PRISMA 2009 Checklist

Section/topic	#	Checklist item	Reported on page #
TITLE			
Title	1	Identify the report as a systematic review, meta-analysis, or both.	1
ABSTRACT			
Structured summary	2	Provide a structured summary including, as applicable: background; objectives; data sources; study eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number.	3
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of what is already known.	5
Objectives	4	Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS).	6
METHODS			
Protocol and registration	5	Indicate if a review protocol exists, if and where it can be accessed (e.g., Web address), and, if available, provide registration information including registration number.	6
Eligibility criteria	6	Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale.	5-6
Information sources	7	Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched.	5
Search	8	Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated.	5-6
Study selection	9	State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis).	7
Data collection process	10	Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators.	6-8
Data items	11	List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made.	7
Risk of bias in individual studies	12	Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis.	8
Summary measures	13	State the principal summary measures (e.g., risk ratio, difference in means).	8-9
Synthesis of results	14	Describe the methods of handling data and combining results of studies, if done, including measures of consistency (e.g., I^2) for each meta-analysis.	8-10

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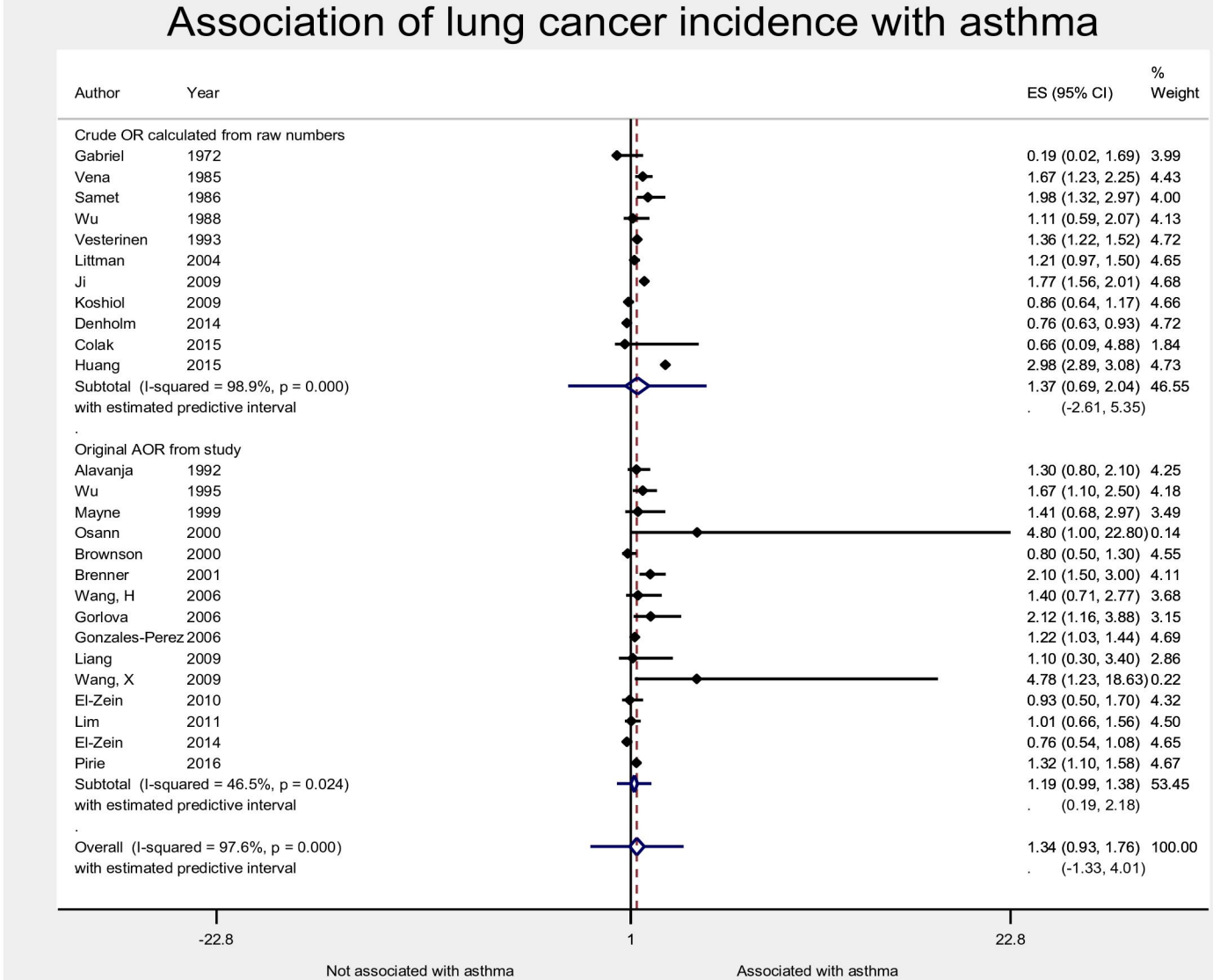
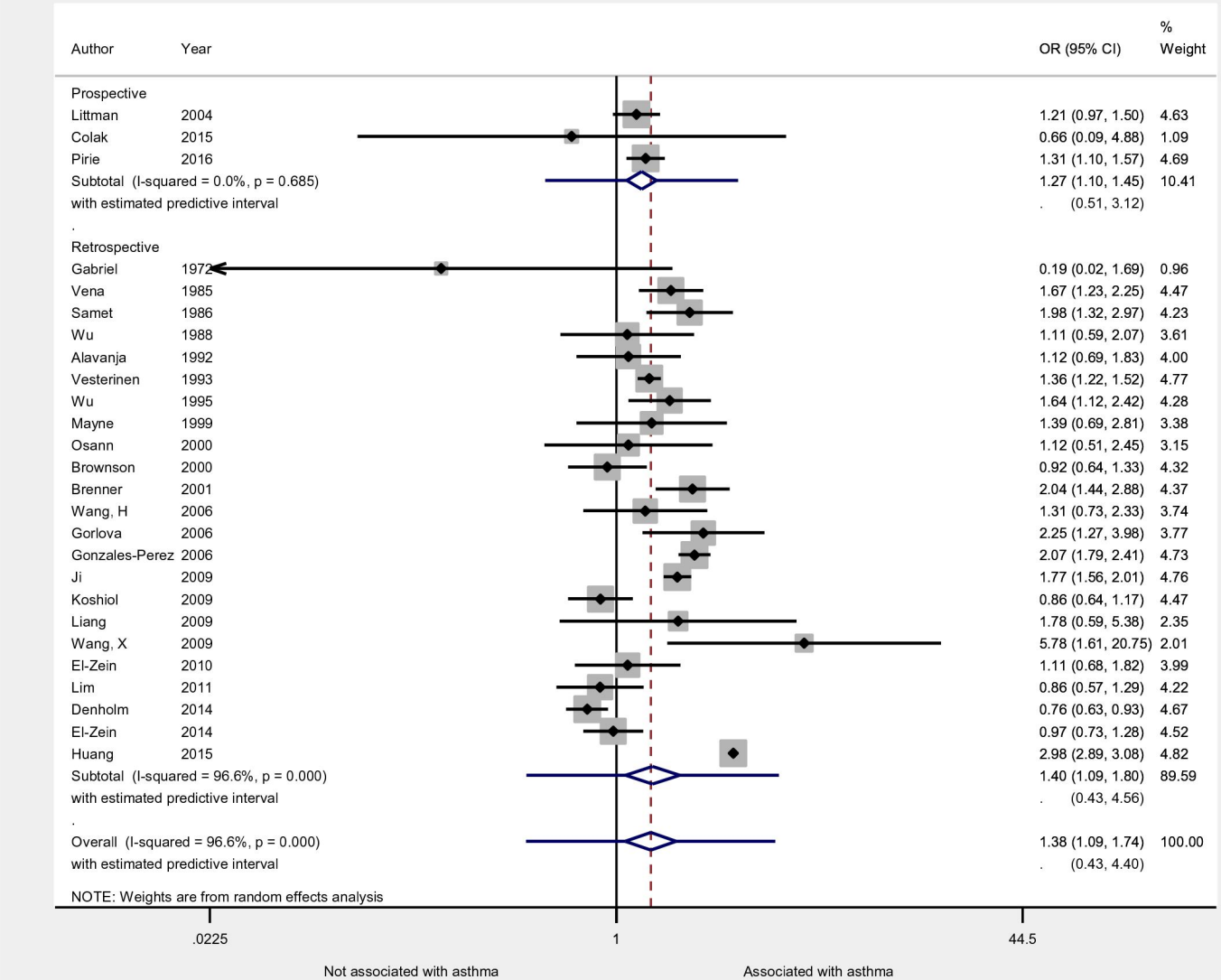
Risk of bias across studies	15	Specify any assessment of risk of bias that may affect the cumulative evidence (e.g., publication bias, selective reporting within studies).	11
