INTERNATIONAL EVIDENCE

ON

PASSIVE SMOKING AND

ADULT ASTHMA INDUCTION

(PROJECT IASTAD)

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EXECUTIVE SUMMARY

Methods used to collect and analyse the data and scope of the information obtained

Based on papers available up to the end of 2004, 17 studies have been identified which provide information from epidemiological case-control, prospective or cross-sectional studies of prevalent or incident asthma in non-smoking adults. Only studies where the endpoint was 'asthma' were included, and studies of 'wheeze', 'wheezing bronchitis', 'chronic wheezing', 'asthma or wheeze' or 'asthmatic bronchitis' were excluded.

Two linked databases have been set up. One contains details of the characteristics of each study, while the other contains relative risk data relating to certain aspects of passive smoke exposure (for parental or household exposure, when exposed, and who smoked; biochemically assessed exposure; workplace exposure). For each study, the study database contains details of the study itself, the definition of asthma used, and the potential confounding variables considered. For each of the 117 relative risks included, the relative risk database contains not only the relative risks and 95% confidence intervals, but precise details of their definition and information on how they were derived.

This report starts by describing the methods used to identify relevant papers, which involved examining over 400 papers, and classifying them into separate studies. 16 principal studies were identified, plus one subsidiary study which was a subset of another study. The report then describes in detail the structure of the databases and the methods used for entry and checking of data. The methods by which relative risks were derived from data presented in various ways are also described.

One multi-centre study was conducted in 17 countries, and the other studies were conducted in 10 countries. Only two studies started before 1988. 10 were of cross-sectional design, and all but two include both males and females. The largest study involved nearly 2500 asthma cases with a further four studies involving between 200 and 500 cases. Nine studies give results for lifetime or incident asthma, and nine studies for current (active) asthma. Data on total ETS exposure are available

for seven studies, while data on household exposure are available for 13, and on workplace exposure for eight. Data on amount of passive smoke exposure are available for four studies. The potential non smoking confounding variables most commonly taken into account are age (13 studies), sex (9), location (8), education (5) and occupation (4). Fuller details of the studies are given in this report.

Of the 117 relative risks, 115 relate to the principal studies. The number of relative risks per principal study varies widely, from only one in three studies, to over 10 in three, the largest being a study with 48 relative risks entered. 92 relative risks are for sexes combined, and all relate to results for the full age range of the study and to all races within the study scope. 24 relate to lifetime asthma prevalence, 77 to current asthma prevalence and 16 to asthma incidence. 44 risks relate to total ETS exposure, with 45 relating to household smoking and 28 to workplace exposure. 53 relate to current exposure, 7 to exposure as an adult and 12 to exposure as a child, with the remainder relating to lifetime or unspecified exposure. None relate to *in utero* exposure. 75 are adjusted for at least one variable. 13 have no relative risk value but a statement of significance or non-significance. 74% of the relative risks and confidence intervals are as given originally or calculated directly from the numbers in the relevant 2×2 table. The rest involve more complex calculations. Fuller details of the relative risks are given in the report.

The report also describes the techniques used for conducting meta-analyses and the format of the tables presenting the results. The process of selecting which relative risks to include in an analysis is described in detail. It has to be quite complex to ensure that all the relevant data are included, while at the same time avoiding double-counting.

Results

Results are presented of a series of meta-analyses of the database aimed at giving insight into how the relative risk of asthma varies by the source, timing and amount of ETS exposure, the definition of the asthma outcome, the sex and age of the subject, the location, timing, size and type of study, the source of the information on exposure and diagnosis, and the extent of adjustment for confounding variables.

The main conclusions reached from the analyses are as follows:

There is an association between ETS exposure and asthma in adults. Including results for nonsmokers as well as for never smokers, and giving preference to exposure estimates as early in life as available and to results for lifetime rather than current asthma, meta-analysis relative risk estimates (95% confidence limits) for total ETS exposure (or nearest equivalent), based on 18 independent results, are 1.14 (1.06-1.23) using the fixed-effects model and 1.19 (1.04-1.35) using the random-effects model. Corresponding meta-analysis estimates for household exposure (n = 14) are 1.13 (1.04-1.23) fixed-effects and 1.16 (1.00-1.35) random-effects. For workplace exposure (n = 6), they are 1.37 (1.18-1.59) fixed-effects and 1.36 (1.09-1.70) random-effects. Restricting results to those for never smokers, giving preference to most recent exposure estimates or giving preference to current rather than lifetime asthma affects the conclusions little, the meta-analyses generally being consistent with a weak, but statistically significant, association, with risk about 20% higher in the ETS exposed group. (However, some of the similarity in the various alternative analyses arises because some studies only provide limited estimates, e.g. for a single timing of exposure or a single definition of asthma.) Meta-analyses for childhood ETS exposure are also consistent with about a 20% increased risk, but are not statistically significant, being based on only 4 estimates (1.27, 1.04-1.54 fixed-effects; 1.26 , 0.88-1.81 random-effects).

Data on dose-response are rather limited, with only 4 studies providing estimates by level of exposure, an additional 2 studies providing results of trend analyses. However, the overall results are consistent with a significantly increased risk in the highest exposure group, a conclusion which is independent of the sources and measures of ETS exposure considered.

There is evidence of significant heterogeneity between estimates in virtually all the meta-analyses conducted. Investigation of heterogeneity is limited by the small number of studies considered, and by the fact that one large study has a very large weight and that individual studies have unusually high or low relative risk estimates for reasons that are not clear. Although there is evidence that associations are

stronger in European studies than in studies conducted elsewhere, in case-control than in prospective studies, and in smaller than in larger studies, the extent to which these observed significant variations represent independent or meaningful differences is unclear.

There is a tendency for smaller studies to provide larger relative risk estimates, but formal testing of publication bias using Egger's method did not show any significant evidence of it. Although it is possible that some publication bias may exist, the fact that 15 of the 18 estimates included in the total exposure meta-analysis cited above are greater than 1.0 makes it unlikely that publication bias could explain the whole association.

There was no direct evidence that diagnostic bias, lack of representativeness or misclassification of exposure is an important issue in the interpretation of the results. However, the data available to investigate this are limited. Nor is there any evidence that our decision to include estimates for nonsmokers (i.e. including former smokers) in our analyses materially affected the findings. We preferred to exclude estimates for the whole population (i.e. including current smokers) because of reports that smoking caused asthma.

There is no clear evidence of confounding by a variety of non-smoking lifestyle factors, although a number of different approaches were used to investigate this. Although most studies took into account potential confounders, factors that might be considered important were only rarely taken account of (e.g. pets only in one study, and diet, exercise and exposure to infections in none).

In our corresponding report on asthma induction in children, we showed a stronger association with maternal smoking in pregnancy than with ETS exposure. Although one of the studies we considered reported that excluding mothers who ever smoked made little difference to their findings, a limitation of the evidence is that none of the studies provided any results relating to *in utero* exposure.

Our meta-analyses have deliberately excluded studies of asthmatic adults which relate specifically to asthma exacerbation, data on which will be presented

elsewhere. As such, one cannot make inferences regarding asthma exacerbation from the data presented here. While the results considered here show an association of ETS exposure with asthma, it is important to realise that there are difficulties in interpreting all the findings strictly in terms of asthma induction. Indeed, we consider that only four studies provide relevant data, with the ETS exposure known to occur before onset of asthma. Though the findings from these studies are suggestive of a possible association of ETS exposure with induction of asthma in adults, the relatively limited data and the somewhat heterogeneous nature of the results preclude a confident conclusion.

Our general conclusion is that the data are consistent with ETS exposure causing asthma induction in adults, but do not clearly demonstrate a causal effect. Limitations of the evidence include the relatively small number of studies (particularly those that specifically relate to induction), the lack of consideration of *in utero* exposure and the lack of control for relevant confounding variables.

The review ends with a brief summary of the findings of various other reviews. As shown there, conclusions reached are somewhat variable, and often based on a literature review that includes studies we consider inappropriate (e.g. not of asthma specifically, or not in nonsmokers) and excludes some studies we consider. A number of reviewers point to the need for additional evidence on asthma in adults. We agree.

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Table F and Appendix Table F

	Outcome (asthma)	Exposure (source)	Exposure (time)	Ex-smokers	Page (Table)	Page (Appendix Table)
F1	lifetime/current	total (or nearest)	earliest	included	88	F1
F2	lifetime/current	total (or nearest)	earliest	excluded	95	F22
F3	lifetime/current	total (or nearest)	most recent	included	98	F32
F4	lifetime/current	total (or nearest), preferring maternal	childhood	included	99	F45
F5	lifetime/current	total (or nearest), preferring paternal	childhood	included	102	F57
F6	current/lifetime	total (or nearest)	earliest	included	103	F69
F7	lifetime/current	household	earliest	included	104	F82
F8	lifetime/current	household	most recent	included	107	F94
F9	lifetime/current	workplace	earliest	included	108	F106
F10	lifetime/current	workplace	most recent	included	111	F118

Table G and Appendix Table G

	Exposure (source)	Dose	Measure of dose	Page (Table)	Page (Appendix Table)
G1	total (or nearest)	low	cigs/hours	112	G1
G2	total (or nearest)	high	cigs/hours	112	G11
G3	household	low	cigs/hours	113	G21
G4	household	high	cigs/hours	113	G26
G5	workplace	low	cigs/hours	114	G31
G6	workplace	high	cigs/hours	114	G36
G7	total (or nearest)	low	pkyrs/cigs/hours	115	G41
G8	total (or nearest)	high	pkyrs/cigs/hours	115	G51
G9	household	low	pkyrs/cigs/hours	116	G61
G10	household	high	pkyrs/cigs/hours	116	G66
G11	workplace	low	pkyrs/cigs/hours	117	G71
G12	workplace	high	pkyrs/cigs/hours	117	G76

1.   Introduction

Individuals may be asthmatic or non-asthmatic, the asthmatic state implying the propensity for an asthmatic attack. An agent may "induce" the asthmatic state, causing an individual previously classified as non-asthmatic to be reclassified as asthmatic. An agent may also "exacerbate" asthma, by causing an attack in a known asthmatic or by increasing the severity of symptoms of asthma.

This report is one of a series of documents relating ETS to asthma. A review of the epidemiological evidence relating ETS to asthma induction in children has already been prepared, and this report similarly reviews evidence relating ETS to asthma induction in non-smoking adults. Other reports relating to exacerbation of asthma by ETS exposure are also in preparation.

The review of adult asthma induction has been organized in a similar way to the childhood review, and many aspects of the methods have been fully described there (Lee et al., 2004a; Lee et al., 2004b). The work involved a number of stages. These included:

i)   **Identification of the studies**   Attention has been restricted to epidemiological case-control, prospective or cross-sectional studies which refer either to prevalent asthma (lifetime or current), or to incident (i.e. newly occurring) asthma. Only studies where the endpoint was 'asthma' were included, with studies of endpoints such as 'wheeze' or 'asthmatic bronchitis' excluded. Only studies with results restricted to non-smokers were included. Studies relating to any form of passive smoke exposure were considered relevant.

ii)   **Setting up databases to allow entry of relevant data**   In-house software (ROELEE) has been used. The structure involves two linked databases. One contained study details, with a record for each study. The other contained relative risk details, with a record for each relative risk (RR). The study database contains details of the study itself (e.g. location, timing, design, treatment of active smokers), the disease

definition, and the potential confounding variables considered. The relative risk database contains all RRs reported relevant to the exposure indices of "major interest" (see next paragraph), for the whole population and broken down by the more important demographic variables, with sufficient detail stored to define the RR precisely.

iii) **Entry and checking of data**   It was anticipated that RRs would be available for four[*] passive smoking exposure indices of "major interest".

> household exposure
> workplace exposure
> total exposure as assessed by questionnaire
> total exposure as assessed biochemically

For these indices, data were entered, where available, for prevalence of lifetime asthma, for prevalence of current asthma and (from prospective studies only) for incidence of asthma. These were entered for the whole population, broken down by sex if available[†]. For prospective studies, data were generally entered for the longest follow-up period available for each exposure type. Any dose-response measures for these indices were also entered. For a few studies, results were also available for certain subsets of the study population. The availability of these data have been noted in the database, but the data have not been entered. Only results restricted to never- or non-smoking adults were selected. If a study had results both for never smokers and for ex-smokers, then only never-smoking results were entered and the availability of the results for ex-smokers was noted.

iv) **Carrying out analyses**   Although a certain amount of analysis using the study database has been carried out to summarise the

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[*] It had also been planned to enter data for maternal smoking in pregnancy (*in utero* exposure), but no such data were found

[†] It had also been planned to enter data broken down by age and race, and to note the availability of results by other stratifying factors, but in fact no such data were found

characteristics of the studies considered and the quantity and type of data available, the main work has involved carrying out meta-analyses to meet the main objectives of the project.

This report describes the work carried out in fuller detail and presents the results of the analyses conducted. Chapter 2 explains the procedures used for identifying the studies. Chapter 3 describes the databases used to hold the data. For both the study database and the relative risk database, the structure of the data entered is described and the distribution of relevant characteristics is summarized. Following Chapter 4, which describes how the meta-analyses were carried out, Chapter 5 presents the results obtained from these meta-analyses. Chapter 6 discusses the overall findings, and in particular the inferences that can be drawn from the data presented regarding the role of ETS in asthma induction in adults, before conclusions are drawn in Chapter 7. Further detail is given where necessary in Appendices A to G.

2.   <u>Identifying the studies</u>

The objective was to identify epidemiological studies of case-control, prospective or cross-sectional design, which either reported RRs relating any aspect of passive smoking to asthma induction in non-smoking adults (or provided data from which such RRs could be calculated), or which commented on the significance or non-significance of the relationship. Uncontrolled case studies were not included, as RRs could not be calculated. Studies of asthma exacerbation were not included. As expected, no studies of asthma mortality were found.

As for the childhood review, only studies where the endpoint was 'asthma' were included. Aspects of this policy have been discussed previously (Lee et al., 2004a).

Identifying potentially relevant papers from the in-house files on smoking and health accumulated by P N Lee Statistics and Computing Ltd (PNLSC) and from Medline searches, classifying papers with relevant results into the separate studies they described, and checking the reference lists of cited papers to identify further potentially relevant papers, were carried out along the lines previously described (Lee et al., 2004a). Here the Medline strategy used was:

> ("asthma"[MeSH Terms]) AND ("adult"[MeSH Terms]) AND
> ("tobacco smoke pollution"[MeSH Terms])

with attention restricted to papers indexed on Medline by the end of 2004.

Overall, 460 papers were identified, of which 454 could be obtained and examined. Of these, 28 contained data relevant to the project, 15 were review papers, and the remaining 411 did not provide relevant data at all.

Ultimately, the project included 28 papers relating to 17 studies.

<u>Table 1</u> gives certain details of the 17 studies; the 6-character reference used to identify the study, a longer study title (which includes information on the location and timing of the study), the reference key to the principal

publication used to extract data and the reference keys to other relevant publications. Reference keys are those used in the PNLSC reference system. Appendix A gives all the reference keys used, in alphabetical order, together with the associated full references.

3.   The databases

3.1   Structure of the two databases

As for the childhood study, there are two linked databases. The first, the study database, contains one record for each study. This record is identified by a unique six-character reference (REF), and holds information relevant to the study as a whole, described more fully in §3.3. The second, the relative risk (RR) database, holds the detailed results, and can contain multiple records for each study. Each record refers to a specific comparison, and contains the information describing that comparison (e.g. smoking by the mother during childhood vs. no smokers in the household, for a particular sex and asthma type) and the actual results. Each record also contains the study REF, which links it to the relevant record in the study database. The RR database is described more fully in §3.4.

3.2   Data entry and checking

Procedures for data entry and checking were as previously described for the childhood study (Lee et al., 2004a). (See Appendix B for details of the automated checks.)

3.3   The study database

3.3.1   Structure of the database

As for the childhood study, the study database contains one record for each study, with each record consisting of "fields" within "cards". The "cards" separate the different main classes of information recorded, while the "fields" contain the individual data items within each class. These are similar to those previously described (Lee et al., 2004a), and are shown in detail in Appendix C.

The six cards used for data entry, together with a brief description of the fields included in each, are as follows:

Study description   This card includes the study short and full title, details of possible overlaps or links with other studies on the database, whether the study is restricted to men or women or is unrestricted, the age range and the race of

the population considered, the location of the study, the period of the study, the year and reference key of the principal publication and the reference keys of any other publications. A free text comment also contains additional detail where required, particularly concerning overlapping studies.

Study design   This card includes the study type (case-control, prospective, or cross-sectional), the type of controls used (e.g. healthy, diseased/hospital), the type of population studied (e.g. general population, farmers). The card also includes details on the source of the ETS exposure data (whether this was ascertained by questionnaire or by biochemical measurement) and the definition used to restrict the analysis to never- or non-smokers. A free text comment also contains additional detail where required.

Asthma   This card includes two fields, indicating whether results are presented for lifetime asthma and for current asthma. For prospective studies, incident asthma is recorded in the 'lifetime' field. The card also includes further fields giving the source of the asthma diagnosis, the timing of the asthma and a text field giving the detailed definition of the asthma. (This is extended by use of a free text comment if more space is required.) For current asthma, it is also recorded whether the asthma was restricted to first occurrence and, in prospective studies, whether current asthma was measured on more than one occasion. This card also includes the number of asthma cases and the total number of subjects included in the study.

Matching factors   For case-control studies, this card includes which matching factors were used.

Confounders considered   The first field on this card gives the total number of potential confounding variables considered for all the RRs entered in the RR database. The remaining fields indicate whether adjustment has occurred for 29 separate potential confounders. On most occasions, data entry is 0 for confounder not adjusted for or 1 for confounder adjusted for. Exceptionally, a greater number than 1 indicates that the confounder was adjusted for by use of more than one variable (e.g. family medical history by several specific

conditions). A further field indicates that other potential confounding factors were formally considered but rejected (e.g. in a step-wise multiple logistic regression model) and these factors are listed in a free-text comment.

Other results   This card records the availability of various data which have not at present been entered on the database. The first field indicates whether the study provides data on other definitions of asthma, which could have been used in this review in place of the outcome(s) chosen. The second field indicates other outcomes related to asthma which would not have qualified for this review, such as wheeze. Further fields indicate the availability of results for other ETS exposure indices (such as smoke exposure outside the home, or changes to parental smoking habits), of results using other definitions of non-smoking (including ex-smoking), and of results stratified by other factors (or restricted to subsets of the study population.)

The record itself is uniquely identified by a six character study reference, usually based on the principal author's name.

3.3.2   The study data

The data recorded on the study database for each of the 17 studies are presented in Appendix D. This is in the form of a computer-generated report. Note that this report is based only on fields which provide positive information. Thus, for example, the card "matching factors" is shown only for case-control studies, and only those factors actually used are shown. Other factors for this card, for which no output is shown, are taken not to be used.

3.3.3   Overlapping studies

In theory, RRs being meta-analysed should come from independent studies involving distinct asthma case. Otherwise, if some asthma cases feature in more than one study, they will be incorrectly "double-counted" in any meta-analysis which includes results from both studies. This is discussed further in the childhood review. However, this proved not to be a major problem in the adult work, where only one pair of overlapping studies was identified.   Results for current asthma from the multicentre   ECRHS

(European Community Respiratory Health Study) were entered as study JANSON and marked as a principal study. In addition, results for lifetime asthma from one of the centres (Bordeaux) were also entered as study RAHERI, and marked as the subsidiary study.

It can also be noted that studies BECKE2 and JAAKK2 are unconnected to the childhood studies with the same principal author, and that results from adult study NHANES, for age 17+, do not overlap with the childhood results previously reported for ages 0-16.

3.3.4   Study characteristics

Table 2 gives the distribution of various selected study characteristics by study type and overall. Except where specified otherwise, the discussion in the rest of this section refers to the principal studies only.

Design   Of the 16 principal studies, 4 are of case-control design, 2 are of prospective design, and 10 are of cross-sectional design. In one of the case-control studies, THORN, and also in the subsidiary study RAHERI, an initial cross-sectional phase was carried out to identify cases. In study JAAKK2, all new asthma cases were identified through all health care facilities in the region supplemented by checks of the National Social Insurance Institution computerized records. The remaining two case-control studies recruited patients at a chest clinic (ORYSZC) and at a hospital emergency department (PLATTS).

Sexes considered   All studies included both sexes, except two which considered females only (JEDRYC in Poland and NG in Singapore).

Age of subjects   The lower age limit was in the range 15-25 in all but two studies – JEDRYC in Poland (65) and MISHRA in India (60). For the case-control studies, the upper age limit was between 50 and 63, while for the cross-sectional studies it was above 60 with one exception (JANSON multicentre study - 48). In the two prospective studies, the age at baseline was 18-30 for BECKE2 and 25+ for ROBBIN.

Race of subjects   In 14 studies, there was no selection on race though clearly variation in the location of the study would cause major variation in the racial distribution. The two studies restricted on race were both conducted in USA – BECKE2 restricted to whites and blacks, and ROBBIN restricted to non-Hispanic whites.

 Location   Studies were most commonly conducted in Europe (8 : three in Sweden and one each in Estonia, Finland, France, Poland and Switzerland) or USA (4 : one nationwide, one multi-state and one each in California and Delaware), with 2 studies in Asia (India and Singapore), one in Australia, and one multi-country study (USA, Australia, New Zealand and 14 European countries).

Timing   The timing of the study was not stated for 3 studies. The two prospective studies were the earliest, starting in 1977 – ROBBIN and 1985 – BECKE2, respectively. All other studies started between 1988 and 1998. For all of the studies, the principal publication year was 1993 or later.

Population studied   Most studies were of the general population with no major restrictions, two exceptions being KRONQV – farmers and ROBBIN – Seventh Day Adventists. Some studies imposed further restrictions which are listed in Table 3 and although these were generally of a minor nature, some may have materially affected the representativeness of the population studied. For instance JEDRYC excluded "residents of old-people's homes or long-stay geriatric wards, who are more likely to have more respiratory problems and poorer lung function." One study gave no information about the population considered.

Although no information has been entered on the database regarding response or retention rates, it can be noted that the two prospective studies based their analysis on subjects who were alive and could be traced for at least one follow-up. One of them (ROBBIN) further restricted attention to subjects who had lived within 5 miles of their baseline address for at least 10 years, and the

cross-sectional study SAPALD restricted analysis to subjects who had lived in the region for 3 years. Thus they may have under-represented subjects from more mobile families.

Type of controls   Among the case-control studies, three used healthy (population) controls – JAAKK2, THORN and subsidiary study RAHERI. PLATTS used patients presenting at the same hospital emergency department with any condition other than breathlessness. ORYSCZ used mainly population controls, but also some recruited through surgery departments and from a check-up centre.

Matching factors   In study PLATTS, the cases and controls were matched on sex and age. There were conflicting reports as to whether study ORYSZC was matched (unmatched according to Oryszczyn et al., 2000 but matched on age, month and centre according to Kauffmann et al., 1997), while the other case-control studies were unmatched.

Respondent   In all studies information about the passive smoke exposure was provided by the subject, with the exception of MISHRA where the head of household responded on behalf of all household members.

Definition of disease outcome – lifetime and incident asthma   Results for lifetime or incident asthma (including prevalent asthma of unspecified timing) were available from 8 principal studies (1 case-control, 5 cross-sectional and the two prospective studies), and also from subsidiary study RAHERI. All these studies were carried out in non-medical settings.

In all but one study, the asthma diagnosis had been made by a doctor, this diagnosis being made in a medical examination as part of the study design in study KRONQV, otherwise as reported by the subject; the exception was study PILOTT which used self-reported asthma. Study ROBBIN presented results for two different definitions of asthma, with one paper (McDonnell et al., 1999) using 'physician-diagnosed asthma' (in relation to household or workplace ETS exposure), and another (Robbins et al., 1993) using 'physician

diagnosed asthma with a history of wheezing' (in relation to total ETS exposure).

Both the prospective studies presented results for onset during the study (i.e. excluding subjects with pre-existing asthma at baseline), while BECKE2 also presented results for baseline prevalence of asthma. In study THORN, only adult-onset asthma was included (onset after age 16 and not more than 15 years ago, the subjects being age 20-50 at the time of the study). Further details of the asthma definition are shown in Table 4.

Definition of disease outcome – current asthma   Results for current (i.e. active) asthma were available from 9 studies, 3 case-control studies, and 6 cross-sectional.   In one of the case-control studies (JAAKK2), this was restricted to being the first episode of asthma, with the cases identified at all health care facilities in the region or through computerized records of prescriptions for asthma medications. In study PLATTS cases were recruited when presenting at a hospital emergency department with acute asthma, in study ORYSZC they were attending a chest clinic, and the other studies were carried out in a non-medical settings.

In all but two studies, an asthma diagnosis was made by a physician (either as reported by the subject or in the course of the study design), usually with the subject also reporting symptoms currently or in the last 12 months; studies JANSON and MISHRA used self- (or proxy-) reported asthma.   Further details are again given in Table 4. Only study SAPALD, and the overlapping pair of studies JANSON/RAHERI, presented results for both lifetime and current asthma.

Availability of alternative disease outcome   Table 5 gives details of the 4 studies from which results are available for alternative asthma definitions; these results have not been entered on the database. The availability of results for wheeze was also noted for 6 studies.

Study size   Where the number of cases was known, for lifetime or incident asthma, it ranged from 69 to 473, with the median being 119. The largest was BECKE2 (with 473 combined baseline and onset cases). For current asthma, the range was 33 to 2479, with median 99.   By far the largest study was MISHRA, conducted in India with 2479 current asthma cases, followed by NHANES in USA with 440. In addition, there were three other large studies (>1000 subjects) for which the number of asthma cases was unknown.

Exposures   For each exposure type, information about the studies for which RRs have been recorded in the relative risk database is presented in §3.4.4. Only study NHANES provided information on other aspects of ETS exposure, for which data have not so far been recorded on the relative risk database. In this study, median serum cotinine was also available in subjects with and without asthma.

Definition of non-smoking   In 11 principal studies, the results referred to self-reported never smokers, or to those whose lifetime smoking history was less than some defined amount. These included 3 case-control studies (and also the subsidiary study RAHERI), and 8 cross-sectional studies. The other studies refer to non smokers (i.e. not currently smoking), based on self-report (PILOTT, PLATTS, ROBBIN), biochemical assessment (BECKE2) or both (NHANES). In the prospective studies, assessment was made at baseline in study BECKE2, while in ROBBIN, subjects are all members of the Seventh Day Adventist Church which does not permit smoking (although subjects may have smoked before joining the church).

Alternative results which have not been entered on the database are available for some studies. Two of the studies providing data for never smokers (JANSON, KRONQV) also presented results for ex-smokers, while SAPALD had results for never smokers validated biochemically. RAHERI also had results for ever smokers restricted to asthma onset before starting to smoke.

Confounders   Three studies did not adjust for any variable at all in analysis, although one of these (PLATTS) was matched on sex and age. About half of

the studies adjusted for four or more potential confounders, with 3 adjusting for 10 or more.

Table 2 also shows all those variables taken account of. Age and sex are the commonest, with 13 and 9 studies adjusting for them respectively. Other commonly used variables were location (8 studies), education (5), occupation (4), aspects of personal (4) or family (3) medical history, cooking methods (3), housing quality, crowding or mould (3), household composition (e.g. number of siblings, marital status) (2), body mass index (2) and race (2).

Never/ex smoking was used as an adjusting factor in one of the studies of non smokers (ROBBIN). Results adjusted for other aspects of passive smoking were available for 4 studies. No study adjusted for maternal smoking in pregnancy, although study SAPALD presented results excluding subjects whose mothers had ever smoked (not entered on database).

Additional confounders were formally considered by the study authors but rejected from analysis in a step-wise multiple logistic regression in 2 studies (KRONQV, ROBBIN).

Other stratifying variables   So far only sex, age and race have been considered as stratifying variables in the relative risk database, and in practice, no results stratified by age, race or by any other stratifying variables were found.   Table 6 presents details of which studies presented results for particular subsets of the subjects.

Derived fields   Fields have been derived holding the total number of RRs, and the number of RRs for each exposure type, that are present for each study in the relative risk database. These are discussed in §3.4.4.

3.4   The relative risk database

3.4.1   Structure of the database

        As described in more detail in Appendix E, the relative risk database contains one record for each relative risk. Again, each record consists of

"fields" within "cards." The four cards used for data entry, together with a brief description of the fields included in each, are as follows:

RR description This includes an RR identification number which is unique within the study, together with details defining the RR. These include the sex, age range, asthma type (lifetime or current) and, for prospective studies, whether the analysis was of prevalence or incidence. The passive smoking exposure is defined by type – household, workplace or total (questionnaire or biochemically assessed), specific source within the family and time of exposure, together with similar information about the unexposed base, or details of the biochemical assessment. See Appendix E for fuller details of the possible levels of the grading systems used. The source of the RR (including reference key, table and page numbers) is also given.

RR adjustment This includes whether or not the RR is adjusted for sex, age, race, other aspect of passive smoking or other confounders, and in the case of other confounders, the number of variables adjusted for. The actual other confounders adjusted for are given in a text comment if they are less than the full set already defined in the study database.

RR data This includes the numbers of exposed and unexposed cases. For unadjusted results only, it also includes the numbers of exposed and unexposed controls or disease-free subjects for prevalence analyses, or the at-risk population or person-years at risk for incidence analyses. For all results, it includes the RR estimate itself and its upper and lower 95% confidence limits (UCL, LCL). For unadjusted data the RR and 95% confidence interval (CI) are calculated from the 2×2 table (if available). For adjusted data, they may be as given in the source paper or as derived by other means, a further variable indicating the method of derivation. The possible methods of derivation are described in §3.4.3.

Discrepancy Any alternative discrepant results are noted here, or results adjusted for alternative variables.

The record includes the six character study reference linking it to the corresponding record on the study database.

3.4.2 Identifying which relative risks to enter

In identifying what RRs to enter, four aspects – passive smoking index, asthma type, confounders adjusted for, and strata – were considered and these are discussed in the following sections. RRs relating to all combinations of these aspects were entered.

RRs based on never-smoking subjects were entered if available, otherwise RRs based on non-smoking subjects were entered.

As discussed above (§3.3.3), it is important in meta-analyses to avoid "double counting", and this applies equally within studies. Although in some circumstances it is quite legitimate for more than one RR from a study to be included in a meta-analysis (for instance by strata such as sex, or for both baseline prevalence and subsequent onset in a prospective study), in other circumstances it is not (for instance if maternally exposed and paternally exposed subjects were each compared to those with no smokers in the family, including both in a meta-analysis of parental smoking would double count the unexposed group). For a simple stratifying variable, it is readily apparent at the analysis stage whether or not inclusion of multiple RRs is valid. However for the other aspects it is not. It was therefore decided that, with the exception of the straightforward strata of sex, all valid combinations would be constructed at the outset. This resulted in larger numbers of RRs being entered for some studies than had been presented in the original papers.

3.4.2.1 Passive smoking indices

Passive smoking exposure was either based on questionnaire responses or on biochemical assessment.

For questionnaire based exposures, it was necessary to define the smoking exposure of the numerator and of the denominator separately for each

RR, exposure being defined according to whether the exposure was from household members smoking (and who specifically smoked), or from workplace or total exposure, any measures of the amount of exposure (such as number of smokers, amount smoked or duration of smoking) and the timing of the exposure. This is defined in the database in a similar way to the childhood exposures as previously described (Lee et al., 2004a). No results were found for maternal smoking in pregnancy (*in utero* exposure).

The only results found for biochemically assessed exposure refer to serum cotinine.

3.4.2.2 Asthma type

Results are entered for lifetime, incident and current asthma, as defined in the study database.

3.4.2.3 Confounders adjusted for

Results are entered unadjusted, and adjusted for the most confounders for which results were available. If the confounders included other aspects of passive smoke exposure as well as other confounders, then results adjusted for the other confounders but not for the other passive smoke exposure are also entered.

3.4.2.4 Strata

Three strata were considered – sex, age and race. Results are entered for males and females separately when available. Combined sex results are only entered when the equivalent results (i.e. for the same passive smoking indices, confounders, age and race) were not available. No results stratified by age or race were found.

3.4.3 Derivation of the relative risks

Adjusted RRs and their 95% CIs are entered as given when available. For an incidence analysis, the odds ratio is entered only if the relative risk is not available (typically when estimated from a multiple logistic regression), and this is noted in the database. Methods of calculating unadjusted RRs from

their 2 × 2 table (which may be constructed by summing groups), and of combining non-independent RRs by the method of Fry and Lee (Fry & Lee, 2000), are as previously described (Lee et al., 2004a). Calculations were mainly carried out using Excel spreadsheets.

3.4.4   Characteristics of the relative risks

A total of 117 relative risks are entered on the database, of which 115 relate to the principal studies and 2 to the subsidiary study. Among the 16 principal studies, 10 have between one and four RRs, and a further 5 have between 5 and 14 RRs, while study JAAKK2 has 48 RRs. (Table 7).

Table 8 gives the distribution of various selected RR characteristics by study type and overall, based on all the 17 studies. Table 9 shows how many of the principal studies or their subsidiary had RRs with selected characteristics, and except where specified otherwise, in the discussion in the rest of this section 'study' refers to 'a principal study or its subsidiary.'

Sex   Only 5 studies give any results for males and females separately, in addition to the two studies which included females only. The great majority of RRs (92, 79%) are for sexes combined

Asthma type   The RRs are predominantly for current (77) asthma prevalence, particularly from the case-control studies (53 RRs, 95%). 24 of the rest refer to lifetime prevalence and 16 refer to incidence, with 14 of these being odds ratios rather than relative risks. SAPALD is the only study that has results for both lifetime and current asthma.

Passive smoking exposure The commonest exposure type is household exposure, with 45 RRs from 13 studies. For total exposure, there are 40 RRs from 6 studies with questionnaire-assessed exposure (mainly home and/or work), and only 4 RRs from 1 study (BECKE2) for biochemically-assessed (serum cotinine) exposure. The remaining 28 RRs from 8 studies are for workplace exposure.

The most frequent timing of the passive smoke exposure is current, with 53 RRs from 10 studies, followed by lifetime exposure with 41 RRs from 3 studies. For study THORN, exposure was while living at 6 most recent homes and before diagnosis of asthma. There are also 10 RRs from 4 studies which refer to childhood exposure (regardless of adult exposure).

For most RRs, the denominator group comprises all those not exposed as defined for the numerator. The exceptions were 4 RRs from study JANSON, where exposure was from a specific household member (mother or father) but the denominator was no household exposure, and 5 RRs from study ROBBIN which refers separately to childhood, adulthood or both exposures relative to neither exposure.

