALYSES BY STUDY TYPE

CASE-CONTROL STUDIES

Log RR (Beta)
WEIGHTED on Beta
Weights

	Deviance	(DF)
Model 1	83.9936	(76)

	Estimate	S.E.	P	RR	95%Cll	95%Clu
Constant	0.0766	0.0441	(+)	1.0796	0.9902	1.1770

PROSPECTIVE STUDIES

Log RR (Beta)
WEIGHTED on Beta
Weights

	Deviance	(DF)
Model 1	9.2189	(15)

	Estimate	S.E.	P	RR	95%Cll	95%Clu
Constant	0.0623	0.0697	N.S.	1.0643	0.9283	1.2202