Additional analyses	16	Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified.	10
RESULTS			
Study selection	17	Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram.	Figure 1
Study characteristics	18	For each study, present characteristics for which data were extracted (e.g., study size, PICOS, follow-up period) and provide the citations.	Table 1
Risk of bias within studies	19	Present data on risk of bias of each study and, if available, any outcome level assessment (see item 12).	Table 1
Results of individual studies	20	For all outcomes considered (benefits or harms), present, for each study: (a) simple summary data for each intervention group (b) effect estimates and confidence intervals, ideally with a forest plot.	S5
Synthesis of results	21	Present results of each meta-analysis done, including confidence intervals and measures of consistency.	11
Risk of bias across studies	22	Present results of any assessment of risk of bias across studies (see Item 15).	10-12
Additional analysis	23	Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression [see Item 16]).	12
DISCUSSION			
Summary of evidence	24	Summarize the main findings including the strength of evidence for each main outcome; consider their relevance to key groups (e.g., healthcare providers, users, and policy makers).	14
Limitations	25	Discuss limitations at study and outcome level (e.g., risk of bias), and at review-level (e.g., incomplete retrieval of identified research, reporting bias).	15
Conclusions	26	Provide a general interpretation of the results in the context of other evidence, and implications for future research.	17-18
FUNDING			
Funding	27	Describe sources of funding for the systematic review and other support (e.g., supply of data); role of funders for the systematic review.	2