Dose response   Most of the categorical dose-response data come from study JAAKK2, which has 36 RRs comprising 6 sets of 2 categories, by number of cigarettes exposed to, and 6 sets of 4 categories, by pack-years. Additionally, studies JANSON and LARSS2 each have one set of 3 categories, by hours per day exposed, and study NG has two sets of 2 categories, by number of cigarettes smoked in the household.

Seven RRs from studies SAPALD and ROBBIN hold results regarding the dose response relationship which could not be expressed in the usual categorical format (Table 10).

Adjustment   75 RRs have some adjustment. In all cases, this includes adjustment for age. 59 (64% of sexes combined RRs) are adjusted for sex. The adjusted RRs come from 13 studies, and 5 studies only have adjusted RRs.

Two studies only have RRs adjusted for other sources of ETS (JANSON where RRs for current exposure are adjusted for childhood exposure and vice versa; and LARSS2 where RRs for workplace exposure are adjusted for household exposure).

2 × 2 table   The full 2 × 2 table is available for 40 of the 42 unadjusted RRs and the numbers of cases for another one.   Among the adjusted RRs, the numbers of cases are available for 36 (48%). There are 6 studies which do not have the numbers of cases for any RR.

RR and CI   Apart from the 7 non-categorical dose-response results already mentioned, 6 RRs have no values for the RR or CI, having only a statement of non-significance (none were significant). Two studies (KRONQV, PLATTS) have no RRs with values for the RR or CI.

The RR values range from 0.30 to 4.80.

The centrality of the RR in the CI was checked using the statistic

$$C = (RR^2) \; / \; (UCL * LCL)$$

which should have the value 1.0.   The value of C was outside the range 0.95 - 1.05 for only one RR, from study THORN, where C=0.907. The RR/CI were given originally to only one decimal place, so the difference is probably due to rounding error.

For case-control and cross-sectional studies, the minimum number of cases and the total number of subjects implied by the CI (Lee, 1999) are compared with the actual numbers, as entered in the study database. No RRs showed a problem by this test. For analyses of prospective studies, the equivalent check on the number of cases is only approximate (see formula 16 of Lee, 1999) and again there were no RRs where a problem was seen.

Derivation method   86 RRs are either as given originally, or are calculated directly from the numbers in the 2 × 2 table. For a further 2 RRs where both the 2 × 2 table and the RR and CI were originally available, the RR and CI are recalculated because of a discrepancy and 4 are calculated after summing categories to obtain a 2 × 2 table. The remaining 12 were estimated using a method for combining non-independent estimates (Fry & Lee, 2000).

Discrepancy   Discrepancies, or the availability of alternative adjusted results, are noted on 14 RRs from 5 studies.

4.   Carrying out meta-analyses

4.1   Introduction

The process of selecting which RRs to include in an analysis based on 'preferences' and the combining of the relative risks using the method of Fleiss and Gross (Fleiss & Gross, 1991) are as previously described in §4 of the childhood report (Lee et al., 2004a).

The layout of the detailed output is also as previously described except that output sections 7 and 8 are now combined. Briefly, each meta-analysis produces a cover page followed by seven sections of output, headed -1 to -7, respectively. The cover page describes the restrictions on the data included, the order of preference for selecting relative risks to be included and a short description of the contents of the table. Sections -1 to -3 relate to 'adjusted' data (i.e. using relative risks adjusted for covariates where available and relative risks unadjusted for covariates otherwise), while sections -4 to -6 relate to 'unadjusted' data (using unadjusted relative risks where available and adjusted relative risks otherwise). Within each of these sets of three tables, the first two (-1, -2 and -4, -5) give details relating to the individual relative risks considered in the meta-analysis, while the third (-3 and -6) give the meta-analysis results. Section -7 gives additional information related to studies and RRs excluded from the meta-analysis.

The tables relate to two broad types of meta-analysis, as follows:

F.   Any exposure

G.   By amount of exposure

Results from Tables F and G are discussed, respectively, in §5.1 and §5.2 of the present report. Note that the full output, including all of section-1 to section-7 for each set of meta-analyses, is presented in Appendix Tables F and G. Reduced output, which only includes the cover page and shortened versions of sections -3 (and sometimes –6) giving the meta-analysis results, is given in Tables F and G. Thus the reader who wishes only to see the main meta-analysis estimates need refer only to the Tables, but the more interested reader who wishes to see full details of the individual relative risks

contributing to the estimates should refer to the corresponding Appendix Tables. The two sets of output always correspond directly.

In the following sections of the methods chapter, some general restrictions to the analyses are noted first (in §4.2), followed by a description of the various ways outcome and exposure are defined (§4.3) and of the various other factors considered in the analysis (§4.4). An explanation is given of how meta-analyses by amount of exposure (§4.5) are conducted and finally (in §4.6), an explanation is given as to certain conventions used in presenting the findings in the results chapter of this report.

4.2   General restrictions to the analyses

The analyses presented all satisfy the following conditions for selecting relative risks:

Results complete enough for use in meta-analysis   Adjusted relative risks which lack a confidence interval are excluded from meta-analyses.

Principal rather than subsidiary studies   As discussed in §3.3.3 only one pair of overlapping studies was identified, and all the meta-analyses use the principal study JANSON.

Sex   Single sex results are preferred to combined sex results (as discussed more fully in §4.1 of Lee et al., 2004a).

4.3   Defining the outcome and the exposure

For each of the main sets of tables (F, G), there is considerable choice as to the outcome and the exposure when selecting the relative risks to be included in the meta-analysis.

Outcome   'Lifetime asthma' is present if, at the time of interest (time of interview for case-control or cross-sectional studies, or time of follow up for prospective studies) the subject has ever had asthma, while 'current asthma' is present if the subject is considered to be asthmatic at the time of interest.

Assuming that people are not asthmatic at birth, lifetime asthma is equivalent to induction of asthma by the time of interest. Since only one study (SAPALD) gave results for both outcomes, the meta-analyses include studies using either outcome, with the lifetime results usually preferred for study SAPALD. This outcome is referred to as 'lifetime/current asthma', and analysis is also carried out for 'current/lifetime asthma' which is similarly defined but in the opposite order for study SAPALD.

Source of exposure to ETS The three main sources of ETS exposure meta-analysed are total exposure (or nearest available), household exposure and workplace exposure. For total exposure, biochemically-assessed exposure is chosen if available from a study, otherwise questionnaire-assessed total exposure is chosen; failing that, results for any household exposure, maternal exposure or workplace exposure are accepted in that order of preference. For household exposure, the order of preference is any household exposure or maternal (i.e. mother smokes irrespective of father's smoking). In addition, some meta-analyses are carried out using paternal exposure in preference to maternal.

Timing of exposure Usually the exposure chosen for meta-analysis is that referring to the earliest exposure during the subject's lifetime. This is chosen from those available from each study in the following order of preference: childhood, lifetime, adulthood, recent (=in last 6 homes), unspecified, current. Meta-analyses are also carried out using an alternative order of preference favouring the most recent exposure available. In addition, separate meta-analyses are carried out for exposure specifically in childhood.

Definition of the unexposed comparison group Generally, the only unexposed group available is the reciprocal of the exposed group, both in terms of the source of exposure and the timing of exposure. In the case of study ROBBIN, results for two unexposed groups are available, and the 'never exposed' group was chosen in preference to the 'non-exposed' group.

Clearly if meta-analyses were conducted for all possible combinations of the four aspects considered in the previous paragraphs, the number of such analyses would be enormous. Consequently, most attention has been given to certain key analyses with full output produced for them. Other analyses involve variation in the definitions from the key analyses, and produce a more limited output, which includes examination of the number of studies for which the change in the definition of the analysis actually changed the relative risks included. The number of relative risks which actually differ between a key analysis and a variant analysis is generally quite small, because many studies do not offer relative risks for any alternative definitions of exposure.

4.4   Factors considered

The meta-analyses first give overall results for all the relative risks selected. Then results of an analysis of risk by the factor **sex** are shown with estimates shown, and compared, for combined sex results and those specifically for males and females. Depending on the particular exposure being considered, further analyses may show results for the following factors:

Asthma   The levels are: lifetime; and current.

Continent   The levels are: NAmer (= North America); Europe; Oth/Mult (= Other/Multiple)

Start year of study   The levels are: <1990; 1990-99; and unknown.

Publication year   The levels are: 1990-99; and 2000+. This refers to the principal publication for the study.

Study type   The levels are: CC (= Case-control); Pr (= Prospective); and CS (= Cross-sectional.

Ex smokers   This refers to how active smoking by the subject was treated in the study (or in the results selected for the database). The levels are: excluded; and included.

Lowest and Highest age in RR   The levels are: 15-19; 20-25; and 60+; and up to 55; 60-69; and 70+ respectively.

Physician diagnosis   The levels are: yes (= diagnosis by physician); and no/mixed (= self-diagnosis, definition based on a list of reported symptoms, or physician-diagnosis plus self-report of symptoms).

Analysis type   The levels are: prev (= prevalence); and onset.

Number of cases   This refers to the number of asthma cases (lifetime or current as relevant to the meta-analysis) in the whole study, rather than in the specific relative risk. The levels are : 1-100; 101-400; 401+; and unknown.

Study adjustment   A number of factors refer to whether any of the relative risks on the data base were adjusted for certain potential confounders, although the specific relative risk included in a meta-analysis may not have been adjusted for that confounder. In each case the levels are yes; and no. The confounders considered are: sex;   age;   race;   location;   SES (= socioeconomic status);   family medical history;   family composition (e.g. number of siblings, single parent);   cooking;   housing quality, crowding, damp, mould;   subject's medical;   ex-smoking or other ETS exposure. For the first two of these confounders considered, matching in the study design (for case-control studies only) was considered equivalent to adjustment for confounding.

Source of ETS exposure   The levels are: Hh (= Household); Hh,Wk (= Household and/or Workplace); Cot (= Serum Cotinine); and Work.

Timing of exposure The levels are: life (= any in subject's lifetime); adult (= in adulthood or in last 6 homes); child (= in childhood); current; and unspec (=unspecified).

Number of adjustment variables This refers the adjustment variables used in the specific relative risk included in the meta-analysis. The levels are: 0; 2; 3-5; 6-9; and 10+.

Relative risk adjustment This refers to the adjustment variables used in the specific relative risk included in the meta-analysis, rather than in the study as a whole, as above. The variables considered, each with levels yes or no, are: sex, age, ex-smoking or other ETS (i.e. other than the specific exposure to which the relative risk refers); any other variables.

Derivation of RR/CI The levels are: Original; Numbers (= calculated from the 2×2 table, adjusted calculation from a 2×2×n table, or recalculation due to a discrepancy between a 2×2 table and an original RR/CI); Sum/F&L (= calculation from 2×2 table after combining categories, or using the method of Fry and Lee, as described in §3.4.3).

4.5   Meta-analysis of results by amount of exposure

Results by amount of exposure generally take the form of a relative risk for each of a set of categories (e.g. mother smokes 1-10, 11-20 etc cigarettes) compared with a common base group, e.g. mother non smoker. These are not independent.

The approach adopted in this report is to use only the first and last from each set of categories, then to carry out a standard meta-analysis for each level. Effectively only one relative risk is chosen from each study for each level, thus ensuring independent results for a valid meta-analysis of 'low dose' and 'high dose' respectively. The sets of categories are included irrespective of the measure of exposure used (number of cigarettes, pack years or hours per day). Only one study (JAAKK2) gives results for more than one measure and

meta-analyses using both are presented. Because the individual studies used different definitions for the categories, the range of values included in the 'low' and 'high' analyses may overlap. For instance, if one study used the categories 1-10 and 11+, while another used 1-19 and 20+, then exposure to 11-19 cigarettes would be included in the low category for one study, but in the high category for the other. However this approach ensures that the same studies are included in both of the low/high pair of analyses, and allows within-study comparisons to be made. No attempt was made to carry out any meta-analysis of 'medium dose'. More complex regression analyses modelling the dose response and allowing all the results to be retained are considered beyond the scope of this report.

4.6   Presentation of findings in the results chapter of this report

Relative risks and 95% confidence intervals are typically referred to simply as e.g. 1.23 (1.18-1.28), where it is obvious in the text that these are what are referred to. On occasion, the abbreviations RR and CI are used. The standard notation may be extended to e.g. 1.23 (1.18-1.28, n=32) or 1.17 (1.10-1.25, $p<0.001$) to indicate the number of relative risk estimates on which a meta-analysis estimate is based or the level of significance. Unless otherwise stated, it should be assumed that meta-analysis relative risk estimates are fixed-effects, and that they are calculated using individual estimates that are adjusted for covariates where there is a choice of unadjusted and adjusted estimates.

5.   Results

5.1   Risk from any exposure – Table F and Appendix Table F

All analyses considered in §5.1, Appendix Table F (which gives the full meta-analysis results) and Table F (which gives the reduced results) relate to the exposed/unexposed comparison and are not concerned with the extent of the exposure. 'Exposure' may be defined as household members smoking, irrespective of whether this is actually in the presence of the subject.   The various analyses summarized in Table F are shown below.

Text Table 5.1   Analyses summarized in Table F

Table	Definition of asthma outcome	Source of ETS exposure	Time of ETS exposure	Definition of non-smoking
F1	Lifetime/current	Total (or nearest)	Earliest	Never/non
F2	Lifetime/current	Total (or nearest)	Earliest	Never
F3	Lifetime/current	Total (or nearest)	Most recent	Never/non
F4	Lifetime/current	Total (or nearest)	Childhood	Never/non
F5	Lifetime/current	Total (or nearest), preferring paternal to maternal	Childhood	Never/non
F6	Current/Lifetime	Total (or nearest)	Earliest	Never/non
F7	Lifetime/current	Household	Earliest	Never/non
F8	Lifetime/current	Household	Most recent	Never/non
F9	Lifetime/current	Workplace	Earliest	Never/non
F10	Lifetime/current	Workplace	Most recent	Never/non

Thus Tables F1, F7 and F9 are the key analyses for the three main sources of exposure, choosing the earliest available exposure, each with a variant choosing the most recent exposure available (F3, F8, F10). Additionally F2 is based on a subset of the results in F1, restricted to studies which excluded ex-smokers, Tables F4 and F5 are variants restricted to exposure in childhood, and Table F6 is a variant choosing current asthma in preference to lifetime for study SAPALD.

5.1.1   Total exposure – Tables F1, F3 and F6

Total exposure (whether assessed biochemically or by questionnaire) is included if available, otherwise household exposure. Exceptionally for study LARSS2 workplace exposure is included, being the only complete result available.   For studies JANSON and LARSS2, results adjusted for other ETS

exposure (childhood and household, respectively) are included, being the only results available. There are a total of 18 relative risks included in the adjusted meta-analysis in Table F1. 15 are >1.00, of which three (LARSS1, SAPALD, THORN-males) are significantly positive (p<0.05), and 3 are <1.00, of which one (BECKE2-baseline prevalence) is borderline significantly negative (p=0.05). Overall there is a significant increased risk in relation to total exposure, with the relative risk estimate 1.14 (1.06-1.23, P<0.001) from the fixed-effects model or 1.19 (1.04-1.35, p<0.05) from the random-effects model. Results from the unadjusted analysis were similar, with three of the 17 RRs significantly positive (THORN having only sexes-combined results here), and none significantly negative (BECKE2 just losing significance, p=0.06). The overall relative risk estimate is 1.16 (1.08-1.24, p<0.001) from the fixed-effects model and 1.17 (1.04-1.32, p<0.01) from the random-effects model. In the following text, we restrict attention to the adjusted analysis. Egger's test (Egger et al., 1997) showed no evidence of publication bias. The heterogeneity chisquared is 37.20 on 17 d.f. (p<0.01). The excess of the chisquared over the degrees of freedom is not obviously explained by any specific outlying study, the largest Q_s values being 10.22 for the THORN-males result (where the lower confidence limit of 2.00 for the RR of 4.80 is higher than any of the other RRs), 8.22 for BECKE2-baseline and 6.74 for LARSS1. By far the largest weights are for study MISHRA, with males – RR= 1.20 (0.80-1.59), weight = 102 and females – RR= 1.05 (0.91-1.21), weight = 189, together accounting for 43% of the total weight of 672.

An alternative relative risk which would have been chosen as higher preference except that it was incomplete was available for study LARSS2. This referred to household exposure and merely stated that there was no significant increase[‡] (thus suggesting no difference from the non-significant increase for workplace exposure included in Table F1). Two other studies (KRONQV and PLATTS) provide only incomplete data, both not significant with no further details.

[‡] In the original paper Larsson et al., 2003 this is given "for respiratory symptoms" but the context suggests this relates specifically to asthma

Variations in relative risk by various factors is shown in Table F1, although the small number of studies available limits the usefulness of the comparisons that can be made, and results are heavily influenced by which factor level study MISHRA falls in.

Sex Although the increase seen in females is not significant, this does not differ significantly from the estimates for males or for sexes combined.

Asthma definition The increase in risk is significant for studies of both lifetime/incident asthma (1.20, 1.06-1.36, p<0.01) and current asthma (1.12, 1.02-1.22, p<0.05), and the difference between them is not significant. Only study SAPALD presented results for both definitions of asthma, and when current asthma was chosen in preference for that study (Table F6) the risk for lifetime/incident asthma reduced slightly and the risk for current asthma increased slightly, but the overall risk remained virtually unchanged (1.14, 1.06-1.24, p<0.001). There was also no difference seen between physician diagnosed asthma and other.

Location The risk estimates vary significantly (p<0.01) by continent, with the risk from the European studies (1.40, 1.21-1.63) significantly higher than from the US studies (0.99, 0.84-1.16).

Timing of study There was weak evidence that risk estimates were higher in studies which started later than in earlier studies (0.05<p<0.1), but the difference was in the opposite direction and non-significant when based on publication year.

Study type and analysis type There is significant evidence of heterogeneity due to study type (χ^2 = 9.32 on 2 d.f., p<0.01), with the highest estimates in case-control studies (1.56, 1.19-2.05, n=5), intermediate in cross-sectional studies (1.15, 1.06-1.26, n=10) and lowest in prospective studies (0.93, 0.76-1.13, n=3). However the risk from the prospective studies is non-significantly >1.00 if the analysis is restricted to onset of asthma (1.11, 0.85-1.45, n=2,

studies BECKE2 and ROBBIN, omitting BECKE2 baseline-prevalence, data not shown). There is also no evidence of a difference between prevalence (1.13, 1.05-1.23, n=15) and onset (1.21, 0.98-1.49, n=3) where the latter category includes the CC study JAAKK2 (first episode of asthma).

Ex smokers There is significant heterogeneity ($\chi^2 = 4.23$ on 1 d.f., p<0.05), with an increased risk seen only in those studies which excluded ex-smokers (1.20, 1.10-1.31, n=13) and not in those which included them (1.00, 0.86-1.16, n=5). The two studies which reported results separately for ex-smokers and never smokers shed little light on this difference. Study KRONQV merely reported no significant association in either ex-smokers or never smokers. Study JANSON did not report results for male ex-smokers because of small numbers, while the risks reported for female ex-smokers were slightly higher than the equivalent results for female never smokers, but still not significant, as shown below.

Text Table 5.2 Odds ratios (95% CIs) for asthma, women, study JANSON

	Never smokers	Ex-smokers[1]
Paternal smoking	0.67 (0.49-0.91)	0.88 (0.53-1.48)
Maternal smoking	1.10 (0.78-1.55)	1.17 (0.78-1.55)

[1] Not entered on database

Analysis restricted to the studies excluding ex-smokers is discussed below (§5.12).

Age Although there is some evidence of heterogeneity (0.05<p<0.1 for lowest age in study, and p<0.05 for highest age), the risk is highest in studies falling in the middle category and this is probably not indicative of any real effect of age on risk.

Size of study There is significant heterogeneity ($\chi^2 = 13.68$ on 3 d.f., p<0.01), with an increased risk seen in smaller studies (1.40, 1.05-1.86, p<0.05 from studies with up to 100 cases, and 1.50, 1.25-1.81, p<0.001 from studies of

101-400 cases), but not in the largest studies (1.05, 0.95-1.15, NS). This represents a significant trend (p<0.01[§])

Adjustment for confounding variables There is little evidence of heterogeneity according to whether the study took into account specific factors as potential confounder, to whether the relative risk itself was adjusted for specific factors, or to the number of factors the relative risk was adjusted for.

Source of exposure The definition of total exposure involves the following order of preference: total-biochemical; total-questionnaire; any household member; mother; workplace. For only one study (BECKE2) are total-biochemical results available (and these are the only result available for that study), while for most of the studies, preferencing led to inclusion of exposure from any household member. Exposure from mother was not chosen by the preferencing for any study, and workplace exposure was chosen for one study (LARSS2). There is some evidence of heterogeneity by source of exposure ($\chi^2 = 11.26$ on 3 d.f., p<0.05), largely due to the low estimates for total-biochemical arising from study BECKE2 (0.84, 0.67-1.04, n=2). The estimates for both total-questionnaire (1.34, 1.13-1.59, n=4) and household (1.16, 1.05-1.27, n=11) are significantly >1.00. Analyses specifically restricted to household and workplace exposures are discussed in §5.1.4 and §5.1.5 respectively.

Timing of exposure In Table F1 the preferencing favoured the earliest exposure in the subject's life (after having chosen the most general source of exposure available as described in the previous paragraph), as follows: childhood; lifetime; adulthood; recent (last 6 homes); unspecified; current. Adulthood and recent were combined in one factor level (and in fact only recent was chosen by the preferencing – study THORN). Despite being the lowest preference, current exposure is the most commonly selected (11 RRs). There is evidence of heterogeneity by time of exposure ($\chi^2 = 18.11$ on 4 d.f., p<0.01). Risk from current exposure (1.07, 0.99-1.17, n=11) was not

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[§] Based on additional analysis (full details not shown) using trend coefficients of 1, 2, 3.

significantly >1.00, and was significantly lower than exposure in adulthood (2.31, 1.35-3.96, n=2, study THORN) or in childhood (1.73, 1.30-2.31, n=2, studies LARSS1 and ROBBIN).

In the variant <u>Table F3</u>, the preferencing favoured the most recent exposure. In fact, the RR altered only for two studies as compared to Table F1, choosing current exposure rather than lifetime for study JAAKK2, and adult rather than childhood for study ROBBIN. This increased the overall estimate of risk slightly, to 1.15 (1.07-1.24) for the fixed-effects model and 1.21 (1.05-1.40) for the random effects model. Heterogeneity remained similar (χ^2 = 17.41 on 4 d.f., p<0.01), with risk from studies of current exposure now marginally significantly increased (1.09, 1.01-1.19, n=12), but still significantly lower than for adult exposure (1.99, 1.40-2.83, n=3, studies ROBBIN, THORN) or childhood (n=1, LARSS1) exposure.

Exposure specifically in childhood is discussed in §5.1.3.

Derivation of RR/CI   There is no evidence of heterogeneity according to whether the relative risk was available directly (n=11), had been calculated directly from the numbers in the 2 × 2 table (n=3), or had been calculated by combining over strata (n=4).

Thus the main sources of heterogeneity appear to be the <u>higher</u> estimates of risk from studies conducted in Europe than elsewhere, and from CC studies than cross-sectional or prospective studies; and <u>lower</u> estimates from studies that included rather than excluded ex-smokers (i.e. restricted to non-smokers rather than to never smokers), from studies that considered biochemical rather than questionnaire assessed exposure, and from studies that considered current exposure rather than earlier or more general exposure timings. However these factors may not be acting independently, with for instance, biochemical exposure inherently current, all case-control studies conducted in Europe, and all prospective studies including ex-smokers, and it

is difficult to distinguish between these effects given the small number of studies available.

5.1.2   Total exposure in never smokers – Table F2

The meta-analysis of Table F1 is repeated in Table F2, but restricted to those studies that excluded ex-smokers, i.e. were restricted to never (or almost never) smokers. Thus 13 relative risk estimates are included in the adjusted analysis, of which 12 are >1.00 (three significantly so), and one is non-significantly <1.00. As has already been noted, the overall fixed-effects adjusted relative risk from this group of studies is higher than from all the studies, 1.20 (1.10-1.31), and this is also the case for the random-effects model, 1.27 (1.09-1.49), and for the unadjusted analysis, 1.20 (1.11-1.29) for the fixed-effects model and 1.24 (1.09-1.42) for the random effects model. Again, we now restrict attention to the adjusted analysis. Heterogeneity remains significant (χ^2 = 25.13 on 12 d.f), with study THORN again the main contributor, with its Q_S value now 9.58. Study MISHRA now represents 58% of the total weight.

The variation in relative risk was examined only for some of the key factors. Even with this reduced list of factors, the usefulness of the analysis is limited, with no studies conducted in US, started before 1990, or of prospective design. Differences seen previously which remain are the higher (p<0.05) estimate of risk from case-control (1.56, 1.19-2.05, n=5) rather than cross-sectional studies (1.16, 1.06-1.27, n=8), and the higher (p<0.05) estimate from studies conducted in Europe (1.40, 1.21-1.63, n=9) than elsewhere (1.11, 1.00-1.23, n=4). Additionally, there is now also evidence of heterogeneity due to sex (χ^2 = 6.96 on 2 d.f., p<0.05) although the pattern is in fact very similar to that seen previously for all studies, and also due to asthma definition (χ^2 = 7.70 on 1 d.f. p<0.001), where the estimate from studies of lifetime asthma is now significantly higher (1.49, 1.25-1.78, n=5) than from studies of current asthma (1.12, 1.01-1.23, n=8).

5.1.3   Total exposure in childhood – Tables F4 and F5

Four studies gave results for exposure in childhood, of which one, KRONQV provided results insufficient to include in meta-analysis (not significant with no further details).   Thus results from three studies are available.   Exposures considered were total (ROBBIN), any household member (LARSS1) and parental (JANSON).   For study JANSON, maternal smoking was chosen for Table F4 and paternal for Table F5; only results adjusted for current ETS exposure are available for this study.

The estimates from studies LARSS1 and ROBBIN (both tables) were >1.00, significantly (p<0.001) so for LARSS1, and these are in fact the same estimates as chosen from these studies for Table F1.   The estimates for maternal exposure (Table F4) from study JANSON are both non-significant, with the male estimate <1.00 and the female >1.00, whereas for paternal exposure (Table F5) they are in the opposite direction and the decrease for females is significant (p=0.01).   The overall estimates of risk from these meta-analyses are all >1.00, but this is only significant (p<0.05) when both the fixed-effects model and maternal exposure are chosen.   It can also be noted that study RAHERI (excluded from the meta-analysis because it is a subset of study JANSON) reported a significant decrease in risk of lifetime asthma associated with childhood exposure (0.30, 0.14-0.61, p<0.005).

Variation in relative risk by the key factors is shown in Tables F4 and F5, but the number of studies available is too small to allow any conclusions to be drawn.

It is also of interest to note that study ROBBIN reported results for childhood and adulthood separately, both against a base of no exposure at either time.   These results, shown below, are not suggestive of any effect of childhood exposure given adult exposure.

Text Table 5.3   Odds ratios (95% CIs) for asthma onset from multiple logistic regression, study ROBBIN

	Unexposed in childhood	Exposed in childhood
Unexposed in adulthood	1.00 (base)	0.74 (0.26-2.06)
Exposed in adulthood	1.57 (0.81-2.97)	1.89 (1.13-3.15)

5.1.4   Household exposure – Tables F7 and F8

Ten studies provide results for household exposure. For two studies, only results adjusted for other ETS exposure (for workplace exposure for JAAKK2 [adjusted analysis] and for current exposure for JANSON) are available. With a preference favouring earliest exposure (Table F7), the adjusted meta-analysis includes 14 RRs, all but three of which (from studies JAAKK2 and JANSON) are in fact the same as those included in Table F1. The overall estimate shows a significant increase in risk, 1.13 (1.04-1.23, p<0.01) from the fixed-effects model or 1.16 (1.00-1.35, p=0.05) from the random-effects model, which, not surprisingly, is quite similar to the total exposure estimate (Table F1). Heterogeneity also remains quite similar (χ^2 = 25.99 on 13 d.f., p<0.05). Analyses studying the variation in relative risk are presented only for the key factors. The pattern of variation is similar to that previously seen, although the only factor showing significant evidence of heterogeneity is definition of asthma (χ^2 = 10.87 on 1 d.f., p<0.001), with a significantly elevated risk seen only from studies of lifetime asthma (1.69, 1.31-2.19, n=4) and not from studies of current asthma (1.07, 0.98-1.18, n=10).

The variant analysis preferring most recent exposure (Table F8) also differs from the total exposure analysis only in the relative risks selected for studies JAAKK2 and JANSON. The estimate for JAAKK2 is rather higher (4.77, 1.29-17.70) than that used in Table F3 (1.97, 1.19-3.25) or Table F7 (1.09, 0.77-1.53). This results in higher overall estimates, slightly for the fixed-effects model (1.17, 1.06-1.28) and more so for the random-effects model (1.26, 1.05-1.53). However the heterogeneity (χ^2 = 27.62 on 12 d.f., p<0.01) and the pattern of results by key factors is not dissimilar from that seen for total exposure (Table F3).

5.1.5   Workplace exposure – Tables F9 and F10

Eight studies gave results for workplace exposure. Studies KNONQV and SAPALD simply reported no significant association without further details, and study ROBBIN reported only trend analyses which are discussed later (§5.2). Thus, results suitable for meta-analysis are available from five studies. For study LARSS2, the exposure was strictly "in smoky rooms outside your home", but we follow the original authors who state that this "mainly related to work, since most of the subjects were of working age" (Larsson et al., 2003). For three studies, only results adjusted for other ETS exposure (for household exposure for JAAKK2 [adjusted analysis] and LARSS2, and for childhood exposure for JANSON) are available.

In the adjusted meta-analysis preferring earliest exposure (Table F9), there are six estimates, of which four are >1.00, three of them significantly so, and two, both from study ORYSZC, are non-significantly <1.00. Study NHANES has the largest weight and represents 48% of the total weight. The overall estimate of risk is highly significantly increased, 1.37 (1.18-1.59, p<0.001) from the fixed-effects model or 1.36 (1.09-1.70, p<0.01) from the random-effects model. There is no evidence of heterogeneity (χ^2 = 7.97 on 5 d.f., p>0.1). Analyses studying the variation in relative risk are presented by the key factors, but as expected when the overall heterogeneity is non-significant, none of the factors showed any significant variation.

The unadjusted analysis preferring earliest exposure, and the variant analyses preferring most recent exposure (Table F10), differ only in the relative risks selected from study JAAKK2 (Table 9 1.55 adjusted or 1.25 unadjusted; Table 10 2.16 adjusted or 1.87 unadjusted). The overall estimates using the adjusted data, 1.39 (1.19-1.63, p<0.001) from the fixed-effects model and 1.40 (1.06-1.85, p<0.05) from the random-effects model, are similar to those in Table F9.

5.2   Risk by amount of exposure – Table G and Appendix Table G

        The analyses considered in §5.2, Appendix Table G (which gives the
full meta-analysis results) and Table G (which gives the reduced results) form
pairs, with the first of each pair relating to a 'low dose' versus unexposed
comparison, and the second relating to a 'high dose' versus unexposed
comparison. The various analyses summarized in Table G are shown below.

Text Table 5.4 Analyses summarized in Table G

Table	Source of ETS exposure	Measure of dose	Dose
G1	Total (or nearest)	Cigarettes or hours	Low
G2	Total (or nearest)	Cigarettes or hours	High
G3	Household	Cigarettes or hours	Low
G4	Household	Cigarettes or hours	High
G5	Workplace	Cigarettes or hours	Low
G6	Workplace	Cigarettes or hours	High
G7	Total (or nearest)	Pack-year, cigarettes or hours	Low
G8	Total (or nearest)	Pack-year, cigarettes or hours	High
G9	Household	Pack-year, cigarettes or hours	Low
G10	Household	Pack-year, cigarettes or hours	High
G11	Workplace	Pack-year, cigarettes or hours	Low
G12	Workplace	Pack-year, cigarettes or hours	High

        Because only study JAAKK2 has a choice of results available for
different exposures and measures of dose, the relative risk chosen for each
table differs only for that study. All studies with relevant results excluded ex-
smokers, and no study had a choice of results for asthma definition or (given
the exposure measure) exposure time.

        In all cases, the overall estimate of risk for low dose does not differ
significantly from 1.00, whereas the overall estimate for high dose generally
shows a significant increase. For instance, for total exposure (or nearest
available) and preferring numbers of cigarettes for study JAAKK2, the overall
adjusted fixed-effects estimate is 1.03 (0.80-1.32, NS, n=4) for low dose and
1.63 (1.19-2.22, p<0.01, n=4) for high dose (Tables G1, G2). Similarly when
restricted to workplace exposure, the adjusted fixed-effects estimate is 1.08
(0.73-1.59, NS, n=2) for low dose and 2.04 (1.26-3.31, p<0.01, n=2) for high
dose (Tables G5, G6). The only exception is the analysis restricted to
household exposure and preferring numbers of cigarettes for study JAAKK2,

where neither the low nor high dose estimate differs significantly from 1.00, and, for the random-effects model, the high dose estimate is actually slightly lower than the low dose estimate (Tables G3, G4). However when pack-years is preferred as the measure of exposure for study JAAKK2, then the usual pattern is again seen for household exposure, although the significance of the high dose increase is weaker ($0.05 < p < 0.1$) (Tables G9, G10).

These dose-response data considered in Table G derive only from those four studies (JAAKK2, JANSON, LARSS2, NG) which present relative risk estimates by level of exposure. As noted earlier, two studies also present results of dose-response analyses expressed as an increase in risk per unit of exposure. As shown in Table 10, study SAPALD reported a significant trend with home/work exposure, whether expressed in terms of hours per day exposed ($p < 0.01$), number of smokers exposed to ($p < 0.05$) or years of exposure ($p < 0.05$). Study ROBBIN, in the 1992 follow-up data, reported a significant association with years worked with a smoker in females ($p < 0.05$) but not males, and a significant association with years lived with a smoker in males ($p < 0.05$) but not females.

Taken together the data considered in Table G and in Table 10 demonstrate the existence of a dose-response relationship.