From: Moher D, Liberati A, Tetzlaff J, Altman DG, The PRISMA Group (2009). Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. PLoS Med 6(6): e1000097. doi:10.1371/journal.pmed1000097

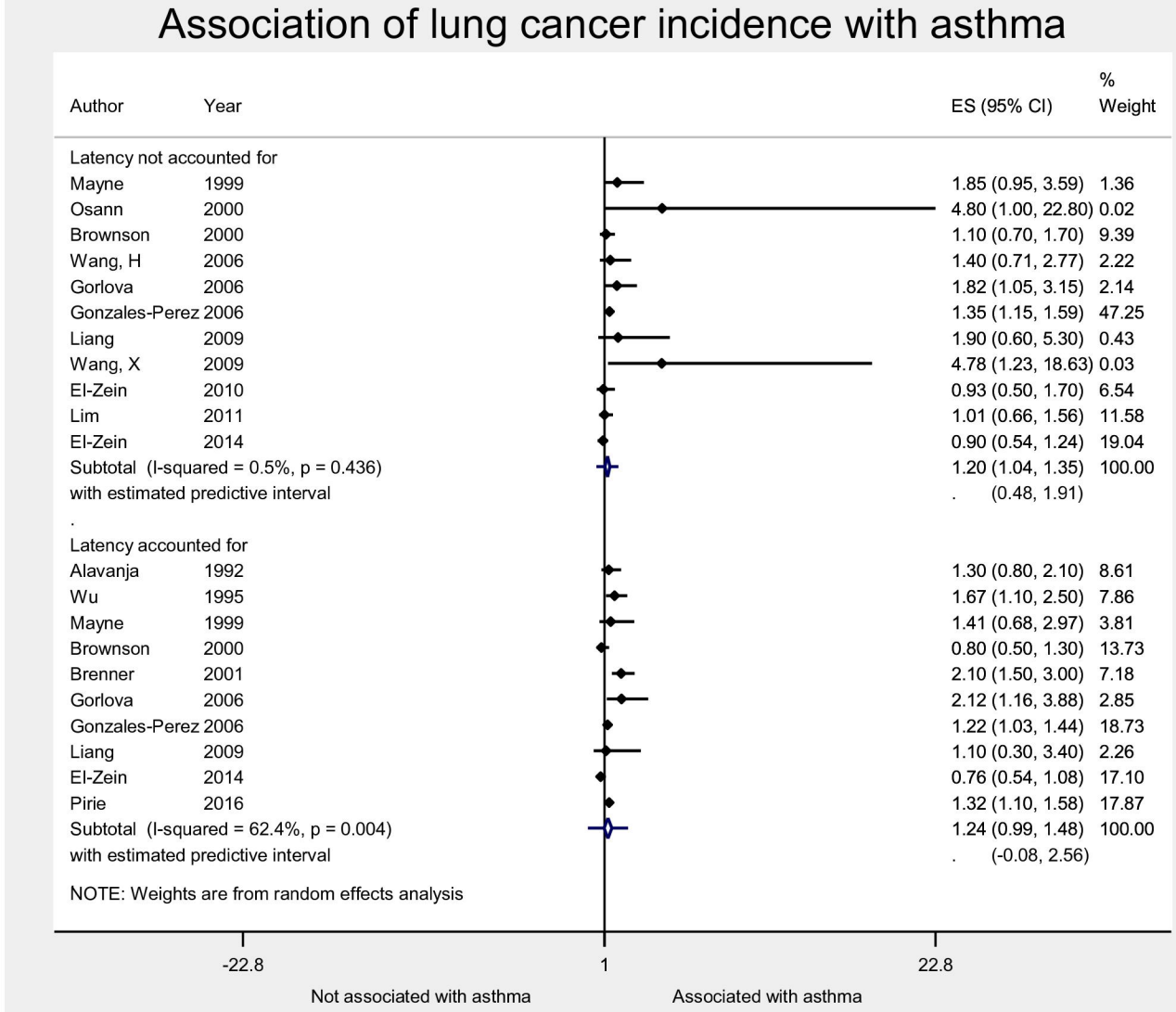
For more information, visit: **www.prisma-statement.org**.



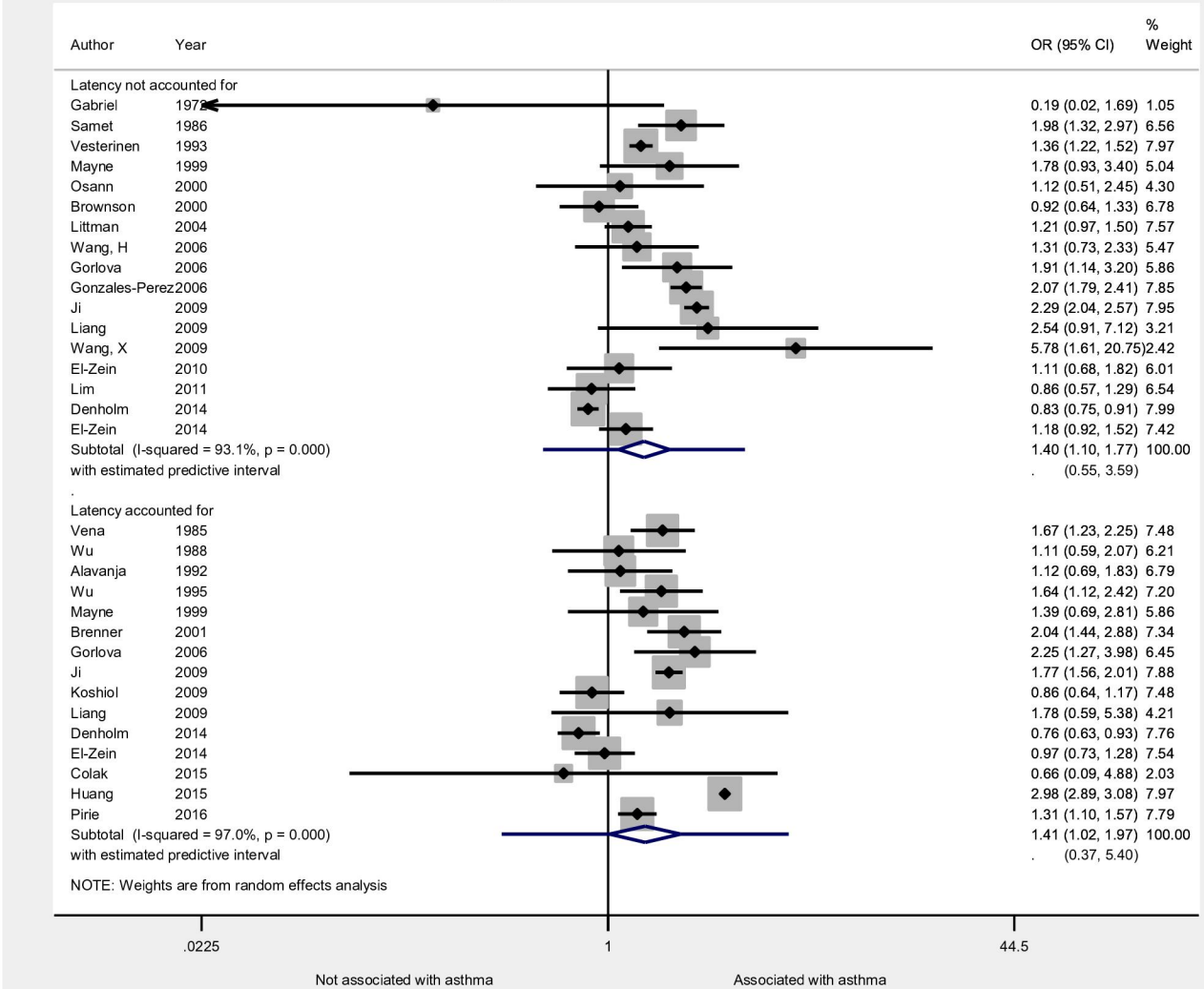
Supplemental Figure S2. Random-effects meta-analysis of association of lung cancer incidence and asthma, with 95% confidence interval (diamond) and estimated predictive interval (lines extending on either side of diamond). These are the same study estimates as in Figure 2, but the forest plot is stratified by whether odds ratios were adjusted by original study, or calculated from raw numbers of the original study (and therefore crude, unadjusted). Estimates that accounted for latency between asthma and lung cancer diagnosis were selected when available. ES, estimate (here, adjusted odds ratio); CI, confidence interval.