6.   Discussion

6.1   Evidence of an association

Text Table 6.1 below summarizes the results of the analyses relating asthma to ETS exposure (irrespective of amount) presented in detail in Appendix Tables F1-F10 and discussed in §5.1. The analyses show an increased risk of asthma in the ETS exposed group, which is always significant except for some of the estimates for childhood exposure, which are based on limited data. The meta-analysis estimates are all consistent with a weak association, with risk about 20% higher in the ETS exposed group, the slightly higher estimates for workplace exposure having relatively wide confidence limits. There is no clear indication that risk estimates vary by type of meta-analysis (fixed-effects or random-effects), source of exposure (total, household, workplace), timing of exposure (earliest, most recent, childhood), by whether ex-smokers are included or excluded from analysis, by whether preference is given to results for lifetime or current asthma or by whether, when childhood exposure is considered, estimates for maternal or paternal smoking are used. The relative risk estimates used in Text-Table 6.1 are adjusted for covariates, where adjusted estimates are available. The same conclusions would have been reached had preference been given to unadjusted estimates.

It should be noted that some of the similarity in the meta-analysis estimates in Text-Table 6.1 arises because, for 8 out of 14 of the studies providing data, only a single adjusted estimate was available, and this estimate contributed to a number of the meta-analyses. Of the other 6 studies, 4 provided only two estimates, and only for studies JAAKK2 and JANSON were a relatively large number of alternative estimates available.

Text Table 6.1 Summary of analyses for ETS exposure (irrespective of amount smoked)

Table	Exposure	Timing of exposure	Variant	N	Fixed effects RR (95% CI)	Random effects RR (95% CI)	Heterogeneity Chisq per df
F1	Total	Earliest		18	1.14 (1.06-1.23)	1.19 (1.04-1.35)	2.19**
F2	Total	Earliest	No ex-smoker	13	1.20 (1.10-1.31)	1.27 (1.09-1.49)	2.09*
F3	Total	Most recent		18	1.15 (1.07-1.24)	1.21 (1.05-1.40)	2.48***
F4	Total	Childhood		4	1.27 (1.04-1.54)	1.26 (0.88-1.81)	3.34*
F5	Total	Childhood	Paternal	4	1.11 (0.93-1.33)	1.18 (0.74-1.90)	6.59***
F6	Total	Earliest	C/L	18	1.14 (1.06-1.24)	1.20 (1.04-1.37)	2.27**
F7	Household	Earliest		14	1.13 (1.04-1.23)	1.16 (1.00-1.35)	2.00*
F8	Household	Most recent		13	1.17 (1.06-1.28)	1.26 (1.05-1.53)	2.30**
F9	Workplace	Earliest		6	1.37 (1.18-1.59)	1.36 (1.09-1.70)	1.59 NS
F10	Workplace	Most recent		6	1.39 (1.19-1.63)	1.40 (1.06-1.85)	2.05 (*)

Key: Exposure: Total includes nearest equivalent if total exposure not available.
Variant: Except for Table F2 analyses may include results for nonsmokers if estimates for never smokers are not available. Except for Table F5 estimates for maternal exposure are preferred to estimates for paternal exposure. Except for Table F6 estimates for lifetime asthma are preferred to estimates for current asthma (L/C). In Table F6 the reverse preference is used (C/L).
N = number of relative risk estimates combined.
Relative risk estimates used are adjusted for covariates where adjusted estimates are available.
Heterogeneity Chisq per df: *** p<0.001, ** p<0.01, * p<0.05, (*) p<0.1, NS p≥0.1.

6.2   Evidence of a dose-response relationship

The data available are rather limited, with only 4 studies providing estimates by level of exposure and 2 studies providing results of trend analyses. Of the 4 studies giving data by level of exposure, 3 only provided a single pair of estimates (for low and high exposure) and only for study JAAKK2, and the two studies providing trend data (SAPALD, ROBBIN) were data available for a variety of ETS exposure sources and measures.

The data for low exposure analysed in Table G consistently show no significant evidence of an increased risk of asthma associated with ETS exposure.   The data for high exposure, however, do show a significant increase, a finding which is supported by significant trends seen in studies SAPALD and ROBBIN.   The relevant data for total cigarettes (or nearest equivalent) are summarized in Text Table 6.2.   Using alternative ETS exposure sources and measures does not affect the general conclusion that the data do provide evidence of an increased risk at higher ETS exposures.

Text Table 6.2 Dose-response data for total ETS exposure (or nearest equivalent)

Study	Sex	Exposure	Level	Relative risk (95% CI)[a]
JAAKK2	M+F	Current, at home or work	1-9 cigs/day 10+ cigs/day	2.13 (1.05-4.30) 2.14 (0.95-4.82)
JANSON	M+F	Current, at home or work	<4 hours/day 4-7 hrs/day 8+ hrs/day	0.99 (0.70-1.40) 1.19 (0.76-1.88) 1.39 (0.86-2.25)
LARSS2	M+F	Current, at work[b]	<1 hrs/day 1-5 hrs/day 6+ hrs/day	0.85 (0.54-1.34) 1.21 (0.71-2.07) 1.79 (1.02-3.16)
NG	F	Lifetime, at home	1-19 cigs/day[c] 20+ cigs/day	0.86 (0.34-2.21) 1.60 (0.69-3.70)
ROBBIN	M	Years lived with smoker	Non-cases Cases	Mean 7.7 Mean 13.5 (p<0.05)[d]
	F	Years lived with smoker	Non-cases Cases	Mean 11.9 Mean 14.0 (NS)[d]
SAPALD	M+F	Current, at home or work	Hours/day	Trend p<0.01
Random-effects meta-analysis – based on first 4 studies			Low High	1.07 (0.75-1.51) 1.63 (1.19-2.22)

[a] Adjusted data if available, unless otherwise stated
[b] Outside home but "mainly related to work" (Larsson et al., 2003)
[c] Maximum consumption of any household smoker
[d] Means given are unadjusted; years lived with a smoker was omitted from multiple logistic   regression analysis as not significant

Clearly the data available show an association and a dose-response relationship that, at least for a number of the exposure indices, cannot be explained by chance. In order to interpret these findings, it is necessary to consider various aspects of the data further.

6.3   Consistency of findings

As shown in Text Table 6.1, there is evidence of heterogeneity in all the Table F analyses, statistically significant except for the limited data for workplace ETS exposure. Identifying the sources of the heterogeneity is not straightforward, partly because one study (MISHRA), which contributes to the analyses in Tables F1-F3 and F6-F8, has a very large weight, and partly because of studies with unusually high estimates (THORN, males, 4.80) and with unusually low estimates (JEDRYC, 0.53) for reasons that are not clear.

Also the number of estimates available is rather small to allow detailed study of sources of heterogeneity.

We have investigated variation in risk on a one factor at a time basis, rather than on a multivariate basis, with Table F1 considering the largest number of factors. There, the most statistically significant (p<0.01) variations in estimate by factor level related to:

continent, with the strongest associations seen in studies conducted in Europe, and no clear association seen in studies conducted in the United States or elsewhere;

study type, with the association strongest for case-control studies, intermediate for cross-sectional studies and not evident for prospective studies;

study size, with the association strongest in the smaller studies ($\leq$400 cases) and not evident in the larger studies (401+ cases) or in the studies with the number of asthma cases unknown; and

time of exposure, with the association not really evident for current exposure or when the time was unspecified, but evident where it was – whether the estimate was based on childhood, adult or lifetime exposure.

The extent to which these observed significant variations represent independent or meaningful differences is unclear, bearing in mind the relatively small number of estimates available at some factor levels (e.g. only 3 for prospective studies), and the likely interrelationships between the factors.

6.4   <u>Publication bias</u>

Though there is a consistent association with a dose-response relationship, this does not of itself imply a cause and effect relationship. Sources of bias and confounding have to be considered. One such source of bias is publication bias. The traditional main sources of publication bias are authors being less willing to submit for publication, and journal editors being less willing to accept for publication, papers which report no association between exposure and disease than papers which report such an association.

Publication bias can be investigated by various possible techniques, all of which involve assumptions which are difficult to justify formally.

In one approach, we found that large studies tended to give lower relative risk estimates than do small studies, suggesting the possibility that some publication bias may exist. This is supported by the observation that there were six cases where a lack of significant association of ETS exposure with asthma was noted, but results sufficient for inclusion in meta-analysis were not presented. However, formal testing using the Egger method (Egger et al., 1997) did not show any significant evidence of publication bias for any of the analyses considered in Appendix Table F. Noting also that 15 of the 18 estimates in Table F1 were greater than 1.0, it seems unlikely that publication bias could explain the whole association.

6.5   Diagnostic bias

Ideally, an epidemiological study of the relationship of an exposure to a disease should involve a disease which has a clearly defined and generally accepted definition, with subjects defined as cases based on accurate diagnostic criteria. Inclusion of cases with other diseases may lead to over- or under-estimation of the relationship of interest, depending on the magnitude and direction of the relationship of the exposure to these other diseases.

While asthma is recognized as a chronic respiratory condition characterized by airway inflammation and episodic airflow limitation, clinical definitions of the disease vary. As for the review of asthma induction in children (Lee et al., 2004a; Lee et al., 2004b), the protocol for the present review specified that only studies where the endpoint was 'asthma' were to be included, with studies of 'wheeze', 'wheezing bronchitis' or 'chronic wheezing' to be excluded. It was further decided, in order to attempt to achieve consistency of definition, to exclude 'asthma or wheeze' and 'asthmatic bronchitis'.

In practice, except for two studies (JANSON, MISHRA) where the asthma was self or proxy reported, the diagnosis of asthma was made by the

physician, usually with the subject also reporting symptoms currently or in the last 12 months. This means that one cannot usefully investigate diagnostic bias by seeing how relative risks vary by the source of diagnosis. It is possible that knowledge of ETS exposure may have affected the diagnosis but the data available provide no means to test this.

6.6   Representativeness

As noted in §3.3.4, most of the studies were of the general population with no major restrictions, though one study (ROBBIN) was of Seventh Day Adventists and another (KRONQV) was of farmers. Other restrictions (see Table 3) seemed mainly to be of a minor nature. It is not evident how the association observed between ETS and asthma could have arisen due to use of unrepresentative populations.

6.7   Misclassification of exposure

The only study to provide relative risk estimates based on biochemically-assessed exposure estimates was BECKE2, which used serum cotinine. Otherwise indices were questionnaire-assessed, based generally on exposure at home and/or at work. Though reported data are generally highly reliable, there is ample documentation that a small proportion of smokers deny smoking on interview (Lee & Forey, 1995) and also that reporting of smoking by others is not completely accurate. Random misclassification of exposed adults as unexposed (or of unexposed adults as exposed) will tend to lead to some underestimation of the true association of exposure with asthma. However, misclassification may not necessarily be random. If having asthma makes it more likely that ETS exposure will be reported (perhaps because the asthmatic is more aware of it), then the relative risk will be systematically overestimated.

If ETS exposure is recorded before onset of asthma, such systematic bias should not occur, but if it is recorded when the subject already has asthma it is more plausible. The observation that an association of ETS exposure with asthma was seen in case-control and cross-sectional studies, but not in prospective studies, might therefore at first sight suggest the association might

be an artefact of systematic bias of this type. However, such an inference is far from reliable. The results for prospective studies are only based on two studies, and in one of these (ROBBIN) it is unclear whether the exposure measure used (based on repeated measurements throughout the study period) actually related to the period before asthma onset. It still remains possible that underestimation of the true relationship due to random misclassification of ETS exposure may be more important than any overestimation due to asthmatics overstating their exposure.

Another possible bias may arise because someone with asthma tends to avoid ETS exposure. If this were true, and ETS exposure caused asthma, one would expect to find a weaker association of asthma with post-onset ETS exposure than with pre-onset ETS exposure. As shown in Text Table 6.1, there was no marked difference in the meta-analysis estimates, whether earliest or most recent ETS exposure was preferred (Table F1 vs F3 for total exposure; Table F7 v F8 for household exposure and Table F9 v F10 for workplace exposure). However, in fact only three studies had alternative estimates relating to differing timing of exposure, with no clear evidence that early or late exposure was more strongly associated with asthma. Some further issues relating to timing of ETS exposure are discussed in §6.11.

6.8   Smoking by the subject

It has been claimed by some (e.g. Larsson, 1994; Beeh et al., 2001) that smoking increases the risk of asthma, though we have never carried out a detailed review of the subject. For that reason we sought data relating ETS exposure to asthma in adults who have never smoked. In practice, the data were so limited that we accepted also data for nonsmokers (i.e. including ex-smokers). Of the 16 principal studies, 11 concerned self-reported never smokers (or those whose lifetime smoking history was less than a small defined amount), 3 concerned self-reported nonsmokers, 1 based nonsmoker status on biochemical assessment and 1 on a combination of self-report and biochemical assessment.

It is known that smoking habits in family members tend much more often to be concordant than would be expected by chance (Lee, 1992). There is also evidence of concordance of smoking habits between work colleagues (Lee et al., 2002). It thus follows that, compared to non ETS exposed nonsmokers, ETS exposed nonsmokers will contain a higher frequency of ex-smokers and a slightly higher frequency of asthma as a result. Given also that a proportion of current smokers deny their smoking on interview (Lee & Forey, 1995), it also follows that ETS exposed nonsmokers (and never smokers) will contain a higher frequency of current smokers. The extent of such bias is difficult to assess, but is probably small, as the association of smoking with asthma is at best weak.

6.9   Confounding

Although the causes of asthma are not fully understood, there is a wide range of potential confounding variables that have been taken into account in at least some of the studies considered. Leaving aside other sources of exposure to tobacco smoke or its constituents, factors considered include the sex, age and race of the subject, location within the study area, education, occupation, body mass index, aspects of medical history of the subject and the family, cooking methods, household composition (e.g. number of siblings, marital status), housing quality, crowding and mould, pets and exposure to allergens. However some of these factors have only been considered in one or two studies and some other factors that might be considered important, such as diet, exercise, exposure to infections and use of air conditioning and humidifiers, have not been considered at all.

There are considerable problems in assessing the extent of confounding, particularly by individual variables. Many studies present only unadjusted or only adjusted relative risks, while those that do present adjusted and unadjusted risks typically only provide estimates adjusted for a number of potential confounding variables, so that the effect of adjustment for specific variables cannot readily be assessed. Furthermore, in some studies, the relative risks presented deliberately do not adjust for certain variables found in preliminary analyses not to have any material confounding effect.

The statistical analyses that we have conducted look at the issue of confounding using various methods.

One method that we used was to compare the results of alternative analyses, one using adjusted risks where possible and unadjusted risks otherwise, the other using unadjusted risks where possible and adjusted risks otherwise. In practice, results did not differ meaningfully between the two analyses. For example in the analyses of overall ETS exposure presented in Table F1, the meta-analysis estimates based on adjusted risks where possible were 1.14 (1.06-1.23) using the fixed-effects model and 1.19 (1.04-1.35) using the random-effects model. In contrast the corresponding results using unadjusted risks where possible were 1.16 (1.08-1.24) using the fixed effects model and 1.17 (1.04-1.32) using the random effects model. Looking at the detailed data, there were 2 studies that presented unadjusted data only, 5 studies that provided adjusted data only and 7 studies that provided both. Of this latter group, adjustment increased the relative risk estimate in 3 studies (by 0.23, 0.20 and 0.06) and decreased the relative risk in 4 studies (by 0.08, 0.07, 0.02 and 0.02).[**] This does not indicate any consistent or major effect of confounder adjustment in these studies.

This conclusion was reinforced by analyses that showed that relative risks did not vary systematically according to the number of confounding variables adjusted for, or whether specific confounding variables were adjusted for. However the relatively small number of studies considered, the variety of variables taken into account, and the fact that studies do not generally present the results of analysis adjusted and not adjusted for specific factors, and the fact that some variables are not considered by any studies at all means that one cannot completely rule out the possibility that some confounding may exist. However any confounding effect is probably not large.

[**] Using combined sex estimates where separate male and female results are available.

6.10   Smoking in pregnancy

Some studies in children have attempted to separate out possible effects of ETS exposure and of maternal smoking in pregnancy. None of the studies of adults provide any results for *in utero* exposure. However in the study SAPALD there is a statement that "Excluding subjects who reported that their mothers smoked at all in pregnancy ... had little impact. Some subjects may not reliably know whether their mothers smoked during pregnancy. They are more likely to know whether their mothers ever smoked, and the third column in Table 3 shows the impact of excluding all subjects whose mothers ever smoked." From their Table 3 the odds ratio for asthma in relation to passive smoke exposure was 1.39 (1.04-1.86) including all the subjects, and 1.43 (1.04-1.96) excluding subjects whose mother ever smoked.

Failure to collect data on smoking in pregnancy is a limitation of the studies considered as, in theory, it could be correlated both with risk of asthma and with indices of ETS exposure.

6.11   Exacerbation or induction?

In one model of asthma, people remain asthma free until some exposure first induces symptoms of the disease and leads to the person being diagnosed as asthmatic. Subsequently other exposures (not necessarily to the same agent) may lead to exacerbation of the asthmatic symptoms. As the main interest of this report is in induction rather than exacerbation, we have not considered here those studies that clearly related to exacerbation, in which the frequency of symptoms in asthmatics is related to ETS exposure (either in everyday life, or controlled in chamber studies). Instead we have limited attention to studies that relate to the whole population and compare the frequency of asthma in exposed and unexposed adults, whether using a prospective, case-control or cross-sectional design.

It is important to realize that there are difficulties in interpreting all the results from these studies strictly in terms of induction. In theory, induction relates to the probability of someone previously asthma free getting the condition for the first time. Ideally, one would conduct a prospective study in

which information is collected on onset of asthma in individuals who are asthma free at the start of the study, and on regularly updated exposure information. Then one would base the analysis (using life-table methods) on data for each of a number of relatively short periods of time, which classified asthma free subjects by exposure at the start of the period and compared the probability of onset of asthma in the different exposure groups. In principle one could also conduct a similar analysis using retrospective data on time of asthma onset and on history of exposure obtained in a case-control or cross-sectional study.

In practice, the data collected rarely conform to this situation. Thus, of the 17 studies considered, there were six cross sectional studies (JANSON, JEDRYC, MISHRA, NG†, NHANES, SAPALD) and two case-control studies (ORYSZC, PLATTS) for which the definition of asthma required the subject to have had symptoms currently or recently but which provided no information on time of onset of the asthmatic condition. This lack of data means that one cannot interpret an association of ETS exposure with asthma as indicating a specific effect on either induction or exacerbation.

More insight might be gained from studies of whether the subject has ever had asthma. Assuming that asthma was not diagnosed at birth, which seems unlikely, the endpoint can be interpreted as induction between birth and current age. There were four cross-sectional studies (KRONQV, LARSS1, LARSS2, RAHERI) and one case-control study (PILOTT) where the definition of asthma was based on having ever had the condition. However, for none of these studies was time of onset of asthma considered and one could not therefore infer that the ETS exposure had occurred before the onset, particularly for study LARSS2 which related current ETS exposure to lifetime asthma. Three of these studies did relate childhood ETS exposure to lifetime asthma, study LARSS1 reporting a significant positive association (1.82, 1.28-2.58), study RAHERI reporting a significant negative association (0.30, 0.14-

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† Asthma was defined as "episodic wheeze and report of asthmatic symptoms diagnosed by a doctor as asthma during the past year" which might be taken to imply a new diagnosis in the last year, but which we have taken to imply the symptoms occurred in the last year but the asthma might have been longstanding.

0.61), and study KRONQV merely reporting no significant relationship. However, even for this index, one cannot be sure whether the exposure was before or after the asthma.

There were in fact only four studies where the exposure occurred before asthma onset:

- Study BECKE2, a prospective study in which serum cotinine was measured at baseline, provided two types of results. One, not relevant to asthma induction, related cotinine level to asthma prevalence at baseline. The other, which is relevant, related cotinine level to onset of asthma over the next 10 years, in those with no history of asthma at baseline. Here no association was seen with the relative onset rate 0.96 (0.70-1.32) for those with cotinine 2-13 ng/ml as compared to those with cotinine <2 ng/ml.

- Study ROBBIN was also a prospective study, with onset after baseline, so childhood exposure was definitely before onset, and showed a non-significant positive relationship (1.57, 0.96-2.58). However, exposure was determined repeatedly during the follow-up period and it is not clear what was used to determine indices of adult exposure.

- Study JAAKK2 was a case-control study where the cases were first occurrences of asthma and previous asthma was also an exclusion for the controls. ETS exposure was determined in the last 12 months or on a lifetime basis, with a large number of indices of exposure studied. For total home and work exposure, an association was seen that was significant (1.97, 1.19-3.25) for most recent exposure, but not for earliest exposure (1.40, 0.99-1.96).

- Study THORN was a case-control study, nested within a cross-sectional study, involving cases with asthma first diagnosed in the previous 15 years. Questions were asked about ETS exposure and period of residence in the last six homes. To be classified as exposed, the case had to report exposure in the year of asthma diagnosis or the years previous to that year,

with a comparable period of potential exposure considered for the controls. This study reported an association with household exposure, significant for males (4.80, 2.00-11.60) but not for females (1.50, 0.80-3.10).

While the data summarized above are suggestive of a possible association of ETS exposure with induction of asthma in adults, the relatively limited number of available studies and the somewhat heterogeneous nature of the results preclude a confident conclusion.

6.12   Other reviews

The 1993 EPA report on respiratory health effects of passive smoking (National Cancer Institute, 1993) included a chapter on "Respiratory disorders other than cancer". However, the section on "Asthma" only considered data for children, while the section on "Respiratory symptoms and lung function in adults" did not consider asthma.

The next year, members of IARC published a review paper (Trédaniel et al., 1994) entitled "Exposure to environmental tobacco smoke and adult non-neoplastic respiratory diseases". This concluded that "no definite conclusion (excluding the acute irritating effect of ETS on respiratory mucous membranes) can be drawn" although there was "a need for further epidemiological studies". The section on "Asthma" was mainly concerned with possible exacerbating and allergenic effects of ETS, citing a number of experimental studies, and did not consider any epidemiological evidence linking asthma onset or prevalence to ETS.

Later that year, the results of study SAPALD were published and an associated editorial entitled "Passive smoking and adults: new evidence for adverse events" (Leaderer & Samet, 1994) summarized its findings and also cited results from ROBBIN and of a study (Dayal et al., 1994) for which the endpoint was obstructive airway disease and not asthma. The authors argued that the new studies "suggest a need for reconsideration of the evidence on passive smoking and respiratory symptoms and illnesses in adults".

A later review was entitled "Effects of environmental tobacco smoke exposure on pulmonary function and respiratory health in adults: update 1997" (Witorsch, 1998). This contained quite a detailed analysis of the experimental evidence on ETS exposure in asthmatics. As regards epidemiology, no actual attempt was made to separate out effects on asthmatics and the normal population and of the 18 studies cited of "asthma incidence, exacerbation or symptoms", the only data cited that are relevant to this report relate to studies JEDRYC, NG, ROBBIN and SAPALD. Witorsch regarded the evidence from the 18 studies as inconsistent, though did not present any quantitative overview.

The same year, a review was entitled "Passive smoking and risk of adult asthma and COPD: an update" (Coultas, 1998). Results related to asthma onset (rather than exacerbation) were cited from three studies, two considered by us (ROBBIN, SAPALD) and one from a study (Hu et al., 1997) we rejected as failing to restrict subjects to nonsmokers. Coultas concluded that "While growing evidence suggests that passive smoking is a risk factor for adult onset asthma and COPD, the magnitude of the associations is small. However additional evidence on the relationship between passive smoking and asthma and COPD is needed to fulfil the criteria for causality, particularly the criteria of temporality and dose-response".

The next year, the California EPA published their overview entitled "Health effects of exposure to environmental tobacco smoke" (National Cancer Institute, 1999). In section 6.2.4, they reviewed evidence on "Chronic pulmonary disease and respiratory symptoms (adults)". Most of the studies reviewed were not relevant to this report, but data were summarized from studies NG, ROBBIN and SAPALD (though not from studies JEDRYC or PLATTS which had been reported well before this report). Later in the report, in section 6.4, the California EPA conclude that "There is consistent and compelling evidence that ETS is a risk factor for induction of new cases of asthma". However, this conclusion seems to have been based mainly on the

findings for children, discussed in our earlier report (Lee et al., 2004b), as no conclusions regarding asthma induction in adults are made, other than to note (in section 6.2.4) that "The results of Leuenberger et al. (1994), Robbins et al. (1993) and other recent papers, however, suggest that ETS exposure may make a significant contribution to chronic respiratory symptoms in adults".

In the same year, a short review was published on "Environmental tobacco smoke exposure and asthma in adults" (Weiss et al., 1999). In the section "The role of ETS in causing asthma in adults", results were reviewed from studies we considered (ROBBIN, SAPALD) and from studies we rejected (Flodin et al., 1995; Hu et al., 1997) as not being restricted to nonsmokers. The authors concluded: "These studies have differing designs – cross-sectional, cohort, and case-control – but their findings provide an indication of potential effects of ETS exposure in the workplace on persons with asthma. Their results may be subject to the complex biases considered above – both selection bias and both differential and nondifferential misclassification of exposure. They highlight the difficulty and challenge of accurately assessing workplace exposure and of interpreting findings that may be subject to selection bias that cannot be characterized readily. In summary, at present there are limited epidemiologic data on the relationship of ETS exposure as a cause of adult asthma".

A longer review entitled "Environmental tobacco smoke and adult asthma" (Eisner & Blanc, 2000) concluded that "The evidence indicates that adults who are exposed to ETS have a greater risk of developing asthma". The studies cited in the relevant table (6.1) only extend by one those considered in the previous review (Weiss et al., 1999), including additionally the study (Dayal et al., 1994) for which the endpoint was obstructive airway disease. Although section 6.8 "ETS exposure and adult asthma: evidence for a causal association" discusses issues such as confounding, biased report of exposure, and dose-response, there is no discussion of the problems of separating out potential effects of ETS exposure on induction and exacerbation. The limited number of relevant studies is also not really put

over, especially when one restricts attention specifically to induction of asthma in nonsmokers.

Another review published in the same year, on "Environmental tobacco smoke and respiratory diseases" (Jaakkola, 2000) was broad ranging. In the section on adults, a subsection deals with "Induction of asthma". Five studies are cited; three we consider (NG, ROBBIN, SAPALD) and two (Flodin et al., 1995; Hu et al., 1997) which were not of nonsmokers. Jaakkola concludes that "These findings provide evidence that ETS causes asthma in adulthood, but more studies, especially with a longitudinal design, are needed before making any definite conclusions". A further review by the same author in 2002 (Jaakkola & Jaakkola, 2002) added study JAAKK2 and presented effectively unchanged conclusions.

A brief editorial the following year (Bousquet & Vignola, 2001) was entitled "Exposure to environmental tobacco smoke and asthma". It stated that there were "only five studies examining exposure to ETS and adult onset asthma", three of which related to studies considered by us (ROBBIN, SAPALD, THORN) with two (Flodin et al., 1995; Hu et al., 1997) not of nonsmokers. The authors concluded that "In these studies, some methodological barriers mostly inherent in the study design limited the available data and the evaluation of the adequacy of the data for risk assessment. Thus, more epidemiologic studies are needed to confirm the causative role of ETS in asthma".

A further review by Eisner in 2002 entitled "Environmental tobacco smoke and adult asthma" (Eisner, 2002) included a section "Environmental tobacco smoke and new-onset adult asthma" which considered data from far more studies than he considered in 2000. Data from seven of the studies we considered are included (KRONQV, JANSON, LARSS1, NG, ROBBIN, SAPALD, THORN) as well as from studies we have rejected, three (Dayal et al., 1994; Flodin et al., 1995; Hu et al., 1997) for reasons noted above and one (Iribarren et al., 2001) because the outcome was hay fever or asthma not

asthma. It should be noted that, although the title of the section refers to "new-onset" adult asthma, some of the studies (e.g. JANSON, NG, SAPALD) only required cases to have recent occurrences, so the asthma could have started years earlier and is not necessarily "new-onset" at all. As with the previous review (Eisner & Blanc, 2000), the discussion considers induction and exacerbation together, without looking at the difficulties of disentangling the two. Nevertheless, he concludes that "the evidence suggests a causal relationship between ETS exposure and new-onset asthma".

In 2004, a short but wide-ranging review on "The effect of passive smoking on respiratory health in children and adults" was published (Janson, 2004). Only one paragraph on asthma in adults was cited reporting the associations seen in the studies LARSS2, ROBBIN, SAPALD and THORN. There was no discussion of any potential bias or of separating potential effects of ETS on induction and exacerbation. The review concluded that "Passive smoking is a widespread, important and avoidable risk factor for respiratory symptoms in both children and adults".

In the recent draft of the "Proposed Identification of Environmental Tobacco Smoke as a Toxic Air Contaminant" (California Environmental Protection Agency, 2004), the California EPA include "asthma induction and exacerbation in children and adults" in this list of "Effects Causally Associated with ETS Exposure". They note that though the findings for asthma induction in adults in their earlier report (National Cancer Institute, 1999), based on only two studies, were "suggestive", their latest report includes evidence from a further nine studies. Table 6.18 "ETS and new-onset adult asthma" in section 6.2.1.2 gives the relevant data for the additional studies. Based on this table, one can see that, of the 11 papers cited there, three are not of nonsmokers (Flodin et al., 1995; Hu et al., 1997; Eagan et al., 2004), one is not of asthma (Iribarren et al., 2001) and two (Greer et al., 1993; McDonnell et al., 1999) are (as recognized by the authors) reports from the same study (ROBBIN). The others do relate to studies we consider (JAAKK2, JANSON, KRONQV,

LARSS1, THORN), but three of these (KRONQV, JANSON, LARSS1) do not relate to "new-onset" asthma (see Table 4). The report also notes that the earlier report considered five studies of ETS and adult asthma, one rejected by us as not being of asthma specifically (Dayal et al., 1994), two relate to studies we consider (NG, SAPALD) but are not of "new-onset" asthma, and two (Greer et al., 1993; Robbins et al., 1993) are papers we consider on the ROBBIN study. Overall, the report includes 7 of the 17 studies we consider, and a number we exclude as not relevant.

The report does not contain any sections giving an overall meta-analysis or interpretation of the data specifically on asthma induction in adults, section 6.2.1.2 merely giving a description of each of the studies published since the previous report that they considered relevant. The next section, 6.2.1.3, is headed "Conclusions – asthma in children and adults" but actually seems to relate to adults. However, it includes evidence on asthma-like symptoms, lung function and exacerbation, and that relating specifically to asthma induction in adults is not clearly delineated. The authors point out that most studies "examined at least some potential confounders" with the association "probably not explained by confounding" and refer to the possibilities of exposure bias. They note the existence of dose-response relationships, as we find (see Text Table 6.2), but argue unreasonably (see §6.11) that "the temporal relationship between ETS and the development of asthma or asthma-like symptoms was clearly delineated in most studies". They note that "a key issue is distinguishing the development of incident adult-onset asthma, as opposed to exacerbation of previously established disease", citing in support one study not of nonsmokers (Hu et al., 1997) and three we consider as most relevant in §6.11 (JAAKK2, ROBBIN, THORN), though failing to cite the fourth relevant study (BECKE2) which finds no association.

The report concludes that "In sum, studies of ETS and adult-onset asthma have controlled for bias and confounding. They have demonstrated temporality, exposure-response relationship, consistency, coherence, and

biologic plausibility, supporting a causal relationship". This seems to overstate the evidence from a rather limited database.

7. <u>Summary and conclusions</u>

    <u>Methods used to collect and analyse the data and scope of the information</u>
    <u>obtained</u>

    Based on papers available up to the end of 2004, 17 studies have been
identified which provide information from epidemiological case-control,
prospective or cross-sectional studies of prevalent or incident asthma in non-
smoking adults. Only studies where the endpoint was 'asthma' were included,
and studies of 'wheeze', 'wheezing bronchitis', 'chronic wheezing', 'asthma
or wheeze' or 'asthmatic bronchitis' were excluded.

    Two linked databases have been set up. One contains details of the
characteristics of each study, while the other contains relative risk data relating
to certain aspects of passive smoke exposure (for parental or household
exposure, when exposed, and who smoked; biochemically assessed exposure;
workplace exposure). For each study, the study database contains details of
the study itself, the definition of asthma used, and the potential confounding
variables considered. For each of the 117 relative risks included, the relative
risk database contains not only the relative risks and 95% confidence intervals,
but precise details of their definition and information on how they were
derived.

    This report starts by describing the methods used to identify relevant
papers, which involved examining over 400 papers, and classifying them into
separate studies. 16 principal studies were identified, plus one subsidiary study
which was a subset of another study. The report then describes in detail the
structure of the databases and the methods used for entry and checking of data.
The methods by which relative risks were derived from data presented in
various ways are also described.

    One multi-centre study was conducted in 17 countries, and the other
studies were conducted in 10 countries. Only two studies started before 1988.
10 were of cross-sectional design, and all but two include both males and
females. The largest study involved nearly 2500 asthma cases with a further

four studies involving between 200 and 500 cases. Nine studies give results for lifetime or incident asthma, and nine studies for current (active) asthma. Data on total ETS exposure are available for seven studies, while data on household exposure are available for 13, and on workplace exposure for eight. Data on amount of passive smoke exposure are available for four studies. The potential non smoking confounding variables most commonly taken into account are age (13 studies), sex (9), location (8), education (5) and occupation (4). Fuller details of the studies are given in this report.

Of the 117 relative risks, 115 relate to the principal studies. The number of relative risks per principal study varies widely, from only one in three studies, to over 10 in three, the largest being a study with 48 relative risks entered. 92 relative risks are for sexes combined, and all relate to results for the full age range of the study and to all races within the study scope. 24 relate to lifetime asthma prevalence, 77 to current asthma prevalence and 16 to asthma incidence. 44 risks relate to total ETS exposure, with 45 relating to household smoking and 28 to workplace exposure. 53 relate to current exposure, 7 to exposure as an adult and 12 to exposure as a child, with the remainder relating to lifetime or unspecified exposure. None relate to *in utero* exposure. 75 are adjusted for at least one variable. 13 have no relative risk value but a statement of significance or non-significance. 74% of the relative risks and confidence intervals are as given originally or calculated directly from the numbers in the relevant 2×2 table. The rest involve more complex calculations. Fuller details of the relative risks are given in the report.

The report also describes the techniques used for conducting meta-analyses and the format of the tables presenting the results. The process of selecting which relative risks to include in an analysis is described in detail. It has to be quite complex to ensure that all the relevant data are included, while at the same time avoiding double-counting.

Results

 Results are presented of a series of meta-analyses of the database aimed at giving insight into how the relative risk of asthma varies by the source, timing and amount of ETS exposure, the definition of the asthma outcome, the sex and age of the subject, the location, timing, size and type of study, the source of the information on exposure and diagnosis, and the extent of adjustment for confounding variables.

 The main conclusions reached from the analyses are as follows:

 There is an association between ETS exposure and asthma in adults. Including results for nonsmokers as well as for never smokers, and giving preference to exposure estimates as early in life as available and to results for lifetime rather than current asthma, meta-analysis relative risk estimates (95% confidence limits) for total ETS exposure (or nearest equivalent), based on 18 independent results, are 1.14 (1.06-1.23) using the fixed-effects model and 1.19 (1.04-1.35) using the random-effects model. Corresponding meta-analysis estimates for household exposure (n = 14) are 1.13 (1.04-1.23) fixed-effects and 1.16 (1.00-1.35) random-effects. For workplace exposure (n = 6), they are 1.37 (1.18-1.59) fixed-effects and 1.36 (1.09-1.70) random-effects. Restricting results to those for never smokers, giving preference to most recent exposure estimates or giving preference to current rather than lifetime asthma affects the conclusions little, the meta-analyses generally being consistent with a weak, but statistically significant, association, with risk about 20% higher in the ETS exposed group. (However, some of the similarity in the various alternative analyses arises because some studies only provide limited estimates, e.g. for a single timing of exposure or a single definition of asthma.) Meta-analyses for childhood ETS exposure are also consistent with about a 20% increased risk, but are not statistically significant, being based on only 4 estimates (1.27, 1.04-1.54 fixed-effects; 1.26 , 0.88-1.81 random-effects).

 Data on dose-response are rather limited, with only 4 studies providing estimates by level of exposure, an additional 2 studies providing results of trend analyses. However, the overall results are consistent with a significantly

increased risk in the highest exposure group, a conclusion which is independent of the sources and measures of ETS exposure considered.

There is evidence of significant heterogeneity between estimates in virtually all the meta-analyses conducted. Investigation of heterogeneity is limited by the small number of studies considered, and by the fact that one large study has a very large weight and that individual studies have unusually high or low relative risk estimates for reasons that are not clear. Although there is evidence that associations are stronger in European studies than in studies conducted elsewhere, in case-control than in prospective studies, and in smaller than in larger studies, the extent to which these observed significant variations represent independent or meaningful differences is unclear.

There is a tendency for smaller studies to provide larger relative risk estimates, but formal testing of publication bias using Egger's method did not show any significant evidence of it. Although it is possible that some publication bias may exist, the fact that 15 of the 18 estimates included in the total exposure meta-analysis cited above are greater than 1.0 makes it unlikely that publication bias could explain the whole association.

There was no direct evidence that diagnostic bias, lack of representativeness or misclassification of exposure is an important issue in the interpretation of the results. However, the data available to investigate this are limited. Nor is there any evidence that our decision to include estimates for nonsmokers (i.e. including former smokers) in our analyses materially affected the findings. We preferred to exclude estimates for the whole population (i.e. including current smokers) because of reports that smoking caused asthma.

There is no clear evidence of confounding by a variety of non-smoking lifestyle factors, although a number of different approaches were used to investigate this. Although most studies took into account potential confounders, factors that might be considered important were only rarely taken account of (e.g. pets only in one study, and diet, exercise and exposure to infections in none).

In our corresponding report on asthma induction in children, we showed a stronger association with maternal smoking in pregnancy than with ETS exposure. Although one of the studies we considered reported that excluding mothers who ever smoked made little difference to their findings, a limitation of the evidence is that none of the studies provided any results relating to *in utero* exposure.

Our meta-analyses have deliberately excluded studies of asthmatic adults which relate specifically to asthma exacerbation, data on which will be presented elsewhere. As such, one cannot make inferences regarding asthma exacerbation from the data presented here. While the results considered here show an association of ETS exposure with asthma, it is important to realise that there are difficulties in interpreting all the findings strictly in terms of asthma induction. Indeed, we consider that only four studies provide relevant data, with the ETS exposure known to occur before onset of asthma. Though the findings from these studies are suggestive of a possible association of ETS exposure with induction of asthma in adults, the relatively limited data and the somewhat heterogeneous nature of the results preclude a confident conclusion.

Our general conclusion is that the data are consistent with ETS exposure causing asthma induction in adults, but do not clearly demonstrate a causal effect. Limitations of the evidence include the relatively small number of studies (particularly those that specifically relate to induction), the lack of consideration of *in utero* exposure and the lack of control for relevant confounding variables.

The review ends with a brief summary of the findings of various other reviews. As shown there, conclusions reached are somewhat variable, and often based on a literature review that includes studies we consider inappropriate (e.g. not of asthma specifically, or not in nonsmokers) and excludes some studies we consider. A number of reviewers point to the need for additional evidence on asthma in adults. We agree.

8.   References

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Table 1 The 17 studies considered and the reference keys used for each

Study Ref	Study title	Principal publication	Additional publication(s)
BECKE2	CARDIA[1] 4 city PS 1985 - 1996	BECKET2001	FRIEDM1988A
JAAKK2	Pirkanmaa incident asthma CC 1997-2000	JAAKKO2003B	-
JANSON	ECRHS[2] multicentre CS 1990-94	JANSON2001	SVANES2004, DEMARC2004
JEDRYC	Cracow elderly TB screening CS (ca 1994?)	JEDRYC1995B	-
KRONQV	Gotland farmers CS 1996	KRONQV1999	-
LARSS1	Swedish part of FinEsS[3], Orebro CS 1995-6	LARSSO2001	-
LARSS2	Estonian part of FinEsS[3], 3 centre CS 1995	LARSSO2003	-
MISHRA	Indian NFHS-2[4] elderly CS 1998-99	MISHRA2003	-
NG	Singapore CS (ca 1992?)	NG1993A	-
NHANES	NHANES III[5] nationwide CS 1988-94	EISNER2002B	-
ORYSZC	French EGEA[6] CC (ca 1996?)	ORYSZC2000	KAUFFM1997
PILOTT	Port Adelaide CS 1995	PILOTT1999	-
PLATTS	Wilmington acute asthma CC 1988-89	PLATTS1993	GELBER1993, MOYER1993
RAHERI	ECRHS[2] Bordeaux centre CS 1991-92	RAHERI2003	-
ROBBIN	California 7th Day Adventist PS 1977-87	ROBBIN1993	GREER1993, MCDONN1999
SAPALD	SAPALDIA[7] CS 1991	LEUENB1994	LEUENB1993, ZEMP1999, KUNZLI2000
THORN	Alvsborg nested CC 1994	THORN2001	-

1   CARDIA = Coronary Artery Risk Development in Young Adults
2   ECRHS = European Community Respiratory Health Study
3   FinEsS = epidemiologic studies in Finland, Estonia and Sweden
4   NFHS-2 = 2nd National Family Health Survey
5   NHANES = Third National Health and Nutrition Examination Survey
6   EGEA = Epidemiological Study of the Genetics and Environment of Asthma
7   SAPALDIA = Swiss Study on Air Pollution and Lung Diseases in Adults

The references corresponding to the reference keys are given in Appendix A

Table 2   Characteristics of the 17 studies

Characteristic	Level	Study type				
		CC	Prosp	CrSec	Subsid	Total
Total		4	2	10	1	17
Study sex	both	4	2	8	1	15
	female	0	0	2	0	2
Lowest age in study	15	1	0	3	0	4
	17	0	0	1	0	1
	18	0	1	2	0	3
	20	1	0	2	1	4
	21	1	0	0	0	1
	25	1	1	0	0	2
	60	0	0	1	0	1
	65	0	0	1	0	1
	missing					
Highest age in study (at baseline for prospective studies)	30	0	1	0	0	1
	44	0	0	0	1	1
	48	0	0	1	0	1
	50	1	0	0	0	1
	54	1	0	0	0	1
	55	1	0	0	0	1
	60	0	0	1	0	1
	63	1	0	0	0	1
	64	0	0	1	0	1
	65	0	0	1	0	1
	69	0	0	1	0	1
	74	0	0	1	0	1
	no upper limit	0	1	4	0	5
	missing					
Highest age in study at final followup (prospective studies)	40	-	1	-	-	1
	no upper limit	-	1	-	-	1
Study race	all (in country)	4	0	10	1	15
	whites and blacks	0	1	0	0	1
	non-Hispanic whites	0	1	0	0	1
Continent	N America	1	2	1	0	4
	Europe	3	0	5	1	9
	Asia	0	0	2	0	2
	Australia	0	0	1	0	1
	multi	0	0	1	0	1
US state	all	0	0	1	0	1
	multi	0	1	0	0	1
	California	0	1	0	0	1
	Delaware	1	0	0	0	1

Table 2 (continued)

Characteristic	Level	Study type				
		CC	Prosp	CrSec	Subsid	Total
Country in Europe	Estonia	0	0	1	0	1
	Finland	1	0	0	0	1
	France	1	0	0	1	2
	Poland	0	0	1	0	1
	Sweden	1	0	2	0	3
	Switzerland	0	0	1	0	1
Country in Asia	India	0	0	1	0	1
	Singapore	0	0	1	0	1
Start year of study	1970-1979	0	1	0	0	1
	1980-1989	1	1	1	0	3
	1990-1999	2	0	7	1	10
	missing	1	0	2	0	3
End year of study (of baseline for prospective studies)	1970-1979	0	1	0	0	1
	1980-1989	1	1	0	0	2
	1990-1999	1	0	8	1	10
	2000	1	0	0	0	1
	missing	1	0	2	0	3
Final follow up year (prospective studies)	1990-1999	-	2	-	-	2
Principal publication year	1990-1999	1	1	5	0	7
	2000-2003	3	1	5	1	10
Type of population[1] (for CC studies refers to cases)	all	2	0	1	0	3
	randomly selected	1	2	6	1	10
	farmers	0	0	1	0	1
	random households	0	0	2	0	2
	unstated	1	0	0	0	1
Type of controls (for CC studies)	healthy	2	-	-	1	3
	diseased/hospital	1	-	-	0	1
	both	1	-	-	0	1
Type of control population (Case-control studies)	same as cases	4	-	-	0	4
	without history of asthma	0	-	-	1	1
Matching factors (Case-control studies)	sex	1	-	-	0	1
	age	1	-	-	0	1

Table 2 (continued/2)

Characteristic	Level	Study type				
		CC	Prosp	CrSec	Subsid	Total
Respondent (for ETS exposure information)	subject	4	2	9	1	16
	head of household (subject or proxy)	0	0	1	0	1
Lifetime[2]/incidence asthma available		1	2	5	1	9
Source of lifetime[2]/ incidence asthma diagnosis	Medical records	0	0	1	0	1
	Self report (physician diagnosis)	1	1	3	1	6
	Self report (other/ unspecified/mixed)	0	1	1	0	2
Timing of lifetime[2] asthma	lifetime	0	1	1	1	3
	unspecified	0	0	4	0	4
	from age 16	1	0	0	0	1
	NA (incidence only)	0	1	0	0	1
Timing of incidence asthma	since baseline (earlier excl)	0	2	0	0	2
	NA (prevalence analysis only)	1	0	5	1	7
Number of lifetime[2]/ incidence asthma cases	1-100	1	1	0	1	2
	101-200	0	0	1	0	1
	201-500	0	1	1	0	2
	N	1	2	2	1	6
	Median	69	276.5	215	96	119.5
	Min	69	8	143	96	69
	Max	69	473	287	96	473
	Missing	0	0	3	0	3
Current asthma available		3	0	6	0	9
Current asthma is first occurrence		1	0	0	0	1
Repeat measures for current asthma (prospective studies)		0	0	0	0	0
Source of current asthma diagnosis	Medical records	2	0	0	0	2
	Self report (physician diagnosis)	0	0	3	0	3
	Self report (other/ unspecified/mixed)	1	0	2	0	3
	Proxy report (other/ unspecified/mixed)	0	0	1	0	1

Table 2 (continued/3)

Characteristic	Level	Study type				
		CC	Prosp	CrSec	Subsid	Total
Timing of current asthma	current diagnosis	2	0	1	0	3
	last 12 months	1	0	3	0	4
	current NOS	0	0	2	0	2
Number of current asthma cases	1-100	2	0	2	0	4
	101-200	0	0	0	0	0
	201-500	1	0	1	0	2
	501-1000	0	0	0	0	0
	>1000	0	0	1	0	1
	N	3	0	4	0	7
	Median	51	-	269.5	-	99
	Min	48	-	33	-	33
	Max	239	-	2479	-	2479
	Missing	0	0	2	0	2
Total number of subjects	1-100	1	0	0	0	1
	101-200	1	0	0	0	1
	201-500	1	0	0	0	1
	501-1000	1	0	1	1	3
	1001-5000	0	2	5	0	7
	>5000	0	0	4	0	4
	N	4	2	10	1	17
	Median	313	3365	3490.5	544	1282
	Min	89	3128	581	544	89
	Max	726	3602	28020	544	28020
	Missing	0	0	0	0	0
Other definitions of asthma available		0	1	3	0	4
Wheezing/wheezing bronchitis available		0	0	6	1	7
Other exposures available		0	0	1	0	1
Non-smoker definition	Never smoked NOS	2	0	2	0	4
	Smoked <1 cig/day for 1 year	0	0	2	0	2
	Never smoked, not even a few per week	0	0	1	0	1
	Never smoked regularly/daily	1	0	1	0	2
	Smoked <20 packs cigarettes or 360g tobacco in lifetime	0	0	1	0	1
	Smoked <1 cigarette/day or 1 cigar/week for a year, or 360g tobacco in lifetime	0	0	1	0	1
	Smoked for <1 year /continued	0	0	0	1	1

Table 2 (continued/4)

Characteristic	Level	Study type				
		CC	Prosp	CrSec	Subsid	Total
Non-smoker definition (continued)	Not current smoker	0	1	1	0	2
	Not active smoker	1	0	0	0	1
	Serum cotinine <14 ng/ml	0	0	1	0	1
	Not current smoker and serum cotinine <14 ng/ml	0	1	0	0	1
Results for other definition of non smokers available		0	0	3	1	4
Total number of adjustment factors used	none	2	0	1	0	3
	2	1	0	0	0	1
	3	0	0	3	0	3
	4	0	0	1	0	1
	5	0	1	0	0	1
	6	0	0	2	0	2
	7	0	1	0	0	1
	8	0	0	1	0	1
	10	0	0	0	1	1
	11	1	0	0	0	1
	12	0	0	1	0	1
	15	0	0	1	0	1
Confounders considered[3]:	sex	1	2	6	1	10
	age	2	2	9	1	14
	race	0	1	1	0	2
	location within study area (including urban/rural, air pollution)	0	2	6	0	8
	family medical history	1	0	2	1	4
	SES	0	0	1	0	1
	household composition	0	0	2	0	2
	cooking	0	0	3	0	3
	mould in home or workplace	1	0	0	0	1
	housing quality	0	0	2	0	2
	pets	1	0	0	0	1
	exposure to allergens	0	0	1	0	1
	occupation	1	0	3	0	4
	religion	0	0	1	0	1
	education	1	2	2	0	5

/continued

Table 2 (continued/5)

Characteristic	Level	Study type				
		CC	Prosp	CrSec	Subsid	Total
Confounders considered[3] (continued):	personal medical history (by 1-3 variables)	1	1	1	0	3
	personal medical history (by >3 variables)	0	0	1	1	2
	body mass index	0	0	2	0	2
	active smoking (never/ex)	0	1	0	0	1
	childhood ETS	0	0	1	0	1
	total (adult) ETS	0	0	1	0	1
	household ETS exposure	1	0	2	0	3
	workplace ETS	1	1	2	0	4
Other confounders considered but rejected		0	1	1	0	2
Results by other stratifying factors available		0	0	3	0	3

CC = case-control; Prosp = prospective; CrSec = Cross-sectional; Subsid = Subsidiary
[1] Refers to persons within the study area, age group etc as defined by other variables
[2] Includes asthma of unspecified timing.
[3] By up to 3 variables, unless stated otherwise.

Table 3 Exclusions from study population

Study Ref	

	A Medical exclusions
BECKE2	Long-term illness or disability (including blind, deaf, mute, mentally retarded, unable to walk), emotionally unstable, pregnant or <3 months post partum
JAAKK2	Previous asthma
JEDRYC	Residents of old people's home and geriatric wards (i.e. incapable of self-care or independent living)
KRONQV	From an initial screening, sampling was 19% among healthy subjects, 75% among those with single-organ hypersensitivity (either lungs or nose/eyes), 99% among those with multiple organ hypersensitivity and 100% among those with allergic alveolitis
LARSS1	Family history of asthma
NG	History of cardiac disease
	B Other exclusions
JEDRYC	Use electric or coal stoves for cooking
LARSS2	Subjects who said they did not leave home
NHANES	Institutionalized persons and non-civilians
ROBBIN	Resident near baseline address <10y. Died before follow-up (1987: ROBBIN1993, GREER1993 or 1992: MCDONN1999). Includes only Seventh Day Adventists
SAPALD	Residents for <3 yrs

The references corresponding to the reference keys are given in Appendix A

Table 4 Diagnostic criteria for asthma

Basis of diagnosis	Study Ref	Description of asthma
		A Lifetime or incident asthma
Medical records	KRONQV	History of episodic shortness of breath, wheezing, and breathing difficulties
Physician diagnosis	BECKE2	Taking medication typically used to treat asthma or ever told by doctor or nurse had asthma
	LARSS1	Asthma
	LARSS2	Asthma
	RAHERI	Asthma
	SAPALD	Asthma
	THORN	Physician-diagnosed asthma, onset after age 16 (and not more than 15 years ago)
Other/mixed	PILOTT	Asthma
	ROBBIN	Definite asthma (physician-diagnosed asthma, and breathing sounded wheezy or attacks of SOB with wheezing) - ROBBIN1993, GREER1993; Doctor-told asthma (ever told by doctor had asthma) - MCDONN1999
		B Current asthma
Medical records	JAAKK2	At least one asthma-like symptom (prolonged cough, wheezing, attacks of or exercise-induced dyspnea, or nocturnal cough or wheezing) and demonstration of reversible airway obstruction in lung function investigations
	PLATTS	Acute asthma (presenting at ER with breathlessness for which the physician on call prescribed urgent treatment for airway obstruction)
Physician diagnosis	NG	Episodic wheeze and asthmatic symptoms diagnosed as asthma in past year
	JEDRYC	Current treatment by medical doctor for bronchial asthma
	NHANES	Ever been told by a doctor that had asthma, still has asthma, and never had physician diagnosis of emphysema
Other/mixed	JANSON	Ever had asthma and had attack in last 12 months (JANSON2001); using current asthma medication or asthma attacks in last 12 months (SVANES2004)
	ORYSZC	Attending chest clinic and positive answer to 4 questions (ever had attacks of breathlessness at rest with wheezing; ever had asthma attacks; diagnosis confirmed by a doctor; had asthma attack in last 12 months), or positive answers to 2-3 of the questions and examination of medical records
	MISHRA	Asthma
	SAPALD	Ever had physician diagnosed asthma, and wheezing or usual cough in last 12 months

The references corresponding to the reference keys are given in Appendix A

Table 5 Other asthma outcomes for which results are available but which have not been entered on the relative risk database

Study Ref	Other asthma outcomes
LARSS1	Results available for ever had asthma (self defined), and for use of asthma medication
ROBBIN	Results also available for adult-onset asthma (GREER1993)
JANSON	Results also available for 3+ asthma symptoms (SVANES2004)
SAPALD	Results available for physician-diagnosed asthma or wheeze without cold in last 12 months (KUNZLI2000)

The references corresponding to the reference keys are given in Appendix A

Table 6   Subsets of the study population for which results are available but which have not been entered on the relative risk database

Study Ref	Subsets of the study population
LARSS1	Results with additional subjects with family history of asthma are also available, including results stratified by age (but lacking CIs)
NG	Results available for housewives (i.e. excluding subjects who might have workplace ETS exposure)
SAPALD	Results available excluding subjects whose mother ever smoked

Table 7   Number of relative risks per study

Study Type	Study Ref	Exposure type			
		Total ETS	Household	Workplace	Total
Case-control	JAAKK2	16	16	16	48
	ORYSZC	0	2	2	4
	PLATTS	1	0	0	1
	RAHERI[1]	2	0	0	2
	THORN	0	3	0	3
Prospective	BECKE2	4	0	0	4
	ROBBIN	10	2	2	14
Cross-sectional	JANSON	4	5	1	10
	JEDRYC	0	1	0	1
	KRONQV	1	1	1	3
	LARSS1	0	2	0	2
	LARSS2	0	1	4	5
	MISHRA	0	4	0	4
	NG	0	6	0	6
	NHANES	0	1	1	2
	PILOTT	0	1	0	1
	SAPALD	6	0	1	7

[1] subsidiary study

Table 8   Characteristics of the 117 relative risks

Characteristic	Level	Study Type				
		CC	Prosp	CrSec	Subsid	Total
Total		56	18	41	2	117
Sex	both	50	14	26	2	92
	male	3	2	4	0	9
	female	3	2	11	0	16
Time of asthma	lifetime	3	18	17	2	40
	current	53	0	24	0	77
Onset	No	56	2	41	2	101
	yes	0	16	0	0	16
Odds ratio (onset analysis)	No	-	2	-	-	2
	yes	-	14	-	-	14
Exposure type	Household	21	2	22	0	45
	Workplace	18	2	8	0	28
	Total	17	14	11	2	44
Household - who smoked	not applicable	35	16	19	2	72
	all	21	2	18	0	41
	mother	0	0	2	0	2
	father	0	0	2	0	2
Total - source	not applicable	39	4	30	0	73
	total NOS	1	0	1	2	4
	home and/or work	16	10	10	0	36
	serum cotinine	0	4	0	0	4
Exposure - when smoked	lifetime	30	5	6	0	41
	current (now)	22	4	27	0	53
	childhood (youth)	0	2	7	1	10
	adult	0	2	0	0	2
	recent years	3	0	0	0	3
	unspecified	1	0	1	1	3
	childhood but not adult	0	2	0	0	2
	adult but not childhood	0	2	0	0	2
	both adult and child	0	1	0	0	1
Dose-response	all (not dose response)	20	14	28	2	64
	level 1	12	0	4	0	16
	level 2	12	0	4	0	16
	level 3	6	0	2	0	8
	level 4	6	0	0	0	6
	per unit dose regression	0	4	0	0	4
	other	0	0	3	0	3

Table 8 (continued)

Characteristic	Level	Study Type				
		CC	Prosp	CrSec	Subsid	Total
Measure of exposure	yes/no	20	10	28	2	60
	cigarettes/day	12	0	4	0	16
	years	0	4	1	0	5
	pack-years	24	0	0	0	24
	hours/day	0	0	7	0	7
	persons	0	0	1	0	1
	ng/ml	0	4	0	0	4
Unexposed - time	non	56	13	41	2	112
	never	0	5	0	0	5
Unexposed - source	none (or low)	17	14	12	2	45
	none of type (as in EXPOS)	39	4	25	0	68
	not specified household member	0	0	4	0	4
N adjusted for	0	30	2	9	1	42
	2	2	0	0	0	2
	3	0	0	3	0	3
	4	0	13	3	0	16
	5	0	3	5	0	8
	6	0	0	7	0	7
	7	8	0	0	0	8
	8	16	0	6	0	22
	9	0	0	4	0	4
	10	0	0	2	1	3
	12	0	0	2	0	2
Adjusted for:	sex	24	12	22	1	59
	age	26	16	32	1	75
	race	0	2	3	0	5
	active smoking (never/ex)	0	12	0	0	12
Adjusted for other sources of ETS	None	40	17	26	2	85
	1	16	1	13	0	30
	2	0	0	2	0	2
Adjusted for other confounders	None	30	2	9	1	42
	1	2	0	2	0	4
	2	0	12	9	0	21
	3	0	4	0	0	4
	4	0	0	7	0	7
	5	24	0	0	0	24
	6	0	0	12	0	12
	8	0	0	0	1	1
	11	0	0	2	0	2

Table 8 (continued /2)

Characteristic	Level	Study Type				
		CC	Prosp	CrSec	Subsid	Total
Numbers of cases available (Unadjusted RRs)	no	1	0	0	0	1
	yes	29	2	9	1	41
Numbers of controls/at risk available (Unadjusted RRs)	no	1	0	0	1	2
	yes	29	2	9	0	40
Full 2 × 2 table available (Unadjusted RRs)	no	1	0	0	1	2
	yes	29	2	9	0	40
Numbers of cases available (Adjusted RRs)	no	2	14	22	1	39
	yes	24	2	10	0	36
Relative risk	0.01-1.00	17	10	19	1	47
	1.01-2.00	27	8	22	1	58
	2.01-4.00	10	0	0	0	10
	4.01+	2	0	0	0	2
	N	55	14	33	2	104
	Median	1.52	1.49	1.15	0.96	1.32
	Min	0.43	0.66	0.53	0.30	0.30
	Max	4.80	1.89	1.90	1.62	4.80
	Miss	1	4	8	0	13
CI available	no	1	4	8	0	13
	yes	55	14	33	2	104
Derivation of RR/CI	original	23	5	22	2	52
	RR/CI from numbers	24	2	8	0	34
	RR/CI recalc from numbers	2	0	0	0	2
	Sum over exposure levels	3	0	1	0	4
	non-significant	1	3	5	0	9
	significant	0	1	3	0	4
	F&L over exposure levels	3	7	2	0	12
discrepancy or alternative adjustment available	no	52	14	35	2	103
	yes	4	4	6	0	14

CC = case-control; Prosp = prospective; CrSec = Cross-sectional; Subsid = Subsidiary

Table 9   Relative risks characteristics available from the 16 principal studies (or their subsidiary)

Characteristic	Level	Study type			
		CC	Prosp	CrSec	Total
Total					
Single sex		2	1	4	7
Lifetime/incidence asthma		1	2	6	9
Current asthma		3	-	6	9
Onset analysis		-	2	-	2
Odds ratio for onset analysis		-	1	-	1
Exposure	Household	3	1	9	13
	Workplace	2	1	5	8
	Total	2	2	3	7
Household – who smoked	All	3	1	9	13
	Mother	0	0	1	1
	Father	0	0	1	1
Total - source	All	1	0	2	3
	Home and/or work	1	1	2	4
	Serum cotinine	0	1	0	1
Exposure – when smoked	Lifetime	1	1	1	3
	Current	2	1	7	10
	Adulthood	0	1	0	1
	Childhood	0	1	3	4
	Recent years	1	0	0	1
	Unspecified	1	0	2	3
	Joint exposures Adult × Child	0	1	0	1
Dose response data		1	0	3	4
Measure of exposure	Yes/No	4	1	10	15
	Cigarettes/day	1	0	1	2
	Years	0	1	1	2
	Pack-years	1	0	0	1
	Hours/day	0	0	3	3
	Persons	0	0	1	1
	ng/ml	0	1	0	1
Unexposed - time	Non	4	2	10	16
	Never	0	1	0	1
Unexposed - source	None (or low)	2	2	3	7
	None of type	3	1	9	13
	Not specific household member	0	0	1	1

Table 9 (continued)

Characteristic	Level	Study type			
		CC	Prosp	CrSec	Total
Adjustment for :	sex	1	2	6	9
	age	2	2	9	13
	race	0	1	1	2
	active smoking (never/ex)	0	1	0	0
	other ETS exposure	1	1	2	4
	other non-ETS variables	2	2	9	13
	any adjustment	2	2	9	13
	no adjustment	4	1	6	11
Number of cases available		3	1	6	10
RR available		3	2	9	14
CI available		3	2	9	14
Derivation of RR/CI	original	2	2	8	12
	from numbers	3	1	5	9
	recalculated	1	0	0	1
	summed levels	1	0	1	2
	significant/non-significant	1	1	3	5
	F&L	1	1	2	4
Discrepancy or alternative adjustment available		1	1	3	5

CC = case-control; Prosp = prospective; CrSec = Cross-sectional

Table 10   Other dose-response results

Study	Asthma	Sex	Exposure	Adjusted	Results
SAPALD	lifetime	both	home / work	yes	Hours per day, significant p=0.0081
SAPALD	lifetime	both	home / work	yes	Number of smokers, significant p=0.028
					(Hours per day × number of smokers also shown graphically without CI)
SAPALD	lifetime	both	home / work	yes	Years, significant p=0.0246
ROBBIN	incidence	male	workplace	yes	At 1992 follow-up: years worked with smoker, not significant, excluded from final MLR model; mean 11.3 (cases), 7.8 (non-cases) p=0.162. Alternative (to 1987 follow-up) RR per 10 years worked with smoker is 1.50 (1.12-2.01)
ROBBIN	incidence	female	workplace	yes	At 1992 follow-up: RR per 7 years worked with smoker is 1.21 (1.04-1.39); mean 7.4 (cases), 4.6 (non-cases) p=0.023. Alternative (to 1987 follow-up) RR per 10 years worked with smoker is 1.50 (1.17-1.92)
ROBBIN	incidence	male	household	yes	At 1992 follow-up: years lived with smoker, not significant, excluded from final MLR model; mean 13.5 (cases), 7.7 (non-cases) p=0.039. Also excluded from final MLR model for 1987 follow-up.
ROBBIN	incidence	female	household	yes	At 1992 follow-up: years lived with smoker, not significant, excluded from final MLR model; mean14.0 (cases), 11.9 (non-cases) p=0.254. Also excluded from final MLR model for 1987 follow-up.

Table F1 -

IASTAD - Meta-analysis of Biochemical/Total/Household/Workplace Exposure (preferring earliest)
Lifetime/Current Asthma

This analysis is restricted to results for:
1) Biochemical, total, household (overall), parental, or workplace exposure
2) Results not by amount of exposure
3) Results complete enough for use in metaanalysis

Within each study, results are then selected (in the following order of preference, within each sex) for:
4) ASTHMA : lifetime, current
5) EXPOS   : biochemical (cotinine), total, household, workplace
6) WHESMO : 3=childhood, 1=lifetime, 10=adult, 7=recent, 6=unspec, 2=current
7) WHOHOU : household overall, mother
8) UNEXTI : unexposed Overall never, non (i.e. not at time defined for exposed Overall)
9) For overlapping studies: principal rather than subsidiary studies
Finally for single sex results (m, f) in preference to results for both sexes combined (b).

Results adjusted for the most potential confounders are then chosen in Section -3
and results adjusted for the least confounders in Section -6. (See corresponding table in Appendix F
for additional output including Random model and Sections -1, -2, -4, -5 and -7)

Table F1 - 3

IASTAD - Meta-analysis of Biochemical/Total/Household/Workplace Exposure (preferring earliest)
Lifetime/Current Asthma
Adjusted

Overall

N	18
NS	14
Wt	671.57
Het Chi	37.20
Het df	17
Het P	**
Fixed RR	1.14
RRl	1.06
RRu	1.23
P	+++
Random RR	1.19
RRl	1.04
RRu	1.35
P	+
Asymm P	N.S.

Sex

	both	male	female	Total
N	10	3	5	18
Het P	*	*	N.S.	**
Fixed RR	1.17	1.28	1.05	1.14
RRl	1.05	1.06	0.92	1.06
RRu	1.30	1.55	1.20	1.23
P	++	++	N.S.	+++
Between P				N.S.

Asthma definition (lifetime/current)

	lifetime	current	Total
N	9	9	18
Het P	***	N.S.	**
Fixed RR	1.20	1.12	1.14
RRl	1.06	1.02	1.06
RRu	1.36	1.22	1.23
P	++	+	+++
Between P			N.S.

Continent

	NAmer	Europe	Oth/Mult	Total
N	4	9	5	18
Het P	(*)	*	N.S.	**
Fixed RR	0.99	1.40	1.11	1.14
RRl	0.84	1.21	1.00	1.06
RRu	1.16	1.63	1.23	1.23
P	N.S.	+++	(+)	+++
Between P				**

Start year of study

	<1990	1990-99	unknown	Total
N	4	10	4	18
Het P	(*)	*	N.S.	**
Fixed RR	0.99	1.21	0.89	1.14
RRl	0.84	1.11	0.57	1.06
RRu	1.16	1.32	1.40	1.23
P	N.S.	+++	N.S.	+++
Between P				(*)

Publication year

	1990-99	2000+	Total
N	5	13	18
Het P	N.S.	**	**
Fixed RR	1.26	1.13	1.14
RRl	1.02	1.04	1.06
RRu	1.55	1.22	1.23
P	+	++	+++
Between P			N.S.