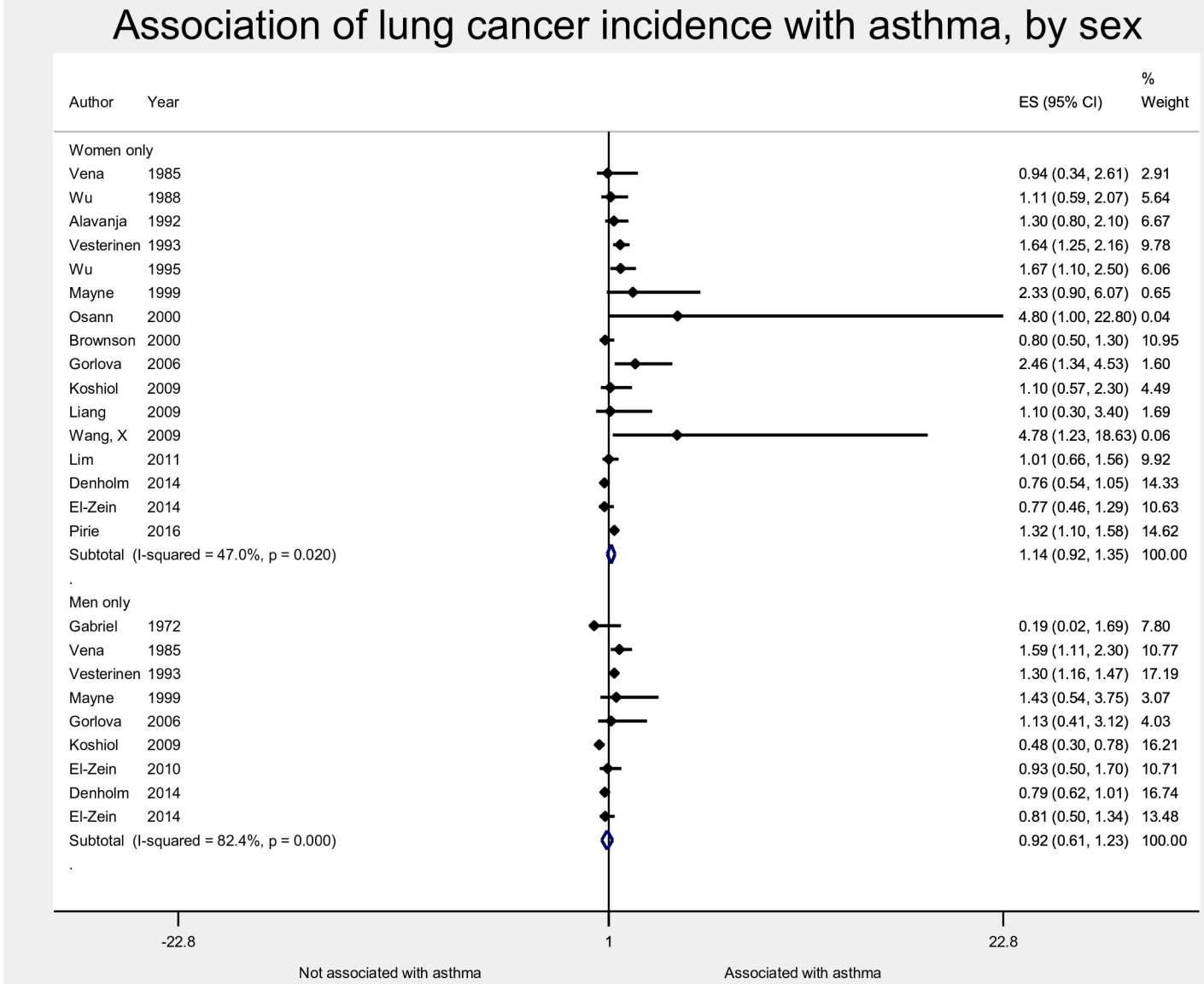
Supplemental Figure S3. Random-effects meta-analysis of association of lung cancer incidence and asthma, with 95% confidence interval (diamond) and estimated predictive interval (lines extending on either side of diamond). Meta-analytic estimates calculated from raw numbers rather than adjusted odds ratios, and stratified by study design. Estimates that accounted for latency between asthma and lung cancer diagnosis were selected when available. ES, estimate (here, adjusted odds ratio); CI, confidence interval.



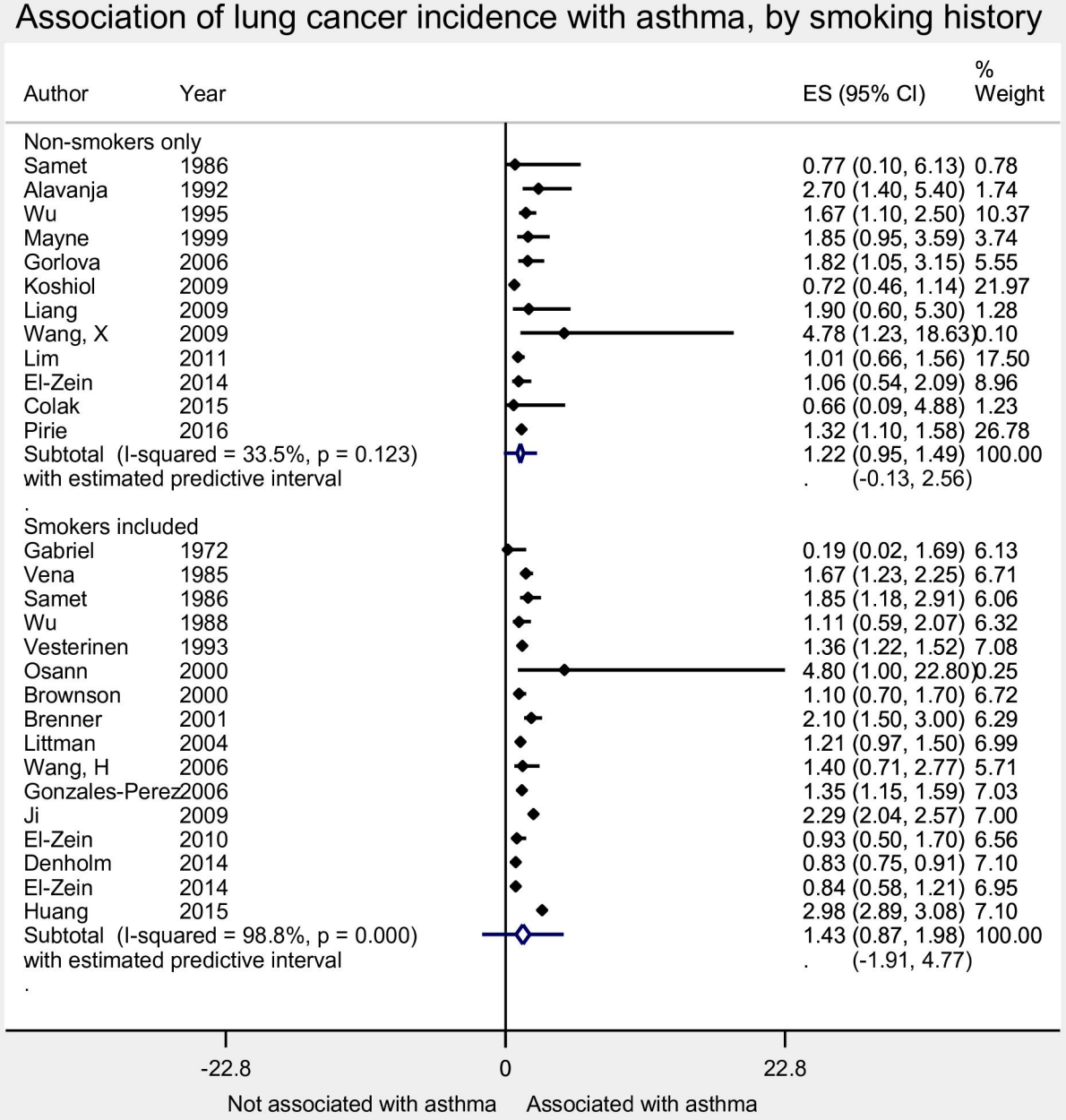
Supplemental Figure S4. Random-effects meta-analysis of association of lung cancer incidence and asthma, with 95% confidence interval (diamond), by whether latency was accounted for. Meta-analytic estimates calculated from adjusted odds ratios, and the plot only includes studies that provided these. Studies that reported latency-corrected and latency-uncorrected figures contribute each, so there is no overall summary estimate. The difference between the subgroups was non-significant in meta-regression (p=0.91). ES, estimate (here, adjusted odds ratio); CI, confidence interval