Study type

	CC	Pr	CS	Total
N	5	3	10	18
Het P	N.S.	*	N.S.	**
Fixed RR	1.56	0.93	1.15	1.14
RRl	1.19	0.76	1.06	1.06
RRu	2.05	1.13	1.26	1.23
P	++	N.S.	++	+++
Between P				**

Table F1 - 3

IASTAD - Meta-analysis of Biochemical/Total/Household/Workplace Exposure (preferring earliest)
Lifetime/Current Asthma
Adjusted

```
            Ex smokers
            excluded included   Total
      N        13        5        18
Het  P          *       (*)       **
Fixed RR      1.20     1.00      1.14
      RRl     1.10     0.86      1.06
      RRu     1.31     1.16      1.23
      P        +++     N.S.      +++
Between P                         *
```

```
            Lowest age in RR
            15-19    20-25    60+     Total
      N        7        8        3        18
Het  P         **      N.S.    N.S.      **
Fixed RR      1.12     1.38     1.08     1.14
      RRl     0.99     1.15     0.97     1.06
      RRu     1.27     1.66     1.21     1.23
      P        (+)      +++     N.S.     +++
Between P                                (*)
```

```
            Highest age in RR
             -55     60-69    70+     Total
      N        7        4        7        18
Het  P         **      N.S.    N.S.      **
Fixed RR      1.02     1.41     1.10     1.14
      RRl     0.86     1.20     1.00     1.06
      RRu     1.20     1.66     1.22     1.23
      P       N.S.      +++      +       +++
Between P                                 *
```

```
            Physician diagnosis
            yes   no/mixed   Total
      N       11       7        18
Het  P       ***      N.S.      **
Fixed RR    1.17     1.12      1.14
      RRl    1.05     1.01      1.06
      RRu    1.31     1.24      1.23
      P        ++       +       +++
Between P                      N.S.
```

```
            Onset (prosp or CC)
            prev    onset    Total
      N       15       3        18
Het  P        **      N.S.      **
Fixed RR    1.13     1.21      1.14
      RRl    1.05     0.98      1.06
      RRu    1.23     1.49      1.23
      P        ++      (+)      +++
Between P                      N.S.
```

```
                  Number of cases
            1-100  101-400   401+   unknown    Total
      N       7       3        5        3        18
Het  P        *      N.S.     N.S.     N.S.      **
Fixed RR    1.40     1.50     1.05     1.13      1.14
      RRl    1.05     1.25     0.95     0.92      1.06
      RRu    1.86     1.81     1.15     1.40      1.23
      P        +       +++     N.S.     N.S.      +++
Between P                                         **
```

```
            Study adjusts for or is matched on sex
            Yes      No      Total
      N        9       9        18
Het  P        **       *        **
Fixed RR    1.18     1.12      1.14
      RRl    1.05     1.01      1.06
      RRu    1.32     1.24      1.23
      P        ++       +       +++
Between P                      N.S.
```

```
                             Table F1 - 3

 IASTAD - Meta-analysis of Biochemical/Total/Household/Workplace Exposure (preferring earliest)
                          Lifetime/Current Asthma
                                 Adjusted
              Study adjusts for or is matched on age
                      Yes       No      Total
           N          15         3        18
   Het  P            ***      N.S.       **
 Fixed  RR          1.15      1.11      1.14
        RRl         1.06      0.86      1.06
        RRu         1.24      1.42      1.23
        P            +++     N.S.       +++
Between  P                               N.S.


              Study adjusts for race
           N           3        15        18
   Het  P           N.S.        *        **
 Fixed  RR          0.86      1.19      1.14
        RRl         0.70      1.10      1.06
        RRu         1.06      1.30      1.23
        P           N.S.      +++       +++
Between  P                               **


              Study adjusts for location
           N          10         8        18
   Het  P           N.S.       **        **
 Fixed  RR          1.09      1.35      1.14
        RRl         1.00      1.15      1.06
        RRu         1.19      1.58      1.23
        P             +       +++       +++
Between  P                                *


              Study adjusts for SES
           N           2        16        18
   Het  P           N.S.       **        **
 Fixed  RR          1.10      1.18      1.14
        RRl         0.98      1.07      1.06
        RRu         1.23      1.30      1.23
        P           N.S.       ++       +++
Between  P                               N.S.


              Study adjusts for family medical history
           N           3        15        18
   Het  P           N.S.       **        **
 Fixed  RR          1.31      1.11      1.14
        RRl         1.09      1.03      1.06
        RRu         1.58      1.21      1.23
        P            ++         +       +++
Between  P                               N.S.


              Study adjusts for family composition
                      Yes       No      Total
           N           3        15        18
   Het  P           N.S.       **        **
 Fixed  RR          1.11      1.18      1.14
        RRl         0.99      1.06      1.06
        RRu         1.23      1.31      1.23
        P            (+)       ++       +++
Between  P                               N.S.


              Study adjusts for cooking, heating
           N           4        14        18
   Het  P           N.S.       **        **
 Fixed  RR          1.09      1.20      1.14
        RRl         0.97      1.08      1.06
        RRu         1.21      1.32      1.23
        P           N.S.      +++       +++
Between  P                               N.S.


              Study adjusts for housing quality, crowding, damp, mould
           N           4        14        18
   Het  P           N.S.       **        **
 Fixed  RR          1.13      1.16      1.14
        RRl         1.01      1.04      1.06
        RRu         1.26      1.29      1.23
        P             +        ++       +++
Between  P                               N.S.
```

```
                              Table F1 - 3

IASTAD - Meta-analysis of Biochemical/Total/Household/Workplace Exposure (preferring earliest)
                          Lifetime/Current Asthma
                                 Adjusted

              Study adjusts for subject's medical history
                       Yes        No      Total
            N           5         13        18
      Het  P          (*)          *        **
    Fixed  RR        1.41       1.10      1.14
           RRl       1.17       1.01      1.06
           RRu       1.69       1.19      1.23
           P          +++         +        +++
  Between  P                              *


              Study adjusts for ex-smoking or other ETS exposure
            N           4         14        18
      Het  P         N.S.         **        **
    Fixed  RR        1.26       1.12      1.14
           RRl       1.05       1.03      1.06
           RRu       1.51       1.22      1.23
           P           +         ++        +++
  Between  P                              N.S.


                          Exposure
                     Hh     Hh,Wk      Cot      Work     Total
            N        11         4        2         1        18
      Het  P          *      N.S.     N.S.      N.S.        **
    Fixed  RR      1.16      1.34     0.84      1.13      1.14
           RRl     1.05      1.13     0.67      0.80      1.06
           RRu     1.27      1.59     1.04      1.59      1.23
           P         ++       +++     N.S.      N.S.       +++
  Between  P                                              *


                  Exposed Overall : when Exposed
                  life     adult    child   current   unspec    Total
            N        2         2        2        11        1        18
      Het  P       N.S.        *     N.S.      N.S.     N.S.        **
    Fixed  RR      1.36      2.31     1.73      1.07     1.09      1.14
           RRl     1.00      1.35     1.30      0.99     0.65      1.06
           RRu     1.85      3.96     2.31      1.17     1.82      1.23
           P        (+)       ++      +++       (+)     N.S.       +++
  Between  P                                                      **


                  Number of adjustment variables
                     0         2       3-5       6-9      10+     Total
            N        3         2        7         4        2        18
      Het  P       N.S.        *       **      N.S.     N.S.        **
    Fixed  RR      1.11      2.31     1.07      1.30     1.10      1.14
           RRl     0.86      1.35     0.93      1.09     0.98      1.06
           RRu     1.42      3.96     1.24      1.55     1.23      1.23
           P       N.S.       ++     N.S.        ++     N.S.       +++
  Between  P                                                      *


                  RR adjusted for sex
                       Yes        No      Total
            N           9          9        18
      Het  P          **          *         **
    Fixed  RR        1.18       1.12      1.14
           RRl       1.05       1.01      1.06
           RRu       1.32       1.24      1.23
           P          ++          +        +++
  Between  P                              N.S.


                  RR adjusted for age
            N          15          3        18
      Het  P         ***        N.S.        **
    Fixed  RR        1.15       1.11      1.14
           RRl       1.06       0.86      1.06
           RRu       1.24       1.42      1.23
           P         +++        N.S.       +++
  Between  P                              N.S.

                  RR adjusted for ex-smoking or other ETS
                       Yes        No      Total
            N           3         15        18
      Het  P         N.S.        **         **
    Fixed  RR        1.21       1.13      1.14
           RRl       0.98       1.05      1.06
           RRu       1.49       1.23      1.23
           P         (+)        ++        +++
  Between  P                              N.S.
```

```
                              Table F1 - 3

IASTAD - Meta-analysis of Biochemical/Total/Household/Workplace Exposure (preferring earliest)
                         Lifetime/Current Asthma
                                Adjusted

              RR adjusted for factor other than sex, age, other ETS
                       Yes        No     Total
              N        15         3        18
      Het  P           ***       N.S.      **
      Fixed RR        1.15       1.11     1.14
            RRl       1.06       0.86     1.06
            RRu       1.24       1.42     1.23
            P          +++       N.S.     +++
      Between P                           N.S.


                         Derivation of RR/CI
                   Original  Numbers  Sum/F&L    Total
              N        11        3        4        18
      Het  P           ***      N.S.     N.S.      **
      Fixed RR        1.12      1.11     1.30     1.14
            RRl       1.03      0.86     1.06     1.06
            RRu       1.22      1.42     1.60     1.23
            P          ++       N.S.      +       +++
      Between P                                   N.S.
```

Table F1 - 6

IASTAD - Meta-analysis of Biochemical/Total/Household/Workplace Exposure (preferring earliest)
Lifetime/Current Asthma
Unadjusted

```
                    Overall
            N        17
           NS        14
           Wt    882.55
      Het Chi     34.66
      Het  df        16
      Het   P        **
   Fixed  RR      1.16
          RRl     1.08
          RRu     1.24
            P      +++
  Random  RR      1.17
          RRl     1.04
          RRu     1.32
            P       ++
    Asymm  P      N.S.
```

```
                    Sex
             both    male   female    Total
        N      11       2        4       17
  Het   P      **     N.S.     N.S.      **
Fixed  RR    1.16    1.34     1.07     1.16
       RRl   1.05    1.15     0.96     1.08
       RRu   1.28    1.56     1.19     1.24
         P     ++     +++     N.S.      +++
Between P                               (*)
```

```
            Asthma definition (lifetime/current)
          lifetime  current    Total
        N        8        9       17
  Het   P      ***     N.S.       **
Fixed  RR     1.18     1.15     1.16
       RRl    1.04     1.06     1.08
       RRu    1.33     1.24     1.24
         P      ++      +++      +++
Between P                       N.S.
```

```
                    Continent
          NAmer   Europe Oth/Mult    Total
        N     4        8        5       17
  Het   P    (*)        *     N.S.       **
Fixed  RR  1.00     1.30     1.16     1.16
       RRl 0.85     1.13     1.07     1.08
       RRu 1.16     1.50     1.27     1.24
         P N.S.      +++      +++      +++
Between P                                *
```

```
            Start year of study
          <1990  1990-99  unknown    Total
        N     4        9        4       17
  Het   P    (*)        *     N.S.       **
Fixed  RR  1.00     1.21     0.88     1.16
       RRl 0.85     1.12     0.57     1.08
       RRu 1.16     1.30     1.38     1.24
         P N.S.      +++     N.S.      +++
Between P                                *
```

```
            Study type
            CC       Pr       CS    Total
        N     4        3       10       17
  Het   P  N.S.        *      (*)       **
Fixed  RR  1.39     0.94     1.18     1.16
       RRl 1.07     0.77     1.09     1.08
       RRu 1.79     1.14     1.26     1.24
         P    +     N.S.      +++      +++
Between P                                *
```

```
            Ex smokers
          excluded included    Total
        N      12        5       17
  Het   P       *     N.S.       **
Fixed  RR    1.20     1.00     1.16
       RRl   1.11     0.86     1.08
       RRu   1.29     1.16     1.24
         P    +++     N.S.      +++
Between P                         *
```

Table F2 -

IASTAD - Meta-analysis of Biochemical/Total/Household/Workplace (preferring earliest) - Ex-smokers excluded
Lifetime/Current Asthma

This analysis is restricted to results for:
1) Biochemical, total, household (overall), parental, or workplace exposure
2) Ex-smokers excluded
3) Results not by amount of exposure
4) Results complete enough for use in metaanalysis

Within each study, results are then selected (in the following order of preference, within each sex) for:
5) ASTHMA : lifetime, current
6) EXPOS   : biochemical (cotinine), total, household, workplace
7) WHESMO : 3=childhood, 1=lifetime, 10=adult, 7=recent, 6=unspec, 2=current
8) WHOHOU : household overall, mother
9) UNEXTI : unexposed Overall never, non (i.e. not at time defined for exposed Overall)
10) For overlapping studies: principal rather than subsidiary studies
Finally for single sex results (m, f) in preference to results for both sexes combined (b).

Results adjusted for the most potential confounders are then chosen in Section -3
and results adjusted for the least confounders in Section -6. (See corresponding table in Appendix F
for additional output including Random model and Sections -1, -2, -4, -5 and -7)

Table F2 - 3

IASTAD - Meta-analysis of Biochemical/Total/Household/Workplace (preferring earliest) - Ex-smokers excluded
Lifetime/Current Asthma
Adjusted

	Overall
N	13
NS	10
Wt	503.93
Het Chi	25.13
Het df	12
Het P	*
Fixed RR	1.20
RRl	1.10
RRu	1.31
P	+++
Random RR	1.27
RRl	1.09
RRu	1.49
P	++
Asymm P	N.S.

Sex

	both	male	female	Total
N	5	3	5	13
Het P	N.S.	*	N.S.	*
Fixed RR	1.35	1.28	1.05	1.20
RRl	1.17	1.06	0.92	1.10
RRu	1.56	1.55	1.20	1.31
P	+++	++	N.S.	+++
Between P				*

Asthma definition (lifetime/current)

	lifetime	current	Total
N	5	8	13
Het P	*	N.S.	*
Fixed RR	1.49	1.12	1.20
RRl	1.25	1.01	1.10
RRu	1.78	1.23	1.31
P	+++	+	+++
Between P			**

Continent

	NAmer	Europe	Oth/Mult	Total
N		9	4	13
Het P		*	N.S.	*
Fixed RR		1.40	1.11	1.20
RRl		1.21	1.00	1.10
RRu		1.63	1.23	1.31
P		+++	(+)	+++
Between P				*

Start year of study

	<1990	1990-99	unknown	Total
N		9	4	13
Het P		**	N.S.	*
Fixed RR		1.21	0.89	1.20
RRl		1.11	0.57	1.10
RRu		1.32	1.40	1.31
P		+++	N.S.	+++
Between P				N.S.

Study type

	CC	Pr	CS	Total
N	5		8	13
Het P	N.S.		(*)	*
Fixed RR	1.56		1.16	1.20
RRl	1.19		1.06	1.10
RRu	2.05		1.27	1.31
P	++		++	+++
Between P				*

Table F2 - 3

Table F2 - 6

IASTAD - Meta-analysis of Biochemical/Total/Household/Workplace (preferring earliest) - Ex-smokers excluded
Lifetime/Current Asthma
Unadjusted

Overall

N	12
NS	10
Wt	709.28
Het Chi	22.68
Het df	11
Het P	*
Fixed RR	1.20
RRl	1.11
RRu	1.29
P	+++
Random RR	1.24
RRl	1.09
RRu	1.42
P	++
Asymm P	N.S.

Sex

	both	male	female	Total
N	6	2	4	12
Het P	*	N.S.	N.S.	*
Fixed RR	1.31	1.34	1.07	1.20
RRl	1.14	1.15	0.96	1.11
RRu	1.49	1.56	1.19	1.29
P	+++	+++	N.S.	+++
Between P				*

Asthma definition (lifetime/current)

	lifetime	current	Total
N	4	8	12
Het P	*	N.S.	*
Fixed RR	1.40	1.16	1.20
RRl	1.18	1.06	1.11
RRu	1.65	1.25	1.29
P	+++	+++	+++
Between P			*

Continent

	NAmer	Europe	Oth/Mult	Total
N		8	4	12
Het P		*	N.S.	*
Fixed RR		1.30	1.17	1.20
RRl		1.13	1.07	1.11
RRu		1.50	1.27	1.29
P		+++	+++	+++
Between P				N.S.

Start year of study

	<1990	1990-99	unknown	Total
N		8	4	12
Het P		*	N.S.	*
Fixed RR		1.21	0.88	1.20
RRl		1.12	0.57	1.11
RRu		1.30	1.38	1.29
P		+++	N.S.	+++
Between P				N.S.

Study type

	CC	Pr	CS	Total
N	4		8	12
Het P	N.S.		*	*
Fixed RR	1.39		1.18	1.20
RRl	1.07		1.10	1.11
RRu	1.79		1.28	1.29
P	+		+++	+++
Between P				N.S.

Table F3 -

IASTAD - Meta-analysis of Biochemical/Total/Household/Workplace Exposure (preferring most recent)
Lifetime/Current Asthma

This analysis is restricted to results for:
1) Biochemical, total, household (overall), parental, or workplace exposure
2) Results not by amount of exposure
3) Results complete enough for use in metaanalysis

Within each study, results are then selected (in the following order of preference, within each sex) for:
4) ASTHMA : lifetime, current
5) EXPOS   : biochemical (cotinine), total, household, workplace
6) WHESMO : 2=current, 7=recent, 6=unspec, 10=adult, 1=lifetime, 3=childhood
7) WHOHOU : household overall, mother
8) UNEXTI : unexposed Overall never, non (i.e. not at time defined for exposed Overall)
9) For overlapping studies: principal rather than subsidiary studies
Finally for single sex results (m, f) in preference to results for both sexes combined (b).

Results adjusted for the most potential confounders are then chosen in Section -3. (See corresponding table in
Appendix F for additional output including factors and Sections -1, -2, -4, -5, -6 and -7)

Table F3 - 3

IASTAD - Meta-analysis of Biochemical/Total/Household/Workplace Exposure (preferring most recent)
Lifetime/Current Asthma
Adjusted

		Overall
	N	18
	NS	14
	Wt	655.68
Het	Chi	42.09
Het	df	17
Het	P	***
Fixed	RR	1.15
	RRl	1.07
	RRu	1.24
	P	+++
Random	RR	1.21
	RRl	1.05
	RRu	1.40
	P	++
Asymm	P	N.S.

Table F4 -

IASTAD - Meta-analysis of Total/Household/Workplace Exposure in Childhood
Lifetime/Current Asthma

This analysis is restricted to results for:
1) Total, household (overall), parental, or workplace exposure
2) Childhood exposure
3) Results not by amount of exposure
4) Results complete enough for use in metaanalysis

Within each study, results are then selected (in the following order of preference, within each sex) for:
5) ASTHMA : lifetime, current
6) EXPOS   : biochemical (cotinine), total, household, workplace
7) WHOHOU : household overall, mother
8) UNEXTI : unexposed Overall never, non (i.e. not at time defined for exposed Overall)
9) For overlapping studies: principal rather than subsidiary studies
Finally for single sex results (m, f) in preference to results for both sexes combined (b).

Results adjusted for the most potential confounders are then chosen in Section -3
and results adjusted for the least confounders in Section -6. (See corresponding table in Appendix F
for additional output including Random model and Sections -1, -2, -4, -5 and -7)

Table F4 - 3

IASTAD - Meta-analysis of Total/Household/Workplace Exposure in Childhood
Lifetime/Current Asthma
Adjusted

	Overall
N	4
NS	3
Wt	102.26
Het Chi	10.01
Het df	3
Het P	*
Fixed RR	1.27
RRl	1.04
RRu	1.54
P	+
Random RR	1.26
RRl	0.88
RRu	1.81
P	N.S.
Asymm P	N.S.

Sex

	both	male	female	Total
N	2	1	1	4
Het P	N.S.	N.S.	N.S.	*
Fixed RR	1.73	0.81	1.10	1.27
RRl	1.30	0.54	0.78	1.04
RRu	2.31	1.22	1.55	1.54
P	+++	N.S.	N.S.	+
Between P				**

Asthma definition (lifetime/current)

	lifetime	current	Total
N	2	2	4
Het P	N.S.	N.S.	*
Fixed RR	1.73	0.97	1.27
RRl	1.30	0.75	1.04
RRu	2.31	1.26	1.54
P	+++	N.S.	+
Between P			**

Continent

	NAmer	Europe	Oth/Mult	Total
N	1	1	2	4
Het P	N.S.	N.S.	N.S.	*
Fixed RR	1.57	1.82	0.97	1.27
RRl	0.96	1.28	0.75	1.04
RRu	2.57	2.58	1.26	1.54
P	(+)	+++	N.S.	+
Between P				*

Start year of study

	<1990	1990-99	unknown	Total
N	1	3		4
Het P	N.S.	*		*
Fixed RR	1.57	1.22		1.27
RRl	0.96	0.99		1.04
RRu	2.57	1.50		1.54
P	(+)	(+)		+
Between P				N.S.

Study type

	CC	Pr	CS	Total
N		1	3	4
Het P		N.S.	*	*
Fixed RR		1.57	1.22	1.27
RRl		0.96	0.99	1.04
RRu		2.57	1.50	1.54
P		(+)	(+)	+
Between P				N.S.

Ex smokers

	excluded	included	Total
N	3	1	4
Het P	*	N.S.	*
Fixed RR	1.22	1.57	1.27
RRl	0.99	0.96	1.04
RRu	1.50	2.57	1.54
P	(+)	(+)	+
Between P			N.S.

Table F4 - 6

IASTAD - Meta-analysis of Total/Household/Workplace Exposure in Childhood
Lifetime/Current Asthma
Unadjusted

Overall

N	4
NS	3
Wt	103.72
Het Chi	10.46
Het df	3
Het P	*
Fixed RR	1.28
RRl	1.05
RRu	1.55
P	+
Random RR	1.27
RRl	0.88
RRu	1.83
P	N.S.
Asymm P	N.S.

Sex

	both	male	female	Total
N	2	1	1	4
Het P	N.S.	N.S.	N.S.	*
Fixed RR	1.75	0.81	1.10	1.28
RRl	1.32	0.54	0.78	1.05
RRu	2.32	1.22	1.55	1.55
P	+++	N.S.	N.S.	+
Between P				**

Asthma definition (lifetime/current)

	lifetime	current	Total
N	2	2	4
Het P	N.S.	N.S.	*
Fixed RR	1.75	0.97	1.28
RRl	1.32	0.75	1.05
RRu	2.32	1.26	1.55
P	+++	N.S.	+
Between P			**

Continent

	NAmer	Europe	Oth/Mult	Total
N	1	1	2	4
Het P	N.S.	N.S.	N.S.	*
Fixed RR	1.57	1.84	0.97	1.28
RRl	0.96	1.31	0.75	1.05
RRu	2.57	2.59	1.26	1.55
P	(+)	+++	N.S.	+
Between P				*

Start year of study

	<1990	1990-99	unknown	Total
N	1	3		4
Het P	N.S.	**		*
Fixed RR	1.57	1.23		1.28
RRl	0.96	1.00		1.05
RRu	2.57	1.52		1.55
P	(+)	(+)		+
Between P				N.S.

Study type

	CC	Pr	CS	Total
N		1	3	4
Het P		N.S.	**	*
Fixed RR		1.57	1.23	1.28
RRl		0.96	1.00	1.05
RRu		2.57	1.52	1.55
P		(+)	(+)	+
Between P				N.S.

Ex smokers

	excluded	included	Total
N	3	1	4
Het P	**	N.S.	*
Fixed RR	1.23	1.57	1.28
RRl	1.00	0.96	1.05
RRu	1.52	2.57	1.55
P	(+)	(+)	+
Between P			N.S.

Table F5 -

IASTAD - Meta-analysis of Total/Household/Workplace Exposure in Childhood (preferring father)
Lifetime/Current Asthma

This analysis is restricted to results for:
1) Total, household (overall), parental, or workplace exposure
2) Childhood exposure
3) Results not by amount of exposure
4) Results complete enough for use in metaanalysis

Within each study, results are then selected (in the following order of preference, within each sex) for:
5) ASTHMA : lifetime, current
6) EXPOS   : biochemical (cotinine), total, household, workplace
7) WHOHOU : household overall, father
8) UNEXTI : unexposed Overall never, non (i.e. not at time defined for exposed Overall)
9) For overlapping studies: principal rather than subsidiary studies
Finally for single sex results (m, f) in preference to results for both sexes combined (b).

Results adjusted for the most potential confounders are then chosen in Section -3. (See corresponding table in
Appendix F for additional output including factors and Sections -1, -2, -4, -5, -6 and -7)

Table F5 - 3

IASTAD - Meta-analysis of Total/Household/Workplace Exposure in Childhood (preferring father)
Lifetime/Current Asthma
Adjusted

		Overall
	N	4
	NS	3
	Wt	117.90
Het	Chi	19.78
Het	df	3
Het	P	***
Fixed	RR	1.11
	RRl	0.93
	RRu	1.33
	P	N.S.
Random	RR	1.18
	RRl	0.74
	RRu	1.90
	P	N.S.
Asymm	P	N.S.

Table F6 -

IASTAD - Meta-analysis of Biochemical/Total/Household/Workplace (preferring earliest, and preferring current asthma)
Current/Lifetime Asthma

This analysis is restricted to results for:
1) Biochemical, total, household (overall), parental, or workplace exposure
2) Results not by amount of exposure
3) Results complete enough for use in metaanalysis

Within each study, results are then selected (in the following order of preference, within each sex) for:
4) ASTHMA : current, lifetime
5) EXPOS   : biochemical (cotinine), total, household, workplace
6) WHESMO : 3=childhood, 1=lifetime, 10=adult, 7=recent, 6=unspec, 2=current
7) WHOHOU : household overall, mother
8) UNEXTI : unexposed Overall never, non (i.e. not at time defined for exposed Overall)
9) For overlapping studies: principal rather than subsidiary studies
Finally for single sex results (m, f) in preference to results for both sexes combined (b).

Results adjusted for the most potential confounders are then chosen in Section -3. (See corresponding table in
Appendix F for additional output including factors and Sections -1, -2, -4, -5, -6 and -7)

Table F6 - 3

IASTAD - Meta-analysis of Biochemical/Total/Household/Workplace (preferring earliest, and preferring current asthma)
Current/Lifetime Asthma
Adjusted

		Overall
	N	18
	NS	14
	Wt	652.19
Het	Chi	38.63
Het	df	17
Het	P	**
Fixed	RR	1.14
	RRl	1.06
	RRu	1.24
	P	+++
Random	RR	1.20
	RRl	1.04
	RRu	1.37
	P	++
Asymm	P	N.S.

Table F7 -

IASTAD - Meta-analysis of Household exposure (preferring earliest)
Lifetime/Current Asthma

This analysis is restricted to results for:
1) Household (overall) or parental exposure
2) Results not by amount of exposure
3) Results complete enough for use in metaanalysis

Within each study, results are then selected (in the following order of preference, within each sex) for:
4) ASTHMA : lifetime, current
5) WHESMO : 3=childhood, 1=lifetime, 10=adult, 7=recent, 6=unspec, 2=current
6) WHOHOU : household overall, mother
7) UNEXTI : unexposed Overall never, non (i.e. not at time defined for exposed Overall)
8) For overlapping studies: principal rather than subsidiary studies
Finally for single sex results (m, f) in preference to results for both sexes combined (b).

Results adjusted for the most potential confounders are then chosen in Section -3
and results adjusted for the least confounders in Section -6. (See corresponding table in Appendix F
for additional output including Random model and Sections -1, -2, -4, -5 and -7)

Table F7 - 3

IASTAD - Meta-analysis of Household exposure (preferring earliest)
Lifetime/Current Asthma
Adjusted

Overall

N	14
NS	10
Wt	513.05
Het Chi	25.99
Het df	13
Het P	*
Fixed RR	1.13
RRl	1.04
RRu	1.23
P	++
Random RR	1.16
RRl	1.00
RRu	1.35
P	+
Asymm P	N.S.

Sex

	both	male	female	Total
N	4	4	6	14
Het P	N.S.	**	N.S.	*
Fixed RR	1.24	1.18	1.05	1.13
RRl	1.04	1.00	0.93	1.04
RRu	1.46	1.41	1.19	1.23
P	+	(+)	N.S.	++
Between P				N.S.

Asthma definition (lifetime/current)

	lifetime	current	Total
N	4	10	14
Het P	*	N.S.	*
Fixed RR	1.69	1.07	1.13
RRl	1.31	0.98	1.04
RRu	2.19	1.18	1.23
P	+++	N.S.	++
Between P			***

Continent

	NAmer	Europe	Oth/Mult	Total
N	1	7	6	14
Het P	N.S.	**	N.S.	*
Fixed RR	1.11	1.39	1.08	1.13
RRl	0.85	1.13	0.98	1.04
RRu	1.44	1.71	1.20	1.23
P	N.S.	++	N.S.	++
Between P				(*)

Start year of study

	<1990	1990-99	unknown	Total
N	1	9	4	14
Het P	N.S.	**	N.S.	*
Fixed RR	1.11	1.15	0.89	1.13
RRl	0.85	1.04	0.57	1.04
RRu	1.44	1.26	1.40	1.23
P	N.S.	++	N.S.	++
Between P				N.S.

Study type

	CC	Pr	CS	Total
N	5		9	14
Het P	*		(*)	*
Fixed RR	1.33		1.11	1.13
RRl	1.01		1.01	1.04
RRu	1.75		1.22	1.23
P	+		+	++
Between P				N.S.

Ex smokers

	excluded	included	Total
N	12	2	14
Het P	**	N.S.	*
Fixed RR	1.14	1.10	1.13
RRl	1.04	0.87	1.04
RRu	1.25	1.39	1.23
P	++	N.S.	++
Between P			N.S.

Table F7 - 6

IASTAD - Meta-analysis of Household exposure (preferring earliest)
Lifetime/Current Asthma
Unadjusted

Overall

N	13
NS	10
Wt	704.11
Het Chi	26.81
Het df	12
Het P	**
Fixed RR	1.17
RRl	1.09
RRu	1.26
P	+++
Random RR	1.18
RRl	1.02
RRu	1.37
P	+
Asymm P	N.S.

Sex

	both	male	female	Total
N	5	3	5	13
Het P	*	(*)	N.S.	**
Fixed RR	1.31	1.26	1.07	1.17
RRl	1.12	1.10	0.97	1.09
RRu	1.53	1.46	1.19	1.26
P	+++	++	N.S.	+++
Between P				(*)

Asthma definition (lifetime/current)

	lifetime	current	Total
N	3	10	13
Het P	(*)	N.S.	**
Fixed RR	1.73	1.13	1.17
RRl	1.35	1.04	1.09
RRu	2.22	1.22	1.26
P	+++	++	+++
Between P			**

Continent

	NAmer	Europe	Oth/Mult	Total
N	1	6	6	13
Het P	N.S.	**	N.S.	**
Fixed RR	1.11	1.38	1.14	1.17
RRl	0.85	1.13	1.05	1.09
RRu	1.44	1.69	1.24	1.26
P	N.S.	++	++	+++
Between P				N.S.

Start year of study

	<1990	1990-99	unknown	Total
N	1	8	4	13
Het P	N.S.	**	N.S.	**
Fixed RR	1.11	1.19	0.88	1.17
RRl	0.85	1.10	0.57	1.09
RRu	1.44	1.28	1.38	1.26
P	N.S.	+++	N.S.	+++
Between P				N.S.

Study type

	CC	Pr	CS	Total
N	4		9	13
Het P	(*)		*	**
Fixed RR	1.31		1.16	1.17
RRl	1.01		1.07	1.09
RRu	1.69		1.25	1.26
P	+		+++	+++
Between P				N.S.

Ex smokers

	excluded	included	Total
N	11	2	13
Het P	**	N.S.	**
Fixed RR	1.18	1.10	1.17
RRl	1.09	0.87	1.09
RRu	1.27	1.39	1.26
P	+++	N.S.	+++
Between P			N.S.

Table F8 -

IASTAD - Meta-analysis of Household exposure (preferring most recent)
Lifetime/Current Asthma

This analysis is restricted to results for:
1) Household (overall) or parental exposure
2) Results not by amount of exposure
3) Results complete enough for use in metaanalysis

Within each study, results are then selected (in the following order of preference, within each sex) for:
4) ASTHMA : lifetime, current
5) WHESMO : 2=current, 7=recent, 6=unspec, 10=adult, 1=lifetime, 3=childhood
6) WHOHOU : household overall, mother
7) UNEXTI : unexposed Overall never, non (i.e. not at time defined for exposed Overall)
8) For overlapping studies: principal rather than subsidiary studies
Finally for single sex results (m, f) in preference to results for both sexes combined (b).

Results adjusted for the most potential confounders are then chosen in Section -3. (See corresponding table in
Appendix F for additional output including factors and Sections -1, -2, -4, -5, -6 and -7)

Table F8 - 3

IASTAD - Meta-analysis of Household exposure (preferring most recent)
Lifetime/Current Asthma
Adjusted

		Overall
	N	13
	NS	10
	Wt	441.99
Het	Chi	27.62
Het	df	12
Het	P	**
Fixed	RR	1.17
	RRl	1.06
	RRu	1.28
	P	++
Random	RR	1.26
	RRl	1.05
	RRu	1.53
	P	+
Asymm	P	N.S.

Table F9 -

<u>IASTAD - Meta-analysis of Workplace Exposure (preferring earliest)</u>
Lifetime/Current Asthma

This analysis is restricted to results for:
1) Workplace exposure
2) Results not by amount of exposure
3) Results complete enough for use in metaanalysis

Within each study, results are then selected (in the following order of preference, within each sex) for:
4) ASTHMA : lifetime, current
5) WHESMO : 3=childhood, 1=lifetime, 10=adult, 7=recent, 6=unspec, 2=current
6) WHOHOU : household overall, mother
7) UNEXTI : unexposed Overall never, non (i.e. not at time defined for exposed Overall)
8) For overlapping studies: principal rather than subsidiary studies
Finally for single sex results (m, f) in preference to results for both sexes combined (b).

Results adjusted for the most potential confounders are then chosen in Section -3
and results adjusted for the least confounders in Section -6. (See corresponding table in Appendix F
for additional output including Random model and Sections -1, -2, -4, -5 and -7)

Table F9 - 3

IASTAD - Meta-analysis of Workplace Exposure (preferring earliest)
Lifetime/Current Asthma
Adjusted

```
              Overall
        N        6
        NS       5
        Wt   166.38
   Het Chi    7.97
   Het df       5
   Het P      N.S.
  Fixed RR    1.37
        RRl   1.18
        RRu   1.59
        P      +++
 Random RR    1.36
        RRl   1.09
        RRu   1.70
        P       ++
  Asymm P     N.S.
```

```
                   Sex
            both    male   female   Total
        N      4       1        1       6
   Het  P   N.S.    N.S.     N.S.    N.S.
  Fixed RR  1.40    0.79     0.43    1.37
        RRl  1.20    0.17     0.13    1.18
        RRu  1.64    3.59     1.45    1.59
        P     +++    N.S.     N.S.     +++
Between  P                            N.S.
```

```
          Asthma definition (lifetime/current)
           lifetime  current   Total
        N        1        5       6
   Het  P     N.S.     N.S.    N.S.
  Fixed RR    1.13     1.44    1.37
        RRl    0.80     1.21    1.18
        RRu    1.59     1.70    1.59
        P      N.S.     +++     +++
Between  P                     N.S.
```

```
                  Continent
           NAmer   Europe Oth/Mult  Total
        N      1        4       1       6
   Het  P   N.S.     N.S.    N.S.    N.S.
  Fixed RR  1.36     1.23    1.90    1.37
        RRl  1.10     0.96    1.25    1.18
        RRu  1.70     1.57    2.88    1.59
        P     ++      (+)      ++     +++
Between  P                            N.S.
```

```
          Start year of study
           <1990  1990-99  unknown   Total
        N      1        3       2       6
   Het  P   N.S.     N.S.    N.S.    N.S.
  Fixed RR  1.36     1.44    0.55    1.37
        RRl  1.10     1.16    0.21    1.18
        RRu  1.70     1.79    1.41    1.59
        P     ++      +++     N.S.     +++
Between  P                            N.S.
```

```
            Study type
            CC       Pr      CS     Total
        N      3               3       6
   Het  P   N.S.           N.S.    N.S.
  Fixed RR  1.34           1.38    1.37
        RRl  0.95           1.16    1.18
        RRu  1.91           1.63    1.59
        P     (+)           +++     +++
Between  P                         N.S.
```

```
            Ex smokers
           excluded included   Total
        N      5        1       6
   Het  P    (*)     N.S.    N.S.
  Fixed RR  1.38     1.36    1.37
        RRl  1.11     1.10    1.18
        RRu  1.70     1.70    1.59
        P     ++       ++     +++
Between  P                    N.S.
```

Table F9 - 6

IASTAD - Meta-analysis of Workplace Exposure (preferring earliest)
Lifetime/Current Asthma
Unadjusted

		Overall
N		6
NS		5
Wt		172.94
Het Chi		7.59
Het df		5
Het P		N.S.
Fixed RR		1.32
RRl		1.14
RRu		1.53
P		+++
Random RR		1.30
RRl		1.06
RRu		1.61
P		+
Asymm P		N.S.

	Sex			
	both	male	female	Total
N	4	1	1	6
Het P	N.S.	N.S.	N.S.	N.S.
Fixed RR	1.35	0.79	0.43	1.32
RRl	1.16	0.17	0.13	1.14
RRu	1.57	3.59	1.45	1.53
P	+++	N.S.	N.S.	+++
Between P				N.S.

	Asthma definition (lifetime/current)		
	lifetime	current	Total
N	1	5	6
Het P	N.S.	N.S.	N.S.
Fixed RR	1.13	1.37	1.32
RRl	0.80	1.16	1.14
RRu	1.59	1.62	1.53
P	N.S.	+++	+++
Between P			N.S.

	Continent			
	NAmer	Europe	Oth/Mult	Total
N	1	4	1	6
Het P	N.S.	N.S.	N.S.	N.S.
Fixed RR	1.36	1.14	1.90	1.32
RRl	1.10	0.90	1.25	1.14
RRu	1.70	1.44	2.88	1.53
P	++	N.S.	++	+++
Between P				N.S.

	Start year of study			
	<1990	1990-99	unknown	Total
N	1	3	2	6
Het P	N.S.	N.S.	N.S.	N.S.
Fixed RR	1.36	1.34	0.55	1.32
RRl	1.10	1.09	0.21	1.14
RRu	1.70	1.65	1.41	1.53
P	++	++	N.S.	+++
Between P				N.S.

	Study type			
	CC	Pr	CS	Total
N	3		3	6
Het P	N.S.		N.S.	N.S.
Fixed RR	1.14		1.38	1.32
RRl	0.83		1.16	1.14
RRu	1.57		1.63	1.53
P	N.S.		+++	+++
Between P				N.S.

	Ex smokers		
	excluded	included	Total
N	5	1	6
Het P	N.S.	N.S.	N.S.
Fixed RR	1.28	1.36	1.32
RRl	1.05	1.10	1.14
RRu	1.57	1.70	1.53
P	+	++	+++
Between P			N.S.

Table F10 -

IASTAD - Meta-analysis of Workplace Exposure (preferring most recent)
Lifetime/Current Asthma

This analysis is restricted to results for:
1) Workplace exposure
2) Results not by amount of exposure
3) Results complete enough for use in metaanalysis

Within each study, results are then selected (in the following order of preference, within each sex) for:
4) ASTHMA : lifetime, current
5) WHESMO : 2=current, 7=recent, 6=unspec, 10=adult, 1=lifetime, 3=childhood
6) UNEXTI : unexposed Overall never, non (i.e. not at time defined for exposed Overall)
7) For overlapping studies: principal rather than subsidiary studies
Finally for single sex results (m, f) in preference to results for both sexes combined (b).

Results adjusted for the most potential confounders are then chosen in Section -3. (See corresponding table in
Appendix F for additional output including factors and Sections -1, -2, -4, -5, -6 and -7)

Table F10 - 3

IASTAD - Meta-analysis of Workplace Exposure (preferring most recent)
Lifetime/Current Asthma
Adjusted

		Overall
	N	6
	NS	5
	Wt	152.36
Het	Chi	10.23
Het	df	5
Het	P	(*)
Fixed	RR	1.39
	RRl	1.19
	RRu	1.63
	P	+++
Random	RR	1.40
	RRl	1.06
	RRu	1.85
	P	+
Asymm	P	N.S.

Tables G1, G2

IASTAD - Meta-analysis of Total/Household/Workplace Exposure : Low/High Dose
Lifetime/Current Asthma

This analysis is restricted to results for:
1) Total, household (overall) or workplace exposure
2) Results for low amount of exposure (G1) or for high amount of exposure (G2)
3) Results complete enough for use in metaanalysis

Within each study, results are then selected (in the following order of preference, within each sex) for:
4) ASTHMA : lifetime, current
5) EXPOS   : total, household, workplace
6) MEAS   : number of cigarettes, hours per day (0 indicates <1)
7) For overlapping studies: principal rather than subsidiary studies
Finally for single sex results (m, f) in preference to results for both sexes combined (b).

Results adjusted for the most potential confounders are then chosen in Section -3
and results adjusted for the least confounders in Section -6. (See corresponding tables in Appendix G
for additional output including Sections -1, -2, -4, -5 and -7)

Table G1

IASTAD - Meta-analysis of Total/Household/Workplace Exposure : Low/High Dose
Lifetime/Current Asthma

	Table G1 - 3 Adjusted		Table G1 - 6 Unadjusted
N	4	N	4
NS	4	NS	4
Wt	62.70	Wt	64.21
Het Chi	4.96	Het Chi	3.26
Het df	3	Het df	3
Het P	N.S.	Het P	N.S.
Fixed RR	1.03	Fixed RR	1.01
RRl	0.80	RRl	0.79
RRu	1.32	RRu	1.29
P	N.S.	P	N.S.
Random RR	1.07	Random RR	1.01
RRl	0.75	RRl	0.78
RRu	1.51	RRu	1.32
P	N.S.	P	N.S.
Asymm P	N.S.	Asymm P	N.S.

Table G2

IASTAD - Meta-analysis of Total/Household/Workplace Exposure : High Dose
Lifetime/Current Asthma

	Table G2 - 3 Adjusted		Table G2 - 6 Unadjusted
N	4	N	4
NS	4	NS	4
Wt	39.90	Wt	42.05
Het Chi	0.96	Het Chi	0.67
Het df	3	Het df	3
Het P	N.S.	Het P	N.S.
Fixed RR	1.63	Fixed RR	1.58
RRl	1.19	RRl	1.16
RRu	2.22	RRu	2.13
P	++	P	++
Random RR	1.63	Random RR	1.58
RRl	1.19	RRl	1.16
RRu	2.22	RRu	2.13
P	++	P	++
Asymm P	N.S.	Asymm P	N.S.

Tables G3, G4

<u>IASTAD - Meta-analysis of Household Exposure : Low/High Dose</u>
Lifetime/Current Asthma

This analysis is restricted to results for:
1) Household (overall) exposure
2) Results for low amount of exposure (G3) or for high amount of exposure (G4)
3) Results complete enough for use in metaanalysis

Within each study, results are then selected (in the following order of preference, within each sex) for:
4) ASTHMA : lifetime, current
5) MEAS : number of cigarettes, hours per day
6) For overlapping studies: principal rather than subsidiary studies
Finally for single sex results (m, f) in preference to results for both sexes combined (b).

Results adjusted for the most potential confounders are then chosen in Section -3
and results adjusted for the least confounders in Section -6. (See corresponding tables in Appendix G
for additional output including Sections -1, -2, -4, -5 and -7)

Table G3

<u>IASTAD - Meta-analysis of Household Exposure : Low Dose</u>
Lifetime/Current Asthma

Table G3 - 3 Adjusted		Table G3 - 6 Unadjusted	
N	2	N	2
NS	2	NS	2
Wt	5.90	Wt	6.36
Het Chi	2.60	Het Chi	1.85
Het df	1	Het df	1
Het P	N.S.	Het P	N.S.
Fixed RR	1.27	Fixed RR	1.16
RRl	0.57	RRl	0.53
RRu	2.85	RRu	2.52
P	N.S.	P	N.S.
Random RR	1.59	Random RR	1.32
RRl	0.37	RRl	0.42
RRu	6.88	RRu	4.18
P	N.S.	P	N.S.
Asymm P		Asymm P	

Table G4

<u>IASTAD - Meta-analysis of Household Exposure : High Dose</u>
Lifetime/Current Asthma

Table G4 - 3 Adjusted		Table G4 - 6 Unadjusted	
N	2	N	2
NS	2	NS	2
Wt	6.71	Wt	7.57
Het Chi	0.59	Het Chi	0.32
Het df	1	Het df	1
Het P	N.S.	Het P	N.S.
Fixed RR	1.39	Fixed RR	1.30
RRl	0.65	RRl	0.64
RRu	2.96	RRu	2.66
P	N.S.	P	N.S.
Random RR	1.39	Random RR	1.30
RRl	0.65	RRl	0.64
RRu	2.96	RRu	2.66
P	N.S.	P	N.S.
Asymm P		Asymm P	

Tables G5, G6

<u>IASTAD – Meta-analysis of Workplace Exposure : Low/High Dose</u>
Lifetime/Current Asthma

This analysis is restricted to results for:
1) Workplace exposure
2) Results for low amount of exposure (G5) or for high amount of exposure (G6)
3) Results complete enough for use in metaanalysis

Within each study, results are then selected (in the following order of preference, within each sex) for:
4) ASTHMA : lifetime, current
5) MEAS   : number of cigarettes, hours per day (0 indicates <1)
6) For overlapping studies: principal rather than subsidiary studies
Finally for single sex results (m, f) in preference to results for both sexes combined (b).

Results adjusted for the most potential confounders are then chosen in Section -3
and results adjusted for the least confounders in Section -6. (See corresponding tables in Appendix G
for additional output including Sections -1, -2, -4, -5 and -7)

Table G5

<u>IASTAD – Meta-analysis of Workplace Exposure : Low Dose</u>
Lifetime/Current Asthma

	Table G5 – 3 Adjusted			Table G5 – 6 Unadjusted
N	2		N	2
NS	2		NS	2
Wt	25.40		Wt	26.47
Het Chi	3.90		Het Chi	3.02
Het df	1		Het df	1
Het P	*		Het P	(*)
Fixed RR	1.08		Fixed RR	1.06
RRl	0.73		RRl	0.72
RRu	1.59		RRu	1.55
P	N.S.		P	N.S.
Random RR	1.26		Random RR	1.17
RRl	0.53		RRl	0.57
RRu	2.97		RRu	2.40
P	N.S.		P	N.S.
Asymm P			Asymm P	

Table G6

<u>IASTAD – Meta-analysis of Workplace Exposure : High Dose</u>
Lifetime/Current Asthma

	Table G6 – 3 Adjusted			Table G6 – 6 Unadjusted
N	2		N	2
NS	2		NS	2
Wt	16.45		Wt	17.75
Het Chi	0.75		Het Chi	0.21
Het df	1		Het df	1
Het P	N.S.		Het P	N.S.
Fixed RR	2.04		Fixed RR	1.93
RRl	1.26		RRl	1.21
RRu	3.31		RRu	3.07
P	++		P	++
Random RR	2.04		Random RR	1.93
RRl	1.26		RRl	1.21
RRu	3.31		RRu	3.07
P	++		P	++
Asymm P			Asymm P	

Tables G7, G8

IASTAD - Meta-analysis of Total/Household/Workplace Exposure : Low/High Dose
Lifetime/Current Asthma

This analysis is restricted to results for:
1) Total, household (overall) or workplace exposure
2) Results for low amount of exposure (G7) or for high amount of exposure (G8)
3) Results complete enough for use in metaanalysis

Within each study, results are then selected (in the following order of preference, within each sex) for:
4) ASTHMA : lifetime, current
5) EXPOS   : total, household, workplace
6) MEAS   : pack-years, number of cigarettes, hours per day (0 indicates <1)
7) For overlapping studies: principal rather than subsidiary studies
Finally for single sex results (m, f) in preference to results for both sexes combined (b).

Results adjusted for the most potential confounders are then chosen in Section -3
and results adjusted for the least confounders in Section -6. (See corresponding tables in Appendix G
for additional output including Sections -1, -2, -4, -5 and -7)

Table G7

IASTAD - Meta-analysis of Total/Household/Workplace Exposure : Low Dose
Lifetime/Current Asthma

Table G7 – 3				Table G7 – 6	
Adjusted				Unadjusted	
N	4			N	4
NS	4			NS	4
Wt	69.14			Wt	71.03
Het Chi	0.56			Het Chi	2.09
Het df	3			Het df	3
Het P	N.S.			Het P	N.S.
Fixed RR	0.90			Fixed RR	0.85
RRl	0.71			RRl	0.68
RRu	1.14			RRu	1.08
P	N.S.			P	N.S.
Random RR	0.90			Random RR	0.85
RRl	0.71			RRl	0.68
RRu	1.14			RRu	1.08
P	N.S.			P	N.S.
Asymm P	N.S.			Asymm P	N.S.

Table G8

IASTAD - Meta-analysis of Total/Household/Workplace Exposure : High Dose
Lifetime/Current Asthma

Table G8 – 3				Table G8 – 6	
Adjusted				Unadjusted	
N	4			N	4
NS	4			NS	4
Wt	55.91			Wt	60.38
Het Chi	0.83			Het Chi	0.49
Het df	3			Het df	3
Het P	N.S.			Het P	N.S.
Fixed RR	1.66			Fixed RR	1.55
RRl	1.28			RRl	1.20
RRu	2.16			RRu	1.99
P	+++			P	+++
Random RR	1.66			Random RR	1.55
RRl	1.28			RRl	1.20
RRu	2.16			RRu	1.99
P	+++			P	+++
Asymm P	N.S.			Asymm P	N.S.

Tables G9, G10

<u>IASTAD - Meta-analysis of Household Exposure : Low/High Dose</u>
Lifetime/Current Asthma

This analysis is restricted to results for:
1) Household (overall) exposure
2) Results for low amount of exposure (G9) or for high amount of exposure (G10)
3) Results complete enough for use in metaanalysis

Within each study, results are then selected (in the following order of preference, within each sex) for:
4) ASTHMA : lifetime, current
5) MEAS   : pack-years, number of cigarettes, hours per day
6) For overlapping studies: principal rather than subsidiary studies
Finally for single sex results (m, f) in preference to results for both sexes combined (b).

Results adjusted for the most potential confounders are then chosen in Section -3
and results adjusted for the least confounders in Section -6. (See corresponding tables in Appendix G
for additional output including Sections -1, -2, -4, -5 and -7)

Table G9

<u>IASTAD - Meta-analysis of Household Exposure : Low Dose</u>
Lifetime/Current Asthma

	Table G9 - 3 Adjusted			Table G9 - 6 Unadjusted	
N	2		N	2	
NS	2		NS	2	
Wt	17.26		Wt	19.51	
Het Chi	0.03		Het Chi	0.03	
Het df	1		Het df	1	
Het P	N.S.		Het P	N.S.	
Fixed RR	0.93		Fixed RR	0.78	
RRl	0.58		RRl	0.50	
RRu	1.48		RRu	1.21	
P	N.S.		P	N.S.	
Random RR	0.93		Random RR	0.78	
RRl	0.58		RRl	0.50	
RRu	1.48		RRu	1.21	
P	N.S.		P	N.S.	
Asymm P			Asymm P		

Table G10

<u>IASTAD - Meta-analysis of Household Exposure : High Dose</u>
Lifetime/Current Asthma

	Table G10 - 3 Adjusted			Table G10 - 6 Unadjusted	
N	2		N	2	
NS	2		NS	2	
Wt	24.03		Wt	28.35	
Het Chi	0.10		Het Chi	0.01	
Het df	1		Het df	1	
Het P	N.S.		Het P	N.S.	
Fixed RR	1.42		Fixed RR	1.50	
RRl	0.95		RRl	1.04	
RRu	2.12		RRu	2.17	
P	(+)		P	+	
Random RR	1.42		Random RR	1.50	
RRl	0.95		RRl	1.04	
RRu	2.12		RRu	2.17	
P	(+)		P	+	
Asymm P			Asymm P		

Tables G11, G12

IASTAD - Meta-analysis of Workplace Exposure : Low/High Dose
Lifetime/Current Asthma

This analysis is restricted to results for:
1) Workplace exposure
2) Results for low amount of exposure (G11) or for high amount of exposure (G12)
3) Results complete enough for use in metaanalysis

Within each study, results are then selected (in the following order of preference, within each sex) for:
4) ASTHMA : lifetime, current
5) MEAS   : pack-years, number of cigarettes, hours per day (0 indicates <1)
6) For overlapping studies: principal rather than subsidiary studies
Finally for single sex results (m, f) in preference to results for both sexes combined (b).

Results adjusted for the most potential confounders are then chosen in Section -3
and results adjusted for the least confounders in Section -6. (See corresponding tables in Appendix G
for additional output including Sections -1, -2, -4, -5 and -7)

Table G11

IASTAD - Meta-analysis of Workplace Exposure : Low Dose
Lifetime/Current Asthma

	Table G11 - 3 Adjusted			Table G11 - 6 Unadjusted	
N	2		N	2
NS	2		NS	2
Wt	33.97		Wt	36.96
Het Chi	0.86		Het Chi	0.23
Het df	1		Het df	1
Het P	N.S.		Het P	N.S.
Fixed RR	0.98		Fixed RR	0.92
RRl	0.70		RRl	0.67
RRu	1.37		RRu	1.27
P	N.S.		P	N.S.
Random RR	0.98		Random RR	0.92
RRl	0.70		RRl	0.67
RRu	1.37		RRu	1.27
P	N.S.		P	N.S.
Asymm P			Asymm P	

Table G12

IASTAD - Meta-analysis of Workplace Exposure : High Dose
Lifetime/Current Asthma

	Table G12 -3 Adjusted			Table G12 - 6 Unadjusted	
N	2		N	2
NS	2		NS	2
Wt	20.95		Wt	22.95
Het Chi	0.23		Het Chi	0.00
Het df	1		Het df	1
Het P	N.S.		Het P	N.S.
Fixed RR	1.96		Fixed RR	1.78
RRl	1.28		RRl	1.18
RRu	3.01		RRu	2.68
P	++		P	++
Random RR	1.96		Random RR	1.78
RRl	1.28		RRl	1.18
RRu	3.01		RRu	2.68
P	++		P	++
Asymm P			Asymm P	

Appendix A
The references corresponding to the reference keys given in Table 1

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Appendix B
Validation checks on completeness and consistency of the data

1. Study database

Appendix C gives a key to the six character codes used for cards and fields on the study database.

'Blank' data (i.e. no data entered) not allowed for any field in any card

'Missing' data not allowed for field: Card DESCR: STYPE

'Not applicable' (NA) data not allowed for any field in the following cards:
CONFND, OTHRES
or for the following fields:
Card DESCR: TITLE, FTITLE, SSEX, SAGELO, SAGEHI, SRACE, CONT,
                LOCAT,BEGYR, ENDYR, PUBYR, REFID, OVERL, PRINC,
                REFGP
Card DESIGN: POPUL, MEDEXC,OTHEXC, RESPON, NEVSMO,QUEST
Card ASTHMA: LIFAST, CURAST, NTOT

'Zero' data not allowed for fields:
Card DESCR: TITLE, FTITLE, SSEX, SRACE, CONT, USSTAT, EUR, ASIA,
                LOCAT, BEGYR, ENDYR, FINFYR, PUBYR, REFID,
                ADDREF, OVERL, PRINC, REFGP
Card DESIGN: STYPE, CONTRL, CONDIS, POPUL, RESPON, NEVSMO,
                QUEST
Card ASTHMA: DIAGLS, TIMLAS, INCAST, DESLAS, DIAGCS, TIMCAS,
                DESCAS, NLAST, NCAST, NTOT

Other checks on card DESCR
If STYPE=2 (prospective), then –
      SAGELO ≤ SAGEHI ≤ SAGEHF
Otherwise (CC or CS study) – SAGELO ≤ SAGEHI and SAGEHF NA

Fields USSTAT, EUR, ASIA must be NA except when the value of CONT is 1-NAMER, 2- EUR, 3- ASIA respectively, in which case must be +ve.

If STYPE=2 (prospective), then –
      BEGYR ≤ ENDYR ≤ FINFYR
Otherwise (CC or CS study) – BEGYR ≤ ENDYR and FINFYR NA

If OVERL=1, then PRINC must be 1, otherwise a comment must be entered.

If PRINC=1 then REFGP must be same as REF

Other checks on cards DESIGN and MATCH
If STYPE=2,3 (prospective or cross-sectional study), then fields CONTRL, CONDIS, POPCON, MATSEX, MATAGE, MATRACE, MATLOC, MATSES, MATHOS must be NA.

If STYPE=1 (case-control study), then –
>   Fields CONTRL, MATSEX, MATAGE, MATRACE, MATLOC, MATSES,
>   MATHOS must not be NA.
>
>   CONDIS must be NA if and only if CONTRL=1 (i.e. healthy controls)
>
>   MATSEX may only be 1 if SSEX=1.

Other checks on card ASTHMA
Fields DIAGLS, TIMLAS, INCAST, DESLAS must be NA if and only if LIFAST=0.
Fields FIRAST, REPCAS, DIAGCS, TIMCAS, DESCAS must be NA if and only if
CURAST=0.

If NTOT is non-missing, then NLAST < NTOT if LIFAST=1, and NCAST < NTOT
if CURAST=1

Other checks on card CONFND
TOTCO must equal the sum of the other fields in the card excluding COREJE (or
TOTCO may be missing).

If COREJE=1, then a comment must be entered.

COSEX may only be 1 if SSEX=1 (i.e. both sexes in study)

Other checks on card OTHRES
If any field has the value 1, then a comment must be entered.

2. <u>RR database</u>

Appendix E gives a key to the six character codes used for cards and fields on the relative risk database.

'Blank' data (i.e. no data entered) not allowed for any field in any card.

'Missing' data not allowed for any field on the following cards:
RRDEF, RRADJ
or for the following field: Card RRDATA: DERIVE

'Not applicable' (NA) data not allowed for any field in card RRADJ,
or for the following fields:
Card RRDEF: NRR, RSEX, RAGELO, RAGEHI, RRACE, RASTIM, ONSET,
                     EXPOS, WHESMO, DOSER, MEASEX, UNEXTI, UNEXSO,
                     SOURCE, DERIVE
Card RRADJ: ADSEX, ADAGE, ADRACE, ADOETS, ADOTHR
Card RRDATA: CA1, CA0, RR, RRL, RRU, DERIVE

Other checks on card RRDEF
If EXPOS = 1 (i.e. household), then WHOHOU must be +ve; otherwise WHOHOU must be NA.

If EXPOS = 3 (i.e. total), then WHOTOT must be +ve; otherwise WHOTOT must be NA.

ODDSON must be NA if and only if ONSET=0.

If DOSER=1, 11, 12 (i.e. not standard dose-response category) then EXPLO and EXPHI must be NA

If DOSER is in the range 2-10 (i.e. standard dose-response category) then
       MEASEX >0
       EXPLO, EXPHI must not be NA
       EXPLO $\leq$ EXPHI
       UNEXHI $\leq$ EXPLO

UNEXHI may be NA if and only if MEASEX=1 (i.e. not dose-response, and not denominator is "low" exposure), except if DOSER=11.

Either both RAGELO = RAGEHI = 0, or 0 < RAGELO $\leq$ RAGEHI

Other checks on card RRDATA
RRL $\leq$ RR $\leq$ RRU

If CA1, CA0, CO1 and CA0 are all +ve, then RR, RRL, RRU must equal (to 2 decimal places) the relative risk and CI as calculated according to the formula given in §3.4.3 of reference 1; if three are +ve and one zero, then the calculation will include the correction for zero cells described in that section, and DERIVE must be 7.

Consistency checks between cards RRDEF and RRADJ
ADSEX may be +ve only if RSEX=1

Consistency checks between cards RRADJ and RRDATA
CO1 and CO0 must be NA if and only if at least one field in card RRADJ is +ve.

Consistency checks between card RRDEF and study database
RSEX may be 2 only if SSEX is 1 or 2
RSEX may be 3 only if SSEX is 1 or 3
RSEX may be 1 only if SSEX is 1

RAGELO $\geq$ SAGELO (except if RAGELO=RAGEHI=0)
If STYPE is 1, 3 (case-control or cross-sectional study) –
        RAGEHI $\leq$ SAGEHI (except if RAGELO=RAGEHI=0)

        Must not have both RAGELO = SAGELO and RAGEHI = SAGEHI.

If STYPE is 2 (prospective study), similar conditions apply but with SAGEHF
instead of SAGEHI.

RASTIM may be 1 only if LIFAST=1, and it may be 2 only if CURAST=1.

ONSET may be 1 only if STYPE=2 (prospective study).

Consistency checks between card RRADJ and study database
ADSEX may be 1 only if COSEX is 1.
ADAGE may be +ve only if COAGE is +ve.
ADRACE may be +ve only if CORACE is +ve.
ADOTHR may be +ve only if COMSMP, COCETS, COTETS, COHETS or
COWETS is +ve.

ADOTHR+ADACSM+ADOETS $\leq$ TOTCO-COSEX-COAGE-CORACE, except that
ADOTHR may be 20 (meaning +ve but unknown) provided the sum is +ve. If less
than (i.e. not equal) then a comment must be entered.

Consistency checks between card RRDATA and study database
CA1 + CA0 $\leq$ NLAST if RASTIM=1, or CA1 + CA0 $\leq$ NCAST if RASTIM=2.

If ONSET=0 (i.e. prevalence analysis) CA1+CA0+CO1+CO0 $\leq$ NTOT.
If ONSET=1 (i.e. onset analysis) CO1+CO0 $\leq$ NTOT. [This validation requirement
was checked individually and waived for RRs where numbers of man-years at risk
had been entered.]

Reference

1. Lee PN, Forey BA, Young KJ. *International evidence on passive smoking and childhood asthma induction (project IESAST). Part I: The databases; methods used to collect and analyse the data and scope of the informtaion obtained.* Internal. 2004.

Appendix C

Detailed structure of the study database

```
_____
 Card
 Name                           Short Name  Position
        Field
        Name                                    Short Name  Number  Type_____

Study description           DESCR       1
        Study title                             TITLE    8     Character  ( 15 )
        Full study title                        FTITLE   9     Character  ( 50 )
        Study sex                               sSEX     10    Graded     ( system 34 )
        Lowest age in study                     sAGELO   11    Measured   ( 0 to 99 )
        Highest age in study (at baseline)      sAGEHI   12    Measured   ( 0 to 99 )
        Highest age in study at final followup  sAGEHF   13    Measured   ( 0 to 99 )
        Study race                              sRACE    14    Graded     ( system 16 )
        Continent                               CONT     15    Graded     ( system 17 )
        US state                                USSTAT   16    Graded     ( system 36 )
        Country in Europe                       EUR      17    Graded     ( system 19 )
        Country in Asia                         ASIA     18    Graded     ( system 37 )
        Location within country                 LOCAT    19    Character  ( 50 )
        Start year of study                     BEGYR    20    Measured   ( 1900 to 2004 )
        End year of study                       ENDYR    21    Measured   ( 1900 to 2004 )
        Final follow up year                    FINFYR   22    Measured   ( 1900 to 2004 )
        Principal publication year              PUBYR    23    Measured   ( 1900 to 2004 )
        Reference ID of principal publication   REFID    24    Character  ( 12 )
        Reference ID of additional publication(s) ADDREF 25    Character  ( 50 )
        Overlap                                 OVERL    26    Graded>0   ( system 21 )
        Principal/subsidiary study              PRINC    27    Graded>0   ( system 22 )
        REF group                               REFGP    28    Character  ( 6 )

Study design                DESIGN      2
        Study type                              STYPE    33    Graded     ( system 38 )
        Type of controls (for CC studies)       CONTRL   34    Graded     ( system 39 )
        Control diseases                        CONDIS   35    Character  ( 50 )
        Type of population                      POPUL    36    Graded     ( system 25 )
        Medical exclusions                      MEDEXC   37    Character  ( 50 )
        Other exclusions                        OTHEXC   38    Character  ( 50 )
        Type of population - controls (if diff from cases) POPCON 39 Graded ( system 26 )
        Respondent                              RESPON   40    Graded     ( system 27 )
        Never/non smoker definition             NEVSMO   41    Graded>0   ( system 28 )
        Questionnaire                           QUEST    42    Graded     ( system 29 )

Asthma                      ASTHMA      3
        Lifetime/incidence/unspec asthma available LIFAST 47  Presence   ( system 6 )
        Source of lifetime asthma diagnosis     DIAGLS   48    Graded     ( system 30 )
        Timing of lifetime asthma               TIMLAS   49    Graded>0   ( system 35 )
        Timing of incidence asthma              INCAST   50    Graded>0   ( system 32 )
        Description of lifetime asthma          DESLAS   51    Character  ( 50 )
        Current asthma available                CURAST   52    Presence   ( system 6 )
        Current asthma is first occurrence      FIRAST   53    Presence   ( system 6 )
        Repeat measures for current asthma      REPCAS   54    Presence   ( system 6 )
        Source of current asthma diagnosis      DIAGCS   55    Graded     ( system 30 )
        Timing of current asthma                TIMCAS   56    Graded>0   ( system 33 )
        Description of current asthma           DESCAS   57    Character  ( 50 )
        Number of lifetime asthma cases         NLAST    58    Measured   ( 0 to 32765 )
        Number of current asthma cases          NCAST    59    Measured   ( 0 to 32765 )
        Total number of subjects                NTOT     60    Measured   ( 0 to 32765 )

Matching factors            MATCH       4
        Cases and controls matched on sex       MATSEX   65    Presence   ( system 6 )
        Cases and controls matched on age (CC)  MATAGE   66    Presence   ( system 6 )
        Cases and controls matched on race      MATRAC   67    Presence   ( system 6 )
        Matched on location (within study area) MATLOC   68    Presence   ( system 6 )
        Cases and controls matched on socioeconomic status MATSES 69 Presence ( system 6 )
        Matched on hospital admission (ward, date etc) MATHOS 70 Presence ( system 6 )

Confounders considered      CONFND      5
        Total number of adjustment factors used TOTCO    75    Measured   ( 0 to 99 )
        Adjusted for sex                        COSEX    76    Presence   ( system 6 )
        Adjusted for age                        COAGE    77    Measured   ( 0 to 10 )
        Adjusted for race                       CORACE   78    Measured   ( 0 to 10 )
        Adjusted for location within study      COLOC    79    Measured   ( 0 to 10 )
        Adjusted for type of respondent         CORESP   80    Measured   ( 0 to 10 )
```

```
        Adjusted for interview setting              COIVST  81    Measured   ( 0 to 10 )
        Adjusted for religion                       CORELI  82    Measured   ( 0 to 10 )
        Adjusted for family (parent/sibl) medical history  COFMED  83    Measured   ( 0 to 10 )
        Adjusted for SES                            COSES   84    Measured   ( 0 to 10 )
        Adjusted for household composition          COHOCO  85    Measured   ( 0 to 10 )
        Adjusted for air conditioning/humidifier    COAIRC  86    Measured   ( 0 to 10 )
        Adjusted for cooking/heating methods        COCOHE  87    Measured   ( 0 to 10 )
        Adjusted for damp/mould in home             CODAMP  88    Measured   ( 0 to 10 )
        Adjusted for housing quality/age/size       COHOUS  89    Measured   ( 0 to 10 )
        Adjusted for pets in household              COPETS  90    Measured   ( 0 to 10 )
        Adjusted for exposure to food/housedust allergens  COALGN  91    Measured   ( 0 to 10 )
        Adjusted for occupation                     COOCC   92    Measured   ( 0 to 10 )
        Adjusted for education                      COEDUC  93    Measured   ( 0 to 10 )
        Adjusted for mobility                       COMOB   94    Measured   ( 0 to 10 )
        Adjusted for subject's medical history      COSMED  95    Measured   ( 0 to 10 )
        Adjusted for obesity/BMI                    COOBES  96    Measured   ( 0 to 10 )
        Adjusted for exercise                       COEXER  97    Measured   ( 0 to 10 )
        Adjusted for diet/alcohol                   CODIET  98    Measured   ( 0 to 10 )
        Adjusted for active smoking (ex/never)      COACSM  99    Measured   ( 0 to 10 )
        Adjusted for maternal smoking in pregnancy  COMSMP  100   Measured   ( 0 to 10 )
        Adjusted for childhood ETS                  COCETS  101   Measured   ( 0 to 10 )
        Adjusted for total ETS                      COTETS  117   Measured   ( 0 to 10 )
        Adjusted for household ETS exposure         COHETS  102   Measured   ( 0 to 10 )
        Adjusted for workplace ETS exposure         COWETS  103   Measured   ( 0 to 10 )
        Other confounders considered but rejected   COREJE  104   Presence   ( system 6 )

Other results (not current db)  OTHRES       6
        Other definitions of asthma available       OTHAST  109   Presence   ( system 6 )
        Wheezing/wheezing bronchitis available      WHEEZE  110   Presence   ( system 6 )
        Other exposures available                   OTHEXP  111   Presence   ( system 6 )
        Results available other defns of never/non smoking  OTHNSM  112   Presence   ( system 6 )
        Results by other stratifying factors available  OTHSTR  113   Presence   ( system 6 )

Derived fields (1)              DER1         7
        Number of RRs                               NRRS    121   Measured   ( 0 to 100 )
        Household exposure RRs                       EXHH    122   Measured   ( 0 to 100 )
        Workplace exposure RRs                       EXWORK  124   Measured   ( 0 to 100 )
        Total exposure RRs                           EXTOT   125   Measured   ( 0 to 100 )
        Biochemical exposure RRs                     EXBIOC  126   Measured   ( 0 to 100 )
        Total exposure (questionnaire assessed) RRs  EXTOTQ  128   Measured   ( 0 to 100 )
```
_____

The grading systems used are as follows
_____
  Grading Level (character equivalent)   Tumour Type
  System
_____

   6   1 (x) present   0

  16   1 (a) all (in study area)   0
          2 (w) whites (inc hispanic)   0
          3 (b) blacks   0
          4 (4) whites and blacks   0
          5 (5) whites (exc hispanic)   0

  17   1 (1) NAmerica   0
          2 (2) Europe   0
          3 (3) Asia   0
          4 (4) Australia   0
          5 (5) multi   0

  19   1 (1) Estonia   0
          2 (2) Finland   0
          3 (3) France   0
          4 (4) Germany   0
          5 (5) Poland   0
          6 (6) Sweden   0
          7 (7) Switzerland   0

  21   1 (1) No overlap   0
          2 (2) JANSON/RAHERI   0

  22   1 (p) principal   0
          2 (s) subsidiary   0

  25   1 (1) all   0
          2 (2) randomly selected   0
          3 (3) farmers   0
          4 (4) random households   0
          5 (5) unstated   0

  26   2 (2) without history of asthma   0

  27   1 (s) subject   0
          3 (3) subject or proxy   0

  28   1 (1) Never smoked NOS   0
          3 (3) Smoked < 1 cig/day for 1 year   0
          4 (4) Never smoked not even few/week   0
          5 (5) Never smoked regularly/daily   0
          6 (6) Smk <20 pks cigs/360g lifetime   0
          7 (7) <1 cig/d 1 cigr/w 1yr, or 360g   0
          8 (8) Smoked < 1 year   0
          9 (9) Not current smoker   0
         10 (a) Not active smoker   0
         11 (b) Not curr smk and serum cot <14   0
         12 (c) Serum cotinine <14 ng/ml   0