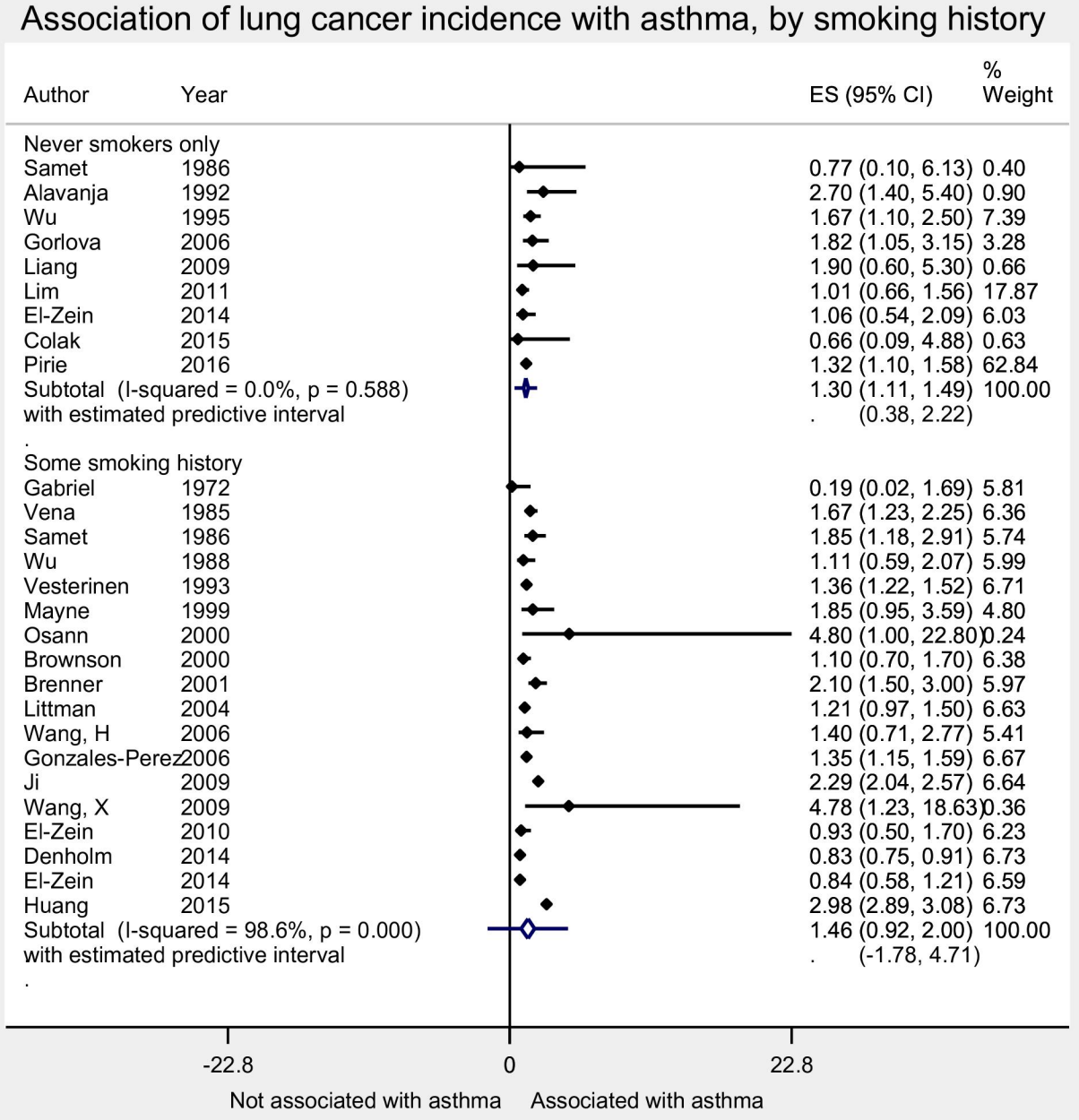


Supplemental Figure S5. Random-effects meta-analysis of association of lung cancer incidence and asthma, with 95% confidence interval (diamond), by whether latency was accounted for. Meta-analytic estimates calculated from raw numbers of participants. Studies that reported latency-corrected and latency-uncorrected figures contribute each, so there is no overall summary estimate. The difference between the subgroups was non-significant (p=0.84). OR, odds ratio; CI, confidence interval.

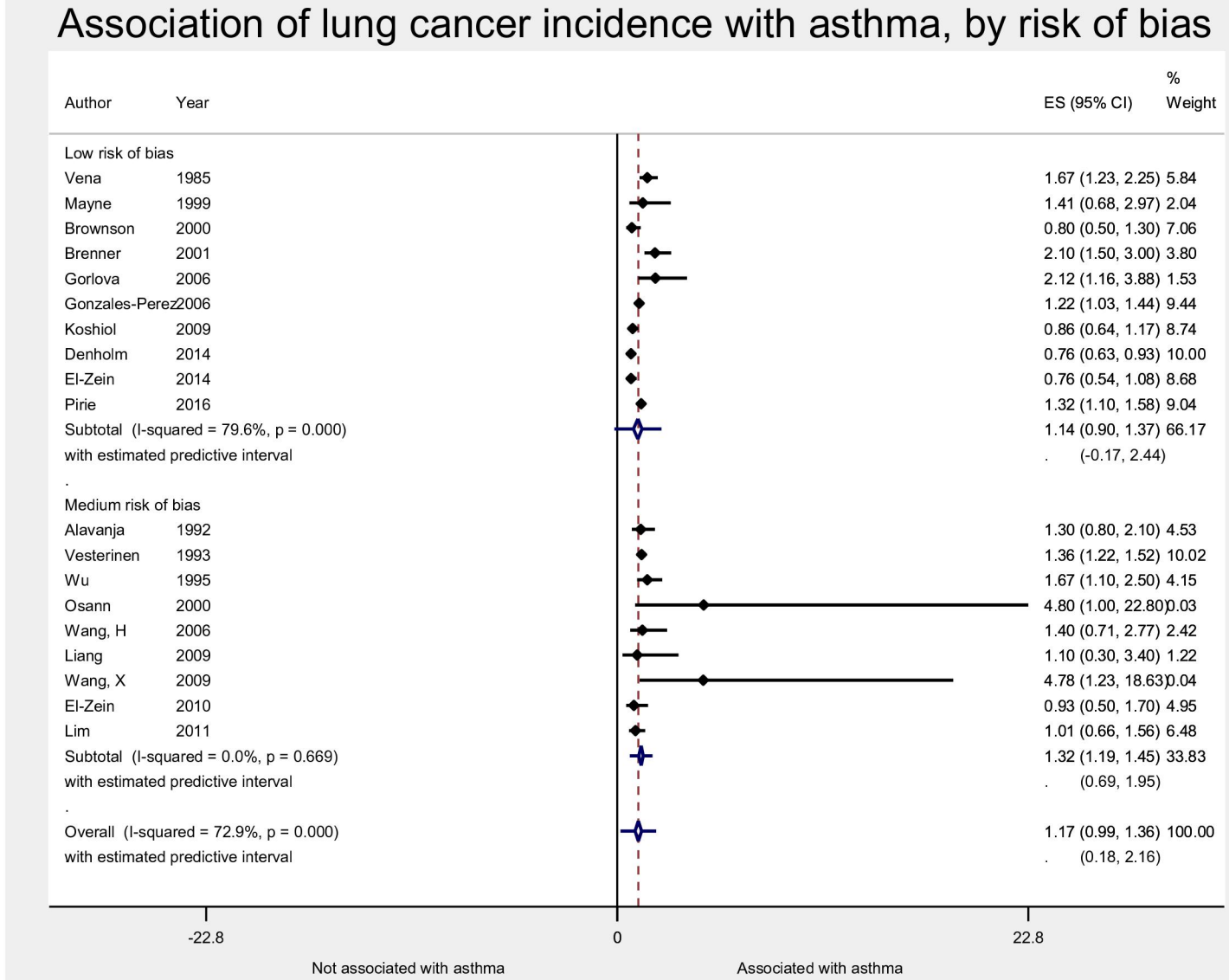


Supplemental Figure S6. Random-effects meta-analysis of association of lung cancer incidence and asthma, stratified by sex. The association of asthma with lung cancer was not statistically significantly different by sex (p=0.14). Meta-analytic estimates calculated from pooled odds ratios, using adjusted odds ratios and those that accounted for latency when provided, but many of the adjusted odds ratios already adjusted for sex. ES, estimate (here, adjusted odds ratio); CI, confidence interval.