  29   1 (1) Non std/NA/NK   0
          4 (4) MRC   0
          5 (5) ECRHS   0

  30   1 (m) Medical records   0
          2 (s) Self report (doctor diag)   0
          3 (3) Self report (other/unspec/mix)   0
          4 (4) Proxy report (doctor diag)   0
          5 (5) Proxy report (other/unsp/mix)   0

  32   1 (1) since baseline (earlier excl)   0
          4 (4) NA (only prevalence analysis)   0

  33   1 (1) current diagnosis   0
          4 (4) in last n months (12<=n<24)   0
          6 (6) current NOS   0

```
34      1 (b) both                                      0
        3 (f) female                                    0

35      1 (1) Lifetime                                  0
        2 (2) NA (incidence only)                       0
        4 (4) from age 16 (ie adult onset)              0
        6 (6) unspecified                               0

36      1 (n) nationwide                                0
        2 (m) multi (not all)                           0
        3 (c) California                                0
        4 (d) Delaware                                  0

37      1 (i) India                                     0
        2 (s) Singapore                                 0

38      1 (c) case/control                              0
        2 (p) prospective                               0
        3 (x) cross sectional                           0

39      1 (h) healthy                                   0
        2 (d) diseased                                  0
        3 (b) both                                      0
```
_____

Appendix D

Study data for the 17 studies

```
BECKE2  Study          Study title       : Beckett
        description    Full study title  : CARDIA 4 city PS 1985 - 1996 (CARDIA = Coronary Artery Risk
                        Development in Young Adults)
                       Study sex         : both
                       Lowest age in study : 18
                       Highest age in study (at baseline): 30
                       Highest age in study at final followup: 40
                       Study race        : whites and blacks
                       Continent         : NAmerica
                       US state          : multi (not all)
                       Location within country: Birmingham, Chicago, Minneapolis, Oakland
                       Start year of study : 1985
                       End year of study   : 1986
                       Final follow up year: 1996
                       Principal publication year: 2001
                       Reference ID of principal publication: BECKET2001
                       Reference ID of additional publication(s): FRIEDM1988A
                       Overlap: No overlap
                       Principal/subsidiary study: principal
                       REF group         : BECKE2

        Study design   Study type        : prospective
                       Type of population : randomly selected
                       Medical exclusions : long-term illness or disablility (including blind, deaf, mute,
                        mentally retarded, unable to walk), emotionally unstable, pregnant or <3 months post
                        partum
                       Respondent        : subject
                       Never/non smoker definition: Serum cotinine <14 ng/ml
                       Questionnaire     : Non std/NA/NK

        Asthma         Lifetime/incidence/unspec asthma available: present
                       Source of lifetime asthma diagnosis: Self report (doctor diag)
                       Timing of lifetime asthma: Lifetime
                       Timing of incidence asthma: since baseline (earlier excl)
                       Description of lifetime asthma: Taking medication typically used to treat asthma or
                        ever told by doctor or nurse had asthma
                       Number of lifetime asthma cases: 473
                       Total number of subjects: 3128

        Confounders    Total number of adjustment factors used: 5
         considered    Adjusted for sex  : present
                       Adjusted for age  : 1
                       Adjusted for race : 1
                       Adjusted for location within study: 1
                       Adjusted for education: 1


JAAKK2  Study          Study title       : Jaakkola
        description    Full study title  : Pirkanmaa incident asthma CC 1997-2000
                       Study sex         : both
                       Lowest age in study : 21
                       Highest age in study (at baseline): 63
                       Study race        : all (in study area)
                       Continent         : Europe
                       Country in Europe : Finland
                       Location within country: Pirkanmaa (South Finland)
                       Start year of study : 1997
                       End year of study   : 2000
                       Principal publication year: 2003
                       Reference ID of principal publication: JAAKKO2003B
                       Overlap: No overlap
                       Principal/subsidiary study: principal
                       REF group         : JAAKK2

        Study design   Study type        : case/control
                       Type of controls (for CC studies): healthy
                       Type of population : all
                       Medical exclusions : previous asthma
                       Respondent        : subject
                       Never/non smoker definition: Never smoked NOS
                       Questionnaire     : Non std/NA/NK
```

```
JAAKK2
(continued)

        Asthma          Current asthma available: present
                        Current asthma is first occurrence: present
                        Source of current asthma diagnosis: Medical records
                        Timing of current asthma: current diagnosis
                        Description of current asthma: at least one asthma-like symptom (prolonged cough,
                         wheezing, attacks of or exercise-induced dyspnea, or nocturnal cough or wheezing) and
                         demonstration of reversible airway obstruction in lung function investigations
                        Number of current asthma cases: 239
                        Total number of subjects: 726

        Confounders     Total number of adjustment factors used: 11
         considered     Adjusted for sex    : present
                        Adjusted for age    : 1
                        Adjusted for family (parent/sibl) medical history: 1
                        Adjusted for damp/mould in home: 1
                        Adjusted for pets in household: 1
                        Adjusted for occupation: 1
                        Adjusted for education: 1
                        Adjusted for household ETS exposure: 2
                        Adjusted for workplace ETS exposure: 2


JANSON  Study           Study title         : Janson
        description     Full study title    : ECRHS multicentre CS 1990-94 (ECRHS = European Community
                         Respiratory Health Study)
                        Study sex           : both
                        Lowest age in study : 20
                        Highest age in study (at baseline): 48
                        Study race          : all (in study area)
                        Continent           : multi
                        Location within country: 37 centres in 17 countries (Australia, Belgium, Denmark,
                         Estonia, France, Germany, Iceland, Ireland, Italy, Netherlands, New Zealand, Norway,
                         Spain, Sweden, Switzerland, UK, USA)
                        Start year of study : 1990
                        End year of study   : 1994
                        Principal publication year: 2001
                        Reference ID of principal publication: JANSON2001
                        Reference ID of additional publication(s): SVANES2004, DEMARC2004
                        Overlap: JANSON/RAHERI
                        Principal/subsidiary study: principal
                        REF group           : JANSON
                        Comments            : Results for current asthma from 17 countries (16 omitting
                         Denmark in JANSON2001) entered as study JANSON; results for lifetime asthma from
                         Bordeaux (France) only entered as study RAHERI

        Study design    Study type          : cross sectional
                        Type of population  : randomly selected
                        Respondent          : subject
                        Never/non smoker definition: <1 cig/d 1 cigr/w 1yr, or 360g
                        Questionnaire       : ECRHS

        Asthma          Current asthma available: present
                        Source of current asthma diagnosis: Self report (other/unspec/mix)
                        Timing of current asthma: in last n months (12<=n<24)
                        Description of current asthma: Ever had asthma and had attack in last 12 months
                         (JANSON2001); using current asthma medication or asthma attacks in last 12 months
                         (SVANES2004)
                        Number of current asthma cases: not assessable
                        Total number of subjects: 7882

        Confounders     Total number of adjustment factors used: 15
         considered     Adjusted for sex    : present
                        Adjusted for age    : 1
                        Adjusted for location within study: 1
                        Adjusted for household composition: 1
                        Adjusted for occupation: 1
                        Adjusted for subject's medical history: 5
                        Adjusted for obesity/BMI: 1
                        Adjusted for childhood ETS: 1
                        Adjusted for total ETS: 1
                        Adjusted for household ETS exposure: 1
                        Adjusted for workplace ETS exposure: 1
```

```
JANSON
(continued)

        Other results    Other definitions of asthma available: present Results also available for 3+ asthma
         (not current     symptoms (SVANES2004)
          db)            Wheezing/wheezing bronchitis available: present Results also available for wheeze;
                          wheeze and breathlessness; wheeze without cold
                         Results available other defns of never/non smoking: present Results also available for
                          ex-smokers (SVANES2004)


JEDRYC  Study           Study title        : Jedrychowski
         description     Full study title   : Cracow elderly TB screening CS (ca 1994?)
                         Study sex          : female
                         Lowest age in study : 65
                         Highest age in study (at baseline): 99
                         Study race         : all (in study area)
                         Continent          : Europe
                         Country in Europe  : Poland
                         Location within country: central Cracow
                         Start year of study : not assessable
                         End year of study  : not assessable
                         Principal publication year: 1995
                         Reference ID of principal publication: JEDRYC1995B
                         Overlap: No overlap
                         Principal/subsidiary study: principal
                         REF group          : JEDRYC

        Study design    Study type         : cross sectional
                         Type of population : all
                         Medical exclusions : residents of old people's home and geriatric wards (i.e.
                          incapable of self-care or independent living)
                         Other exclusions   : use electric or coal stoves for cooking
                         Respondent         : subject
                         Never/non smoker definition: Smoked < 1 cig/day for 1 year
                         Questionnaire      : MRC

        Asthma          Current asthma available: present
                         Source of current asthma diagnosis: Self report (doctor diag)
                         Timing of current asthma: current diagnosis
                         Description of current asthma: current treatment by medical doctor for bronchial
                          asthma
                         Number of current asthma cases: 99
                         Total number of subjects: 1252
                         Comments           : Number of cases estimated from % distribution.

        Confounders     Total number of adjustment factors used: 3
         considered      Adjusted for age   : 1
                         Adjusted for cooking/heating methods: 1
                         Adjusted for education: 1


KRONQV  Study           Study title        : Kronqvist
         description     Full study title   : Gotland farmers CS 1996
                         Study sex          : both
                         Lowest age in study : 15
                         Highest age in study (at baseline): 65
                         Study race         : all (in study area)
                         Continent          : Europe
                         Country in Europe  : Sweden
                         Location within country: Gotland (island in Baltic Sea)
                         Start year of study : 1996
                         End year of study  : 1996
                         Principal publication year: 1999
                         Reference ID of principal publication: KRONQV1999
                         Overlap: No overlap
                         Principal/subsidiary study: principal
                         REF group          : KRONQV
```

KRONQV
(continued)

```
        Study design   Study type          : cross sectional
                        Type of population  : farmers
                        Medical exclusions  : From an initial screening, sampling was 19% among healthy
                         subjects, 75% among those with single-organ hypersensitivity (either lungs or nose/
                         eyes), 99% among those with multiple organ hypersensitivity and 100% among those with
                         allergic alveolitis
                        Respondent          : subject
                        Never/non smoker definition: Never smoked NOS
                        Questionnaire       : Non std/NA/NK

        Asthma          Lifetime/incidence/unspec asthma available: present
                        Source of lifetime asthma diagnosis: Medical records
                        Timing of lifetime asthma: unspecified
                        Timing of incidence asthma: NA (only prevalence analysis)
                        Description of lifetime asthma: history of episodic shortness of breath, wheezing, and
                         breathing difficulties
                        Number of lifetime asthma cases: not assessable
                        Total number of subjects: 581
                        Comments            : Number of subjects estimated from percentage of never smokers

        Confounders     Total number of adjustment factors used: 4
         considered     Adjusted for sex    : present
                        Adjusted for age    : 1
                        Adjusted for exposure to food/housedust allergens: 2
                        Other confounders considered but rejected: present
                        Comments            : Variables rejected from MLR were sensitization to various
                         pollens, mites, animal danders and insects

        Other results   Results available other defns of never/non smoking: present Result also available for
         (not current   ex-smokers
         db)


LARSS1  Study           Study title         : Larsson 1
         description    Full study title    : Swedish part of FinEsS, Orebro CS 1995-6
                        Study sex           : both
                        Lowest age in study : 15
                        Highest age in study (at baseline): 69
                        Study race          : all (in study area)
                        Continent           : Europe
                        Country in Europe   : Sweden
                        Location within country: Orebro (mid Sweden)
                        Start year of study : 1995
                        End year of study   : 1996
                        Principal publication year: 2001
                        Reference ID of principal publication: LARSSO2001
                        Overlap: No overlap
                        Principal/subsidiary study: principal
                        REF group           : LARSS1

        Study design    Study type          : cross sectional
                        Type of population  : randomly selected
                        Medical exclusions  : Family history of asthma
                        Respondent          : subject
                        Never/non smoker definition: Never smoked NOS
                        Questionnaire       : MRC
                        Comments            : Only analyses excluding subjects with family history of asthma
                         are entered here, although some (unadjusted) analyses including those subjects are
                         also available

        Asthma          Lifetime/incidence/unspec asthma available: present
                        Source of lifetime asthma diagnosis: Self report (doctor diag)
                        Timing of lifetime asthma: unspecified
                        Timing of incidence asthma: NA (only prevalence analysis)
                        Description of lifetime asthma: Asthma
                        Number of lifetime asthma cases: 143
                        Total number of subjects: 2784
                        Comments            : The subjects included (i.e. without family history of asthma)
                         represent 78% of all subjects, and 61% of all cases
```

```
LARSS1
(continued)

        Confounders      Total number of adjustment factors used: 3
         considered      Adjusted for sex    : present
                         Adjusted for age    : 1
                         Adjusted for occupation: 1

        Other results    Other definitions of asthma available: present Results available for ever had asthma
         (not current     (self defined), and for use of asthma medication
         db)             Wheezing/wheezing bronchitis available: present Results available for wheeze, and for
                          attacks of breathlessness, wheeze or cough when exposed to exercise, cold air,
                          cigarette smoke or pets
                         Results by other stratifying factors available: present Results with additional
                          subjects with family history of asthma are also available, including results
                          stratified by age (but lacking CIs)


LARSS2  Study            Study title         : Larsson 2
         description     Full study title    : Estonian part of FinEsS, 3 centre CS 1995
                         Study sex           : both
                         Lowest age in study : 15
                         Highest age in study (at baseline): 64
                         Study race          : all (in study area)
                         Continent           : Europe
                         Country in Europe   : Estonia
                         Location within country: Tallinn, Narva and Saaremaa
                         Start year of study : 1995
                         End year of study   : 1996
                         Principal publication year: 2003
                         Reference ID of principal publication: LARSSO2003
                         Overlap: No overlap
                         Principal/subsidiary study: principal
                         REF group           : LARSS2

        Study design     Study type          : cross sectional
                         Type of population  : randomly selected
                         Other exclusions    : Subjects who said they did not leave home
                         Respondent          : subject
                         Never/non smoker definition: Never smoked not even few/week
                         Questionnaire       : MRC

        Asthma           Lifetime/incidence/unspec asthma available: present
                         Source of lifetime asthma diagnosis: Self report (doctor diag)
                         Timing of lifetime asthma: unspecified
                         Timing of incidence asthma: NA (only prevalence analysis)
                         Description of lifetime asthma: Asthma
                         Number of lifetime asthma cases: not assessable
                         Total number of subjects: 6817

        Confounders      Total number of adjustment factors used: 6
         considered      Adjusted for sex    : present
                         Adjusted for age    : 1
                         Adjusted for location within study: 1
                         Adjusted for family (parent/sibl) medical history: 1
                         Adjusted for household ETS exposure: 1
                         Adjusted for workplace ETS exposure: 1

        Other results    Wheezing/wheezing bronchitis available: present Results available for wheeze, for
         (not current     wheeze in last 12 months, and for attacks for breathlessness, wheeze or cough when
         db)              exposed to exercise, cold air, dust, tobacco smoke, exhaust fumes, perfumes, pollen
                          or pets
```

```
MISHRA   Study          Study title        : Mishra
          description   Full study title   : Indian NFHS-2 elderly CS 1998-99 (NFHS-2 = 2nd National Family
                         Health Survey)
                        Study sex          : both
                        Lowest age in study : 60
                        Highest age in study (at baseline): 99
                        Study race         : all (in study area)
                        Continent          : Asia
                        Country in Asia    : India
                        Location within country: nationwide
                        Start year of study : 1998
                        End year of study   : 1999
                        Principal publication year: 2003
                        Reference ID of principal publication: MISHRA2003
                        Overlap: No overlap
                        Principal/subsidiary study: principal
                        REF group          : MISHRA

         Study design  Study type         : cross sectional
                        Type of population  : random households
                        Respondent         : subject or proxy
                        Never/non smoker definition: Never smoked regularly/daily
                        Questionnaire      : Non std/NA/NK

         Asthma        Current asthma available: present
                        Source of current asthma diagnosis: Proxy report (other/unsp/mix)
                        Timing of current asthma: current NOS
                        Description of current asthma: Asthma
                        Number of current asthma cases: 2479
                        Total number of subjects: 28020
                        Comments           : Numbers of cases and of subjects estimated from percentage
                         distribution

         Confounders   Total number of adjustment factors used: 12
          considered   Adjusted for age    : 1
                        Adjusted for location within study: 2
                        Adjusted for religion: 1
                        Adjusted for SES    : 2
                        Adjusted for household composition: 1
                        Adjusted for cooking/heating methods: 1
                        Adjusted for housing quality/age/size: 3
                        Adjusted for education: 1


NG       Study         Study title        : Ng
          description  Full study title   : Singapore CS (ca 1992?)
                        Study sex          : female
                        Lowest age in study : 20
                        Highest age in study (at baseline): 74
                        Study race         : all (in study area)
                        Continent          : Asia
                        Country in Asia    : Singapore
                        Location within country: 5 public housing estates
                        Start year of study : not assessable
                        End year of study   : not assessable
                        Principal publication year: 1993
                        Reference ID of principal publication: NG1993A
                        Overlap: No overlap
                        Principal/subsidiary study: principal
                        REF group          : NG

         Study design  Study type         : cross sectional
                        Type of population  : randomly selected
                        Medical exclusions  : history of cardiac disease
                        Respondent         : subject
                        Never/non smoker definition: Smoked < 1 cig/day for 1 year
                        Questionnaire      : MRC

         Asthma        Current asthma available: present
                        Source of current asthma diagnosis: Self report (doctor diag)
                        Timing of current asthma: in last n months (12<=n<24)
                        Description of current asthma: episodic wheeze and asthmatic symptoms diagnosed as
                         asthma in past year
                        Number of current asthma cases: 33
                        Total number of subjects: 1282
```

NG
(continued)

```
        Confounders    Total number of adjustment factors used: 6
         considered    Adjusted for age     : 1
                       Adjusted for race    : 1
                       Adjusted for location within study: 1
                       Adjusted for cooking/heating methods: 1
                       Adjusted for housing quality/age/size: 1
                       Adjusted for occupation: 1

        Other results  Wheezing/wheezing bronchitis available: present Results available for wheeze
         (not current  Results by other stratifying factors available: present Results available for
          db)           housewives (i.e. excluding subjects who might have workplace ETS exposure)


NHANES  Study          Study title        : NHANES III
        description    Full study title   : NHANES III nationwide CS 1988-94 (NHANES = Third National Health
                        and Nutrition Examination Survey)
                       Study sex          : both
                       Lowest age in study : 17
                       Highest age in study (at baseline): 99
                       Study race         : all (in study area)
                       Continent          : NAmerica
                       US state           : nationwide
                       Location within country: Nationwide
                       Start year of study : 1988
                       End year of study   : 1994
                       Principal publication year: 2002
                       Reference ID of principal publication: EISNER2002B
                       Overlap: No overlap
                       Principal/subsidiary study: principal
                       REF group          : NHANES

        Study design   Study type         : cross sectional
                       Type of population : randomly selected
                       Other exclusions   : institutionalized persons and non-civilians
                       Respondent         : subject
                       Never/non smoker definition: Not curr smk and serum cot <14
                       Questionnaire      : Non std/NA/NK

        Asthma         Current asthma available: present
                       Source of current asthma diagnosis: Self report (doctor diag)
                       Timing of current asthma: current NOS
                       Description of current asthma: Ever been told by a doctor that had asthma, still has
                        asthma, and never had physician diagnosis of emphysema
                       Number of current asthma cases: 440
                       Total number of subjects: 10581

        Other results  Other exposures available: present Median serum cotinine also available in subjects
         (not current   with and without asthma
          db)


ORYSZC  Study          Study title        : Oryszczyn
        description    Full study title   : French EGEA CC (ca 1996?) (EGEA = Epidemiological Study of the
                        Genetics and Environment of Asthma)
                       Study sex          : both
                       Lowest age in study : 25
                       Highest age in study (at baseline): 54
                       Study race         : all (in study area)
                       Continent          : Europe
                       Country in Europe  : France
                       Location within country: Paris, Lyon, Marseilles, Montpellier, Grenoble
                       Start year of study : not assessable
                       End year of study   : not assessable
                       Principal publication year: 2000
                       Reference ID of principal publication: ORYSZC2000
                       Reference ID of additional publication(s): KAUFFM1997
                       Overlap: No overlap
                       Principal/subsidiary study: principal
                       REF group          : ORYSZC
```

```
ORYSZC
(continued)

        Study design    Study type          : case/control
                        Type of controls (for CC studies): both
                        Control diseases    : unstated (recruitment at surgery departments and a check up
                         center)
                        Type of population  : unstated
                        Respondent          : subject
                        Never/non smoker definition: Never smoked regularly/daily
                        Questionnaire       : MRC,ATS,ECRHS
                        Comments            : Additional results for relatives of asthma cases have not been
                         entered here

        Asthma          Current asthma available: present
                        Source of current asthma diagnosis: Self report (other/unspec/mix)
                        Timing of current asthma: in last n months (12<=n<24)
                        Description of current asthma: Attending chest clinic and positive answer to 4
                         questions (ever had attacks of breathlessness at rest with wheezing; ever had asthma
                         attacks; diagnosis confirmed by a doctor; had asthma attack in last 12 months), or
                         positive answers to 2-3 of the questions and examination of medical records
                        Number of current asthma cases: 51
                        Total number of subjects: 139

        Matching        Comments            : According to ORYSZC2000, no matching was performed but
         factors         comparability was controlled to avoid disparities by centre, season, sex and age.
                         However according to KAUFFM1997 controls were matched on age, month and centre


PILOTT  Study           Study title         : Pilotto
         description    Full study title    : Port Adelaide CS 1995
                        Study sex           : both
                        Lowest age in study : 18
                        Highest age in study (at baseline): 99
                        Study race          : all (in study area)
                        Continent           : Australia
                        Location within country: Port Adelaide (South Australia)
                        Start year of study : 1995
                        End year of study   : 1995
                        Principal publication year: 1999
                        Reference ID of principal publication: PILOTT1999
                        Overlap: No overlap
                        Principal/subsidiary study: principal
                        REF group           : PILOTT

        Study design    Study type          : cross sectional
                        Type of population  : random households
                        Respondent          : subject
                        Never/non smoker definition: Not current smoker
                        Questionnaire       : Non std/NA/NK

        Asthma          Lifetime/incidence/unspec asthma available: present
                        Source of lifetime asthma diagnosis: Self report (other/unspec/mix)
                        Timing of lifetime asthma: unspecified
                        Timing of incidence asthma: NA (only prevalence analysis)
                        Description of lifetime asthma: Asthma
                        Number of lifetime asthma cases: not assessable
                        Total number of subjects: 1123

        Confounders     Total number of adjustment factors used: 3
         considered     Adjusted for sex    : present
                        Adjusted for age    : 1
                        Adjusted for location within study: 1

        Other results   Wheezing/wheezing bronchitis available: present Results available for wheeze
         (not current
         db)
```

```
PLATTS  Study           Study title        : Platts-Mills
        description     Full study title   : Wilmington acute asthma CC 1988-89
                        Study sex          : both
                        Lowest age in study : 15
                        Highest age in study (at baseline): 55
                        Study race         : all (in study area)
                        Continent          : NAmerica
                        US state           : Delaware
                        Location within country: Wilmington (Delaware)
                        Start year of study : 1988
                        End year of study  : 1989
                        Principal publication year: 1993
                        Reference ID of principal publication: PLATTS1993
                        Reference ID of additional publication(s): GELBER1993, MOYER1993
                        Overlap: No overlap
                        Principal/subsidiary study: principal
                        REF group          : PLATTS

        Study design    Study type         : case/control
                        Type of controls (for CC studies): diseased
                        Control diseases   : Presenting at ER with any condition other than breathlessness
                        Type of population : all
                        Respondent         : subject
                        Never/non smoker definition: Not active smoker
                        Questionnaire      : Non std/NA/NK
                        Comments           : It is not clear whether the analysis includes never or non
                         smokers

        Asthma          Current asthma available: present
                        Source of current asthma diagnosis: Medical records
                        Timing of current asthma: current diagnosis
                        Description of current asthma: Acute asthma (presenting at ER with breathlessness for
                         which the physician on call prescribed urgent treatment for airway obstruction)
                        Number of current asthma cases: 48
                        Total number of subjects: 89

        Matching        Cases and controls matched on sex: present
         factors        Cases and controls matched on age (CC): present


RAHERI  Study           Study title        : Raherison
        description     Full study title   : ECRHS Bordeaux centre CS 1991-92 (ECRHS = European Community
                         Respiratory Health Study)
                        Study sex          : both
                        Lowest age in study : 20
                        Highest age in study (at baseline): 44
                        Study race         : all (in study area)
                        Continent          : Europe
                        Country in Europe  : France
                        Location within country: Bordeaux
                        Start year of study : 1991
                        End year of study  : 1992
                        Principal publication year: 2003
                        Reference ID of principal publication: RAHERI2003
                        Overlap: JANSON/RAHERI
                        Principal/subsidiary study: subsidiary
                        REF group          : JANSON
                        Comments           : Results for current asthma from 17 countries entered as study
                         JANSON; results for lifetime asthma from Bordeaux (France) only entered as study
                         RAHERI

        Study design    Study type         : case/control
                        Type of controls (for CC studies): healthy
                        Type of population : randomly selected
                        Type of population - controls (if diff from cases): without history of asthma
                        Respondent         : subject
                        Never/non smoker definition: Smoked < 1 year
                        Questionnaire      : ECRHS
                        Comments           : Cases were all asthmatics identified in earlier screening phase,
                         controls randomly selected from remainder
```

RAHERI
(continued)

        Asthma   Lifetime/incidence/unspec asthma available: present
                        Source of lifetime asthma diagnosis: Self report (doctor diag)
                        Timing of lifetime asthma: Lifetime
                        Timing of incidence asthma: NA (only prevalence analysis)
                        Description of lifetime asthma: Asthma
                        Number of lifetime asthma cases: 96
                        Total number of subjects: 544

        Confounders   Total number of adjustment factors used: 10
         considered   Adjusted for sex   : present
                        Adjusted for age   : 1
                        Adjusted for family (parent/sibl) medical history: 1
                        Adjusted for subject's medical history: 7

        Other results   Wheezing/wheezing bronchitis available: present Results available for wheeze without
         (not current   asthma
         db)   Results available other defns of never/non smoking: present Results available in ever
                         smokers for asthma onset before start of smoking

ROBBIN Study   Study title   : Robbins
        description   Full study title : California 7th Day Adventist PS 1977-87
                        Study sex   : both
                        Lowest age in study : 25
                        Highest age in study (at baseline): 99
                        Highest age in study at final followup: 99
                        Study race   : whites (exc hispanic)
                        Continent   : NAmerica
                        US state   : California
                        Location within country: California, mainly San Francisco, LA and San Diego
                        Start year of study : 1977
                        End year of study   : 1977
                        Final follow up year: 1992
                        Principal publication year: 1993
                        Reference ID of principal publication: ROBBIN1993
                        Reference ID of additional publication(s): GREER1993, MCDONN1999
                        Overlap: No overlap
                        Principal/subsidiary study: principal
                        REF group   : ROBBIN

        Study design   Study type   : prospective
                        Type of population : randomly selected
                        Other exclusions : Resident near baseline address <10y. Died before follow-up
                         (1987: ROBBIN1993, GREER1993 or 1992: MCDONN1999). Includes only Seventh Day
                         Adventists
                        Respondent   : subject
                        Never/non smoker definition: Not current smoker
                        Questionnaire   : MRC

        Asthma   Lifetime/incidence/unspec asthma available: present
                        Source of lifetime asthma diagnosis: Self report (other/unspec/mix)
                        Timing of lifetime asthma: NA (incidence only)
                        Timing of incidence asthma: since baseline (earlier excl)
                        Description of lifetime asthma: Definite asthma (physician-diagnosed asthma, and
                         breathing sounded wheezy or attacks of SOB with wheezing) - ROBBIN1993, GREER1993;
                         Doctor-told asthma (ever told by doctor had asthma) - MCDONN1999
                        Number of lifetime asthma cases: 80
                        Total number of subjects: 3602
                        Comments   : Numbers of cases and at-risk subjects refer to definite asthma
                         at 1987 follow-up (ROBBIN1993). The numbers for doctor-told asthma at 1992 follow-up
                         are 138 and 2671 respectively (MCDONN1999, cases based on %s)

        Confounders   Total number of adjustment factors used: 7
         considered   Adjusted for sex   : present
                        Adjusted for age   : 1
                        Adjusted for location within study: 1
                        Adjusted for education: 1
                        Adjusted for subject's medical history: 1
                        Adjusted for active smoking (ex/never): 1
                        Adjusted for workplace ETS exposure: 1
                        Other confounders considered but rejected: present
                        Comments   : Rejected variables: SMED, OCCUP, OETS (living with smoker)

ROBBIN
(continued)

      Other results   Other definitions of asthma available: present Results also available for adult-onset
      (not current   asthma (GREER1993)
      db)

SAPALD Study   Study title   : SAPALDIA
      description   Full study title   : SAPALDIA CS 1991 (SAPALDIA = Swiss Study on Air Pollution and
                   Lung Diseases in Adults)
                   Study sex   : both
                   Lowest age in study : 18
                   Highest age in study (at baseline): 60
                   Study race   : all (in study area)
                   Continent   : Europe
                   Country in Europe : Switzerland
                   Location within country: Aarau, Basel, Davos, Geneva, Lugano, Montana, Payerne, Wald
                   Start year of study : 1991
                   End year of study   : 1991
                   Principal publication year: 1994
                   Reference ID of principal publication: LEUENB1994
                   Reference ID of additional publication(s): LEUENB1993,ZEMP1999,KUNZLI2000
                   Overlap: No overlap
                   Principal/subsidiary study: principal
                   REF group   : SAPALD

      Study design   Study type   : cross sectional
                   Type of population : randomly selected
                   Other exclusions   : residents for <3 yrs
                   Respondent   : subject
                   Never/non smoker definition: Smk <20 pks cigs/360g lifetime
                   Questionnaire   : ECRHS

      Asthma   Lifetime/incidence/unspec asthma available: present
                   Source of lifetime asthma diagnosis: Self report (doctor diag)
                   Timing of lifetime asthma: Lifetime
                   Timing of incidence asthma: NA (only prevalence analysis)
                   Description of lifetime asthma: Asthma
                   Current asthma available: present
                   Source of current asthma diagnosis: Self report (other/unspec/mix)
                   Timing of current asthma: in last n months (12<=n<24)
                   Description of current asthma: Ever had physician diagnosed asthma, and wheezing or
                   usual cough in last 12 months
                   Number of lifetime asthma cases: 287
                   Number of current asthma cases: not assessable
                   Total number of subjects: 4197
                   Comments   : Number of subjects included in the analysis (based on serum
                   cotinine <14 ng/ml) exceeds the number of self-reported never and ex-smokers (3218 vs
                   2824, Tables 3-4 BECKET2001)

      Confounders   Total number of adjustment factors used: 8
      considered   Adjusted for sex   : present
                   Adjusted for age   : 1
                   Adjusted for location within study: 1
                   Adjusted for family (parent/sibl) medical history: 3
                   Adjusted for subject's medical history: 1
                   Adjusted for obesity/BMI: 1
                   Comments   : Confounders given here are the Basic model. Some results
                   additionally adjust for education or for occupational exposure, or (in a subset only)
                   for paternal smoking in childhood

      Other results   Other definitions of asthma available: present Results available for
      (not current   physician-diagnosed asthma or wheeze without cold in last 12 months (KUNZLI2000)
      db)   Wheezing/wheezing bronchitis available: present Results available for wheeze without
                   colds
                   Results available other defns of never/non smoking: present Results available also
                   excluding subjects with expired CO >= 7ppm
                   Results by other stratifying factors available: present Results available excluding
                   subjects whose mother ever smoked

```
THORN    Study          Study title        : Thorn
          description   Full study title   : Alvsborg nested CC 1994
                        Study sex          : both
                        Lowest age in study : 20
                        Highest age in study (at baseline): 50
                        Study race         : all (in study area)
                        Continent          : Europe
                        Country in Europe  : Sweden
                        Location within country: Alvsborg (western Sweden)
                        Start year of study : 1994
                        End year of study  : 1994
                        Principal publication year: 2001
                        Reference ID of principal publication: THORN2001
                        Overlap: No overlap
                        Principal/subsidiary study: principal
                        REF group          : THORN

         Study design  Study type         : case/control
                        Type of controls (for CC studies): healthy
                        Type of population : randomly selected
                        Respondent         : subject
                        Never/non smoker definition: Never smoked NOS
                        Questionnaire      : Non std/NA/NK
                        Comments           : Subjects were drawn from a cross-sectional study conducted the
                         previous year

         Asthma         Lifetime/incidence/unspec asthma available: present
                        Source of lifetime asthma diagnosis: Self report (doctor diag)
                        Timing of lifetime asthma: from age 16 (ie adult onset)
                        Timing of incidence asthma: NA (only prevalence analysis)
                        Description of lifetime asthma: Physician-diagnosed asthma, onset after age 16 (and
                         not more than 15 years ago)
                        Number of lifetime asthma cases: 69
                        Total number of subjects: 487

         Confounders    Total number of adjustment factors used: 2
          considered    Adjusted for age   : 1
                        Adjusted for subject's medical history: 1
```