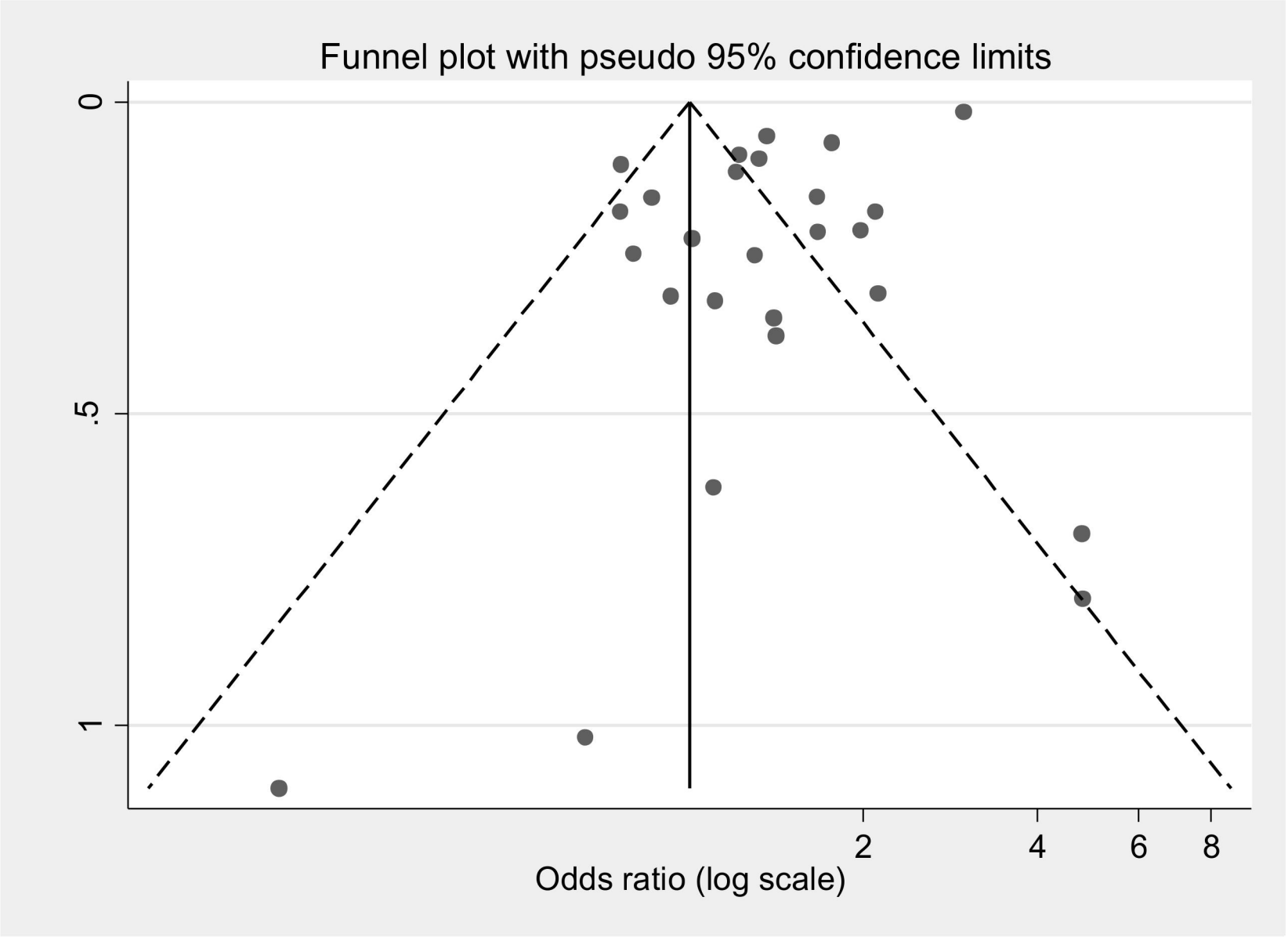




Supplemental Figure S7. Random-effects meta-analysis of association of lung cancer incidence and asthma, stratified by inclusion of any current smokers (***A***) or any ever-smokers (***B***). Meta-analytic estimates from pooled odds ratios, including adjusted odds ratios when provided, noting that many of these already adjusted for smoking. ES, estimate (here, adjusted odds ratio); CI, confidence interval.



Supplemental Figure S8. Random-effects meta-analysis of association of lung cancer incidence and asthma, stratified by risk of bias, and limited to studies at medium or low risk of bias. The association of asthma with lung cancer was not statistically significantly different by study risk of bias (p=0.69). Meta-analytic estimates calculated from pooled odds ratios, using adjusted odds ratios and those that accounted for latency when provided. ES, estimate (here, adjusted odds ratio); CI, confidence interval.



Supplemental Figure S9. Funnel plot of log odds ratio vs standard error of the log odds ratio, with 95% pseudoconfidence limits. The x-axis is subsequently exponentiated to back-transform to an odds ratio. There is statistically significant asymmetry (Egger's test $p<0.001$), suggesting the presence of small-study effects, possibly biasing the effect estimate negatively towards from the null.