Appendix E

Detailed structure of the relative risk database

Card Name	Field Name	Short Name	Position Number	Type	
RR Description		RRDEF	1		
	Number of RR within study	NRR	8	Measured+v	(1 to 440)
	Sex	RSEX	9	Graded>0	(system 16)
	Lowest age in RR	rAGELO	10	Measured	(0 to 99)
	Highest age in RR	rAGEHI	11	Measured	(0 to 99)
	Race	rRACE	12	Graded	(system 27)
	Time of asthma	rASTIM	13	Graded>0	(system 17)
	Onset	ONSET	14	Presence	(system 6)
	Odds ratio used for onset	ODDSON	15	Presence	(system 6)
	Exposure type	EXPOS	16	Graded>0	(system 18)
	Household - who smoked	WHOHOU	17	Graded>0	(system 19)
	Total - who smoked	WHOTOT	18	Graded>0	(system 20)
	Exposure - when smoked	WHESMO	19	Graded	(system 21)
	Dose-response	DOSER	20	Graded>0	(system 22)
	Measure of exposure	MEASEX	21	Graded>0	(system 23)
	Exposed - low value	EXPLO	22	Real	(0.00 to 999.00)
	Exposed - high value	EXPHI	23	Real	(0.00 to 999.00)
	Unexposed - time	UNEXTI	24	Graded>0	(system 24)
	Unexposed - source	UNEXSO	25	Graded>0	(system 25)
	Unexposed - high value	UNEXHI	26	Real	(0.00 to 999.00)
	Source	SOURCE	27	Character	(50)
RR adjustment		RRADJ	2		
	Adjusted for sex	ADSEX	32	Presence	(system 6)
	Adjusted for age	ADAGE	33	Presence	(system 6)
	Adjusted for race	ADRACE	34	Presence	(system 6)
	Adjusted for active smoking (ex/never)	ADACSM	35	Presence	(system 6)
	Adjusted for other sources of ETS	ADOETS	36	Graded	(system 26)
	Adjusted for other variables	ADOTHR	37	Graded	(system 26)
RR data		RRDATA	3		
	Cases exposed	CA1	42	Measured	(0 to 9999)
	Cases, unexposed	CA0	43	Measured	(0 to 9999)
	Controls, exposed	CO1	44	Measured	(0 to 9999)
	Controls, unexposed	CO0	45	Measured	(0 to 9999)
	Relative risk	RR	46	Real	(0.00 to 999.00)
	RR lower 95% CL	RRL	47	Real	(0.00 to 999.00)
	RR upper 95% CL	RRU	48	Real	(0.00 to 999.00)
	Derived RR	DERIVE	49	Graded	(system 28)
Discrepancy		DISCR	4		
Derived 2 - Principal/subsid		DER2	5		
	REF group	REFGP	62	Character	(6)
	Principal/subsidary RR	RPRINC	63	Graded	(system 29)
Derived 3 - RR checks		DER3	6		
	Central RR/CI (should be 1.0)	CENTR	68	Real	(0.000 to 999.000)
	Minimum number of cases (CC/CS study)	MINCAS	69	Real	(0.0 to 16959.0)
	Minimum number of subjects in total (CC/CS study)	MINTOT	70	Real	(0.0 to 16959.0)
Transformed Fields		TRI	-3		
	N adjusted for	ADTOT	58	Measured	(0 to 20)

The grading systems used are as follows
_____

  Grading Level (character equivalent)   Tumour Type
  System
_____

```
    6      1 (x) present                                0

   16      1 (b) both                                   0
           2 (m) male                                   0
           3 (f) female                                 0

   17      1 (l) lifetime                               0
           2 (c) current                                0

   18      1 (h) household                              0
           2 (w) work                                   0
           3 (t) total                                  0

   19      1 (a) all                                    0
           2 (m) mother                                 0
           3 (f) father                                 0

   20      1 (1) total NOS                              0
           2 (2) serum cotinine                         0
           3 (3) home and/or work                       0

   21      1 (l) lifetime                               0
           2 (n) current (now)                          0
           3 (y) childhood (youth)                      0
           4 (e) ever                                   0
           5 (m) marriage                               0
           6 (u) unspecified                            0
           7 (r) recent years                           0
           8 (8) childhood but not adult                0
           9 (9) adult but not childhood                0
          10 (a) adult                                  0
          11 (b) both adult and child                   0

   22      1 (1) all                                    0
           2 (2) level 1                                0
           3 (3) level 2                                0
           4 (4) level 3                                0
           5 (5) level 4                                0
           6 (6) level 5                                0
           7 (7) level 6                                0
           8 (8) level 7                                0
           9 (9) level 8                                0
          10 (a) level 9                                0
          11 (b) per unit dose regression              0
          12 (c) dose response other                   0

   23      1 (1) yes/no                                 0
           2 (n) cigarettes/day                         0
           3 (y) years                                  0
           4 (k) pack-years                             0
           5 (h) hours/day                              0
           6 (b) ng/ml                                  0
           7 (7) persons                                0

   24      1 (1) non                                    0
           2 (2) never                                  0
           3 (3) non+other                              0

   25      1 (1) none (or low)                          0
           2 (2) none of type (as in EXPOS)             0
           3 (3) neither parent                         0
           4 (4) not specified hh menber                0

   26      1 (1) 1                                      0
           2 (2) 2                                      0
           3 (3) 3                                      0
           4 (4) 4                                      0
           5 (5) 5                                      0
```

```
         6 (6) 6                               0
         7 (7) 7                               0
         8 (8) 8                               0
         9 (9) 9                               0
        10 (a) 10                              0
        11 (b) 11                              0
        12 (c) 12                              0
        13 (d) 13                              0
        14 (e) 14                              0
        15 (f) 15                              0
        16 (g) 16                              0
        17 (h) 17                              0
        18 (i) 18                              0
        19 (j) 19                              0
        20 (k) +ve but unknown                 0

27       2 (w) white                           0
         3 (b) black                           0
         4 (4) white exc hispanic              0
         5 (5) hispanic white                  0

28       1 (1) original                        0
         2 (2) RR/CI from numbers              0
         3 (3) RR/CI recalc from numbers       0
         4 (4) Sum over exposure levels        0
        10 (a) non-significant                 0
        11 (b) significant                     0
        14 (e) F&L over exposure levels        0

29       1 (1) principal                       0
         2 (2) subsidiary study                0
```
_____

Appendix Table F1 -

IASTAD - Meta-analysis of Biochemical/Total/Household/Workplace Exposure (preferring earliest)
Lifetime/Current Asthma

This analysis is restricted to results for:
1) Biochemical, total, household (overall), parental, or workplace exposure
2) Results not by amount of exposure
3) Results complete enough for use in metaanalysis

Within each study, results are then selected (in the following order of preference, within each sex) for:
4) ASTHMA : lifetime, current
5) EXPOS   : biochemical (cotinine), total, household, workplace
6) WHESMO : 3=childhood, 1=lifetime, 10=adult, 7=recent, 6=unspec, 2=current
7) WHOHOU : household overall, mother
8) UNEXTI : unexposed group never, non (i.e. not at time defined for exposed group)
9) For overlapping studies: principal rather than subsidiary studies
Finally for single sex results (m, f) in preference to results for both sexes combined (b).

Results adjusted for the most potential confounders are then chosen in Sections -1 to -3
and results adjusted for the least confounders in Sections -4 to -6. (Those least adjusted results which
actually differ from the most adjusted are marked 'x' in column X in Section -4)

Section -7 shows excluded studies, together with the stage (as above) at which no qualifying results
were found. It then lists the potentially overlapping studies which have been included (1=principal,
2=subsidiary), and any results which would have been included in preference except that they had data
not complete enough for use in metaanalysis. It also lists their significance (yes/no), if known.

Appendix Table F1 - 1

IASTAD - Meta-analysis of Biochemical/Total/Household/Workplace Exposure (preferring earliest)
Lifetime/Current Asthma
Adjusted

REF	NRR	SEX	AST	SMOK	AGEL	AGEH	LOC	BEGYR	PUBYR	STTYP	ONS	ADJ	EXPOS	UNEXsrce	EXPOS-time	UNEXTI
BECKE2	2	b	l	Non	18	40	US:mul	1985	2001	Pr	prv	5	Cot	Low	current	non
BECKE2	4	b	l	Non	18	40	US:mul	1985	2001	Pr	ons	5	Cot	Low	current	non
JAAKK2	34	b	c	Never	21	63	Eu:Fin	1997	2003	CC	ons	7	Hh,Wk	None	lifetime	non
JANSON	1	b	c	<1yr	20	48	multi	1990	2001	CS	prv	9	Hh,Wk	None	current	non
JEDRYC	1	f	c	<1yr	65	99	Eu:Pol	*	1995	CS	prv	3	Hh	NoHhMemb	current	non
LARSS1	2	b	l	Never	15	69	Eu:Swe	1995	2001	CS	prv	3	Hh	NoHhMemb	childhood	non
LARSS2	4	b	l	Never	15	64	Eu:Est	1995	2003	CS	prv	5	Work	NotWork	current	non
MISHRA	3	m	c	NevReg	60	99	As:Ind	1998	2003	CS	prv	12	Hh	NoHhMemb	current	non
MISHRA	4	f	c	NevReg	60	99	As:Ind	1998	2003	CS	prv	12	Hh	NoHhMemb	current	non
NG	6	f	c	<1yr	20	74	As:Sin	*	1993	CS	prv	6	Hh	NoHhMemb	lifetime	non
NHANES	1	b	c	Non	17	99	US:nat	1988	2002	CS	prv	0	Hh	NoHhMemb	current	non
ORYSZC	1	m	c	NevReg	25	54	Eu:Fra	*	2000	CC	prv	0	Hh	NoHhMemb	current	non
ORYSZC	2	f	c	NevReg	25	54	Eu:Fra	*	2000	CC	prv	0	Hh	NoHhMemb	current	non
PILOTT	1	b	l	Non	18	99	Austra	1995	1999	CS	prv	3	Hh	NoHhMemb	unspec	non
ROBBIN	10	b	l	Non	25	99	US:Cal	1977	1993	Pr	ons	4	Hh,Wk	None	childhood	never
SAPALD	2	b	l	<20pks	18	60	Eu:Swi	1991	1994	CS	prv	8	Hh,Wk	None	current	non
THORN	2	m	l	Never	20	50	Eu:Swe	1994	2001	CC	prv	2	Hh	NoHhMemb	last6homes	non
THORN	3	f	l	Never	20	50	Eu:Swe	1994	2001	CC	prv	2	Hh	NoHhMemb	last6homes	non

Appendix Table F1 - 2

IASTAD - Meta-analysis of Biochemical/Total/Household/Workplace Exposure (preferring earliest)
Lifetime/Current Asthma
Adjusted

				Numbers						
				Numbers exposed		Non-exposed				
REF	NRR	SEX	ADJ	Case	Cont	Case	Cont	RR	95.00%CI	
BECKE2	2	b	5	63	–	215	–	0.74 (	0.55-	1.00)
*BECKE2	4	b	5	54	–	141	–	0.96 (	0.70-	1.32)
Subtotal BECKE2								0.84 (	0.67-	1.04)
JAAKK2	34	b	7	135	–	104	–	1.40 (	0.99-	1.96)
JANSON	1	b	9	–	–	–	–	1.15 (	0.84-	1.58)
JEDRYC	1	f	3	–	–	–	–	0.53 (	0.24-	1.14)
LARSS1	2	b	3	85	–	58	–	1.82 (	1.28-	2.58)
LARSS2	4	b	5	–	–	–	–	1.13 (	0.80-	1.59)
MISHRA	3	m	12	242	–	835	–	1.20 (	0.99-	1.46)
MISHRA	4	f	12	561	–	829	–	1.05 (	0.91-	1.21)
Subtotal MISHRA								1.10 (	0.98-	1.23)
NG	6	f	6	18	–	15	–	1.18 (	0.57-	2.46)
NHANES	1	b	0	70	1481	370	8660	1.11 (	0.85-	1.44)
ORYSZC	1	m	0	3	4	14	28	1.50 (	0.29-	7.65)
ORYSZC	2	f	0	8	13	26	43	1.02 (	0.37-	2.78)
Subtotal ORYSZC								1.13 (	0.48-	2.67)
PILOTT	1	b	3	–	–	–	–	1.09 (	0.65-	1.82)
*ROBBIN	10	b	4	–	–	–	–	1.57 (	0.96-	2.58)
SAPALD	2	b	8	96	–	191	–	1.39 (	1.04-	1.86)
THORN	2	m	2	–	–	–	–	4.80 (	2.00-	11.60)
THORN	3	f	2	–	–	–	–	1.50 (	0.80-	3.10)
Subtotal THORN								2.31 (	1.35-	3.96)
Partial Totals				1335	1498	2798	8731			

*prospective study

REF	NRR	SEX	ADJ	Ys	Ws	Qs	Ps
BECKE2	2	b	5	-0.30	42.99	8.17	0.0483
*BECKE2	4	b	5	-0.04	38.19	1.18	0.8008
Subtotal BECKE2				-0.61	81.18	9.34	
JAAKK2	34	b	7	0.34	32.94	1.34	0.0535
JANSON	1	b	9	0.14	38.50	0.00	0.3859
JEDRYC	1	f	3	-0.63	6.33	3.75	0.1102
LARSS1	2	b	3	0.60	31.28	6.74	0.0008
LARSS2	4	b	5	0.12	32.57	0.01	0.4855
MISHRA	3	m	12	0.18	101.81	0.23	0.0658
MISHRA	4	f	12	0.05	189.27	1.40	0.5021
Subtotal MISHRA				-0.04	291.08	1.63	
NG	6	f	6	0.17	7.19	0.01	0.6573
NHANES	1	b	0	0.10	56.25	0.06	0.4488
ORYSZC	1	m	0	0.41	1.45	0.11	0.6256
ORYSZC	2	f	0	0.02	3.79	0.05	0.9727
Subtotal ORYSZC				0.15	5.24	0.16	
PILOTT	1	b	3	0.09	14.49	0.03	0.7428
*ROBBIN	10	b	4	0.45	15.72	1.57	0.0737
SAPALD	2	b	8	0.33	45.46	1.72	0.0264
THORN	2	m	2	1.57	4.97	10.22	0.0005
THORN	3	f	2	0.41	8.37	0.61	0.2406
Subtotal THORN				1.70	13.35	10.84	

Appendix Table F1 - 2

IASTAD - Meta-analysis of Biochemical/Total/Household/Workplace Exposure (preferring earliest)
Lifetime/Current Asthma
Adjusted

```
           N       18
          NS       14


          Wt   671.57
  Het Chi    37.20
  Het  df       17
  Het  P        **
Fixed  RR     1.14
         RRl    1.06
         RRu    1.23
          P      +++
Random  RR     1.19
         RRl    1.04
         RRu    1.35
          P        +
Asymm  P      N.S.
```

Appendix Table F1 - 3

IASTAD - Meta-analysis of Biochemical/Total/Household/Workplace Exposure (preferring earliest)
Lifetime/Current Asthma
Adjusted

Overall

```
            N      18
            NS     14


           Wt   671.57
      Het Chi   37.20
      Het  df      17
      Het  P       **
    Fixed  RR    1.14
           RRl   1.06
           RRu   1.23
            P    +++
   Random  RR    1.19
           RRl   1.04
           RRu   1.35
            P      +
    Asymm  P    N.S.
```

	Sex			
	both	male	female	Total
N	10	3	5	18
NS	9	3	5	17
Wt	348.39	108.23	214.95	671.57
Het Chi	20.69	9.15	4.12	37.20
Het df	9	2	4	17
Het P	*	*	N.S.	**
Fixed RR	1.17	1.28	1.05	1.14
RRl	1.05	1.06	0.92	1.06
RRu	1.30	1.55	1.20	1.23
P	++	++	N.S.	+++
Random RR	1.18	2.02	1.05	1.19
RRl	1.01	0.73	0.89	1.04
RRu	1.39	5.56	1.23	1.35
P	+	N.S.	N.S.	+
Between Chi				3.24
Between df				2
Between P				N.S.

	Asthma definition (lifetime/current)		
	lifetime	current	Total
N	9	9	18
NS	7	7	14
Wt	234.06	437.52	671.57
Het Chi	29.72	6.66	37.20
Het df	8	8	17
Het P	***	N.S.	**
Fixed RR	1.20	1.12	1.14
RRl	1.06	1.02	1.06
RRu	1.36	1.22	1.23
P	++	+	+++
Random RR	1.31	1.12	1.19
RRl	1.01	1.02	1.04
RRu	1.70	1.22	1.35
P	+	+	+
Between Chi			0.82
Between df			1
Between P			N.S.

Appendix Table F1 - 3

IASTAD - Meta-analysis of Biochemical/Total/Household/Workplace Exposure (preferring earliest)
Lifetime/Current Asthma
Adjusted

| | | Continent | | | |
		NAmer	Europe	Oth/Mult	Total
	N	4	9	5	18
	NS	3	7	4	14
	Wt	153.15	167.17	351.26	671.57
Het	Chi	7.71	17.60	1.28	37.20
Het	df	3	8	4	17
Het	P	(*)	*	N.S.	**
Fixed	RR	0.99	1.40	1.11	1.14
	RRl	0.84	1.21	1.00	1.06
	RRu	1.16	1.63	1.23	1.23
	P	N.S.	+++	(+)	+++
Random	RR	1.01	1.40	1.11	1.19
	RRl	0.78	1.08	1.00	1.04
	RRu	1.32	1.82	1.23	1.35
	P	N.S.	++	(+)	+
Between	Chi				10.60
Between	df				2
Between	P				**

| | | Start year of study | | | |
		<1990	1990-99	unknown	Total
	N	4	10	4	18
	NS	3	8	3	14
	Wt	153.15	499.67	18.76	671.57
Het	Chi	7.71	20.84	2.74	37.20
Het	df	3	9	3	17
Het	P	(*)	*	N.S.	**
Fixed	RR	0.99	1.21	0.89	1.14
	RRl	0.84	1.11	0.57	1.06
	RRu	1.16	1.32	1.40	1.23
	P	N.S.	+++	N.S.	+++
Random	RR	1.01	1.30	0.89	1.19
	RRl	0.78	1.12	0.57	1.04
	RRu	1.32	1.52	1.40	1.35
	P	N.S.	+++	N.S.	+
Between	Chi				5.91
Between	df				2
Between	P				(*)

| | | Publication year | | |
		1990-99	2000+	Total
	N	5	13	18
	NS	5	9	14
	Wt	89.20	582.38	671.57
Het	Chi	6.28	29.99	37.20
Het	df	4	12	17
Het	P	N.S.	**	**
Fixed	RR	1.26	1.13	1.14
	RRl	1.02	1.04	1.06
	RRu	1.55	1.22	1.23
	P	+	++	+++
Random	RR	1.20	1.18	1.19
	RRl	0.90	1.02	1.04
	RRu	1.60	1.37	1.35
	P	N.S.	+	+
Between	Chi			0.93
Between	df			1
Between	P			N.S.

Appendix Table F1 - 3

IASTAD - Meta-analysis of Biochemical/Total/Household/Workplace Exposure (preferring earliest)
Lifetime/Current Asthma
Adjusted

		CC	Pr	CS	Total
	Study type				
	N	5	3	10	18
	NS	3	2	9	14
	Wt	51.53	96.90	523.14	671.57
Het	Chi	7.37	6.59	13.91	37.20
Het	df	4	2	9	17
Het	P	N.S.	*	N.S.	**
Fixed	RR	1.56	0.93	1.15	1.14
	RRl	1.19	0.76	1.06	1.06
	RRu	2.05	1.13	1.26	1.23
	P	++	N.S.	++	+++
Random	RR	1.69	0.99	1.18	1.19
	RRl	1.06	0.68	1.04	1.04
	RRu	2.69	1.45	1.33	1.35
	P	+	N.S.	++	+
Between	Chi				9.32
Between	df				2
Between	P				**

		excluded	included	Total
	Ex smokers			
	N	13	5	18
	NS	10	4	14
	Wt	503.93	167.65	671.57
Het	Chi	25.13	7.84	37.20
Het	df	12	4	17
Het	P	*	(*)	**
Fixed	RR	1.20	1.00	1.14
	RRl	1.10	0.86	1.06
	RRu	1.31	1.16	1.23
	P	+++	N.S.	+++
Random	RR	1.27	1.02	1.19
	RRl	1.09	0.82	1.04
	RRu	1.49	1.27	1.35
	P	++	N.S.	+
Between	Chi			4.23
Between	df			1
Between	P			*

		15-19	20-25	60+	Total
	Lowest age in RR				
	N	7	8	3	18
	NS	6	6	2	14
	Wt	261.23	112.93	297.41	671.57
Het	Chi	17.81	9.87	4.48	37.20
Het	df	6	7	2	17
Het	P	**	N.S.	N.S.	**
Fixed	RR	1.12	1.38	1.08	1.14
	RRl	0.99	1.15	0.97	1.06
	RRu	1.27	1.66	1.21	1.23
	P	(+)	+++	N.S.	+++
Random	RR	1.13	1.44	1.06	1.19
	RRl	0.91	1.12	0.86	1.04
	RRu	1.40	1.83	1.31	1.35
	P	N.S.	++	N.S.	+
Between	Chi				5.04
Between	df				2
Between	P				(*)

Appendix Table F1 - 3

IASTAD - Meta-analysis of Biochemical/Total/Household/Workplace Exposure (preferring earliest)
Lifetime/Current Asthma
Adjusted

Highest age in RR

	-55	60-69	70+	Total
N	7	4	7	18
NS	4	4	6	14
Wt	138.27	142.25	391.06	671.57
Het Chi	18.51	3.64	6.58	37.20
Het df	6	3	6	17
Het P	**	N.S.	N.S.	**
Fixed RR	1.02	1.41	1.10	1.14
RRl	0.86	1.20	1.00	1.06
RRu	1.20	1.66	1.22	1.23
P	N.S.	+++	+	+++
Random RR	1.20	1.41	1.11	1.19
RRl	0.84	1.18	0.99	1.04
RRu	1.70	1.69	1.24	1.35
P	N.S.	+++	(+)	+
Between Chi				8.47
Between df				2
Between P				*

Physician diagnosis

	yes	no/mixed	Total
N	11	7	18
NS	9	5	14
Wt	306.54	365.04	671.57
Het Chi	33.64	3.26	37.20
Het df	10	6	17
Het P	***	N.S.	**
Fixed RR	1.17	1.12	1.14
RRl	1.05	1.01	1.06
RRu	1.31	1.24	1.23
P	++	+	+++
Random RR	1.22	1.12	1.19
RRl	0.97	1.01	1.04
RRu	1.52	1.24	1.35
P	(+)	+	+
Between Chi			0.29
Between df			1
Between P			N.S.

Onset (prosp or CC)

	prev	onset	Total
N	15	3	18
NS	12	3	15
Wt	584.72	86.85	671.57
Het Chi	33.07	3.81	37.20
Het df	14	2	17
Het P	**	N.S.	**
Fixed RR	1.13	1.21	1.14
RRl	1.05	0.98	1.06
RRu	1.23	1.49	1.23
P	++	(+)	+++
Random RR	1.17	1.24	1.19
RRl	1.01	0.92	1.04
RRu	1.36	1.67	1.35
P	+	N.S.	+
Between Chi			0.32
Between df			1
Between P			N.S.

Appendix Table F1 - 3

<u>IASTAD - Meta-analysis of Biochemical/Total/Household/Workplace Exposure (preferring earliest)</u>
Lifetime/Current Asthma
Adjusted

		<u>Number of cases</u>			
	1-100	101-400	401+	unknown	Total

		1-100	101-400	401+	unknown	Total
	N	7	3	5	3	18
	NS	5	3	3	3	14
	Wt	47.83	109.68	428.51	85.56	671.57
Het	Chi	14.37	1.59	7.53	0.03	37.20
Het	df	6	2	4	2	17
Het	P	*	N.S.	N.S.	N.S.	**
Fixed	RR	1.40	1.50	1.05	1.13	1.14
	RRl	1.05	1.25	0.95	0.92	1.06
	RRu	1.86	1.81	1.15	1.40	1.23
	P	+	+++	N.S.	N.S.	+++
Random	RR	1.39	1.50	1.03	1.13	1.19
	RRl	0.87	1.25	0.89	0.92	1.04
	RRu	2.22	1.81	1.18	1.40	1.35
	P	N.S.	+++	N.S.	N.S.	+
Between	Chi					13.68
Between	df					3
Between	P					**

<u>Study adjusts for or is matched on sex</u>

		Yes	No	Total
	N	9	9	18
	NS	8	6	14
	Wt	292.14	379.43	671.57
Het	Chi	20.50	16.25	37.20
Het	df	8	8	17
Het	P	**	*	**
Fixed	RR	1.18	1.12	1.14
	RRl	1.05	1.01	1.06
	RRu	1.32	1.24	1.23
	P	++	+	+++
Random	RR	1.20	1.17	1.19
	RRl	0.99	0.96	1.04
	RRu	1.44	1.43	1.35
	P	(+)	N.S.	+
Between	Chi			0.45
Between	df			1
Between	P			N.S.

<u>Study adjusts for or is matched on age</u>

		1-100	101-400	Total
	N	15	3	18
	NS	12	2	14
	Wt	610.09	61.49	671.57
Het	Chi	36.97	0.16	37.20
Het	df	14	2	17
Het	P	***	N.S.	**
Fixed	RR	1.15	1.11	1.14
	RRl	1.06	0.86	1.06
	RRu	1.24	1.42	1.23
	P	+++	N.S.	+++
Random	RR	1.20	1.11	1.19
	RRl	1.03	0.86	1.04
	RRu	1.39	1.42	1.35
	P	+	N.S.	+
Between	Chi			0.07
Between	df			1
Between	P			N.S.

Appendix Table F1 - 3

IASTAD - Meta-analysis of Biochemical/Total/Household/Workplace Exposure (preferring earliest)
Lifetime/Current Asthma
Adjusted

Study adjusts for race

		Yes	No	Total
	N	3	15	18
	NS	2	12	14
	Wt	88.37	583.21	671.57
Het	Chi	2.15	26.76	37.20
Het	df	2	14	17
Het	P	N.S.	*	**
Fixed	RR	0.86	1.19	1.14
	RRl	0.70	1.10	1.06
	RRu	1.06	1.30	1.23
	P	N.S.	+++	+++
Random	RR	0.86	1.26	1.19
	RRl	0.69	1.10	1.04
	RRu	1.08	1.43	1.35
	P	N.S.	+++	+
Between	Chi			8.29
Between	df			1
Between	P			**

Study adjusts for location

		Yes	No	Total
	N	10	8	18
	NS	8	6	14
	Wt	526.20	145.38	671.57
Het	Chi	13.24	19.01	37.20
Het	df	9	7	17
Het	P	N.S.	**	**
Fixed	RR	1.09	1.35	1.14
	RRl	1.00	1.15	1.06
	RRu	1.19	1.58	1.23
	P	+	+++	+++
Random	RR	1.10	1.40	1.19
	RRl	0.98	1.01	1.04
	RRu	1.23	1.93	1.35
	P	N.S.	+	+
Between	Chi			4.95
Between	df			1
Between	P			*

Study adjusts for SES

		Yes	No	Total
	N	2	16	18
	NS	1	13	14
	Wt	291.08	380.49	671.57
Het	Chi	1.18	35.23	37.20
Het	df	1	15	17
Het	P	N.S.	**	**
Fixed	RR	1.10	1.18	1.14
	RRl	0.98	1.07	1.06
	RRu	1.23	1.30	1.23
	P	N.S.	++	+++
Random	RR	1.10	1.21	1.19
	RRl	0.97	1.02	1.04
	RRu	1.25	1.44	1.35
	P	N.S.	+	+
Between	Chi			0.79
Between	df			1
Between	P			N.S.

Analysis run on 17-MAR-05

Appendix Table F1 - 3

IASTAD - Meta-analysis of Biochemical/Total/Household/Workplace Exposure (preferring earliest)
Lifetime/Current Asthma
Adjusted

Study adjusts for family medical history

		Yes	No	Total
	N	3	15	18
	NS	3	11	14
	Wt	110.97	560.60	671.57
Het	Chi	1.02	33.73	37.20
Het	df	2	14	17
Het	P	N.S.	**	**
Fixed	RR	1.31	1.11	1.14
	RRl	1.09	1.03	1.06
	RRu	1.58	1.21	1.23
	P	++	+	+++
Random	RR	1.31	1.16	1.19
	RRl	1.09	0.99	1.04
	RRu	1.58	1.36	1.35
	P	++	(+)	+
Between	Chi			2.46
Between	df			1
Between	P			N.S.

Study adjusts for family composition

		Yes	No	Total
	N	3	15	18
	NS	2	12	14
	Wt	329.58	342.00	671.57
Het	Chi	1.25	35.20	37.20
Het	df	2	14	17
Het	P	N.S.	**	**
Fixed	RR	1.11	1.18	1.14
	RRl	0.99	1.06	1.06
	RRu	1.23	1.31	1.23
	P	(+)	++	+++
Random	RR	1.11	1.22	1.19
	RRl	0.99	1.01	1.04
	RRu	1.23	1.47	1.35
	P	(+)	+	+
Between	Chi			0.75
Between	df			1
Between	P			N.S.

Study adjusts for cooking, heating

		Yes	No	Total
	N	4	14	18
	NS	3	11	14
	Wt	304.60	366.98	671.57
Het	Chi	4.54	31.11	37.20
Het	df	3	13	17
Het	P	N.S.	**	**
Fixed	RR	1.09	1.20	1.14
	RRl	0.97	1.08	1.06
	RRu	1.21	1.32	1.23
	P	N.S.	+++	+++
Random	RR	1.08	1.25	1.19
	RRl	0.91	1.05	1.04
	RRu	1.28	1.48	1.35
	P	N.S.	+	+
Between	Chi			1.55
Between	df			1
Between	P			N.S.

Appendix Table F1 - 3

IASTAD - Meta-analysis of Biochemical/Total/Household/Workplace Exposure (preferring earliest)
Lifetime/Current Asthma
Adjusted
Study adjusts for housing quality, crowding, damp, mould

		Yes	No	Total
	N	4	14	18
	NS	3	11	14
	Wt	331.21	340.37	671.57
Het	Chi	2.91	34.16	37.20
Het	df	3	13	17
Het	P	N.S.	**	**
Fixed	RR	1.13	1.16	1.14
	RRl	1.01	1.04	1.06
	RRu	1.26	1.29	1.23
	P	+	++	+++
Random	RR	1.13	1.20	1.19
	RRl	1.01	0.99	1.04
	RRu	1.26	1.45	1.35
	P	+	(+)	+
Between	Chi			0.12
Between	df			1
Between	P			N.S.

Study adjusts for subject's medical history

		Yes	No	Total
	N	5	13	18
	NS	4	10	14
	Wt	113.03	558.54	671.57
Het	Chi	9.28	22.08	37.20
Het	df	4	12	17
Het	P	(*)	*	**
Fixed	RR	1.41	1.10	1.14
	RRl	1.17	1.01	1.06
	RRu	1.69	1.19	1.23
	P	+++	+	+++
Random	RR	1.54	1.10	1.19
	RRl	1.12	0.97	1.04
	RRu	2.11	1.26	1.35
	P	++	N.S.	+
Between	Chi			5.83
Between	df			1
Between	P			*

Study adjusts for ex-smoking or other ETS exposure

		Yes	No	Total
	N	4	14	18
	NS	4	10	14
	Wt	119.73	551.85	671.57
Het	Chi	1.83	34.04	37.20
Het	df	3	13	17
Het	P	N.S.	**	**
Fixed	RR	1.26	1.12	1.14
	RRl	1.05	1.03	1.06
	RRu	1.51	1.22	1.23
	P	+	++	+++
Random	RR	1.26	1.16	1.19
	RRl	1.05	0.99	1.04
	RRu	1.51	1.37	1.35
	P	+	(+)	+
Between	Chi			1.32
Between	df			1
Between	P			N.S.

Appendix Table F1 - 3

IASTAD - Meta-analysis of Biochemical/Total/Household/Workplace Exposure (preferring earliest)
Lifetime/Current Asthma
Adjusted

| | | Exposure | | | |
	Hh	Hh,Wk	Cot	Work	Total
N	11	4	2	1	18
NS	8	4	1	1	14
Wt	425.20	132.62	81.18	32.57	671.57
Het Chi	23.15	1.42	1.37	0.00	37.20
Het df	10	3	1	0	17
Het P	*	N.S.	N.S.	N.S.	**
Fixed RR	1.16	1.34	0.84	1.13	1.14
RRl	1.05	1.13	0.67	0.80	1.06
RRu	1.27	1.59	1.04	1.59	1.23
P	++	+++	N.S.	N.S.	+++
Random RR	1.24	1.34	0.84	1.13	1.19
RRl	1.02	1.13	0.65	0.80	1.04
RRu	1.50	1.59	1.08	1.59	1.35
P	+	+++	N.S.	N.S.	+
Between Chi					11.26
Between df					3
Between P					*

| | | Exposed group : when Exposed | | | | |
	life	adult	child	current	unspec	Total
N	2	2	2	11	1	18
NS	2	1	2	8	1	14
Wt	40.13	13.35	47.00	556.61	14.49	671.57
Het Chi	0.17	4.22	0.23	14.46	0.00	37.20
Het df	1	1	1	10	0	17
Het P	N.S.	*	N.S.	N.S.	N.S.	**
Fixed RR	1.36	2.31	1.73	1.07	1.09	1.14
RRl	1.00	1.35	1.30	0.99	0.65	1.06
RRu	1.85	3.96	2.31	1.17	1.82	1.23
P	(+)	++	+++	(+)	N.S.	+++
Random RR	1.36	2.59	1.73	1.07	1.09	1.19
RRl	1.00	0.83	1.30	0.95	0.65	1.04
RRu	1.85	8.08	2.31	1.19	1.82	1.35
P	(+)	N.S.	+++	N.S.	N.S.	+
Between Chi						18.11
Between df						4
Between P						**

| | | Number of adjustment variables | | | | |
	0	2	3-5	6-9	10+	Total
N	3	2	7	4	2	18
NS	2	1	6	4	1	14
Wt	61.49	13.35	181.57	124.09	291.08	671.57
Het Chi	0.16	4.22	20.66	1.03	1.18	37.20
Het df	2	1	6	3	1	17
Het P	N.S.	*	**	N.S.	N.S.	**
Fixed RR	1.11	2.31	1.07	1.30	1.10	1.14
RRl	0.86	1.35	0.93	1.09	0.98	1.06
RRu	1.42	3.96	1.24	1.55	1.23	1.23
P	N.S.	++	N.S.	++	N.S.	+++
Random RR	1.11	2.59	1.08	1.30	1.10	1.19
RRl	0.86	0.83	0.81	1.09	0.97	1.04
RRu	1.42	8.08	1.43	1.55	1.25	1.35
P	N.S.	N.S.	N.S.	++	N.S.	+
Between Chi						9.95
Between df						4
Between P						*

Appendix Table F1 - 3

IASTAD - Meta-analysis of Biochemical/Total/Household/Workplace Exposure (preferring earliest)
Lifetime/Current Asthma
Adjusted

RR adjusted for sex

		Yes	No	Total
	N	9	9	18
	NS	8	6	14
	Wt	292.14	379.43	671.57
Het	Chi	20.50	16.25	37.20
Het	df	8	8	17
Het	P	**	*	**
Fixed	RR	1.18	1.12	1.14
	RRl	1.05	1.01	1.06
	RRu	1.32	1.24	1.23
	P	++	+	+++
Random	RR	1.20	1.17	1.19
	RRl	0.99	0.96	1.04
	RRu	1.44	1.43	1.35
	P	(+)	N.S.	+
Between	Chi			0.45
Between	df			1
Between	P			N.S.

RR adjusted for age

		Yes	No	Total
	N	15	3	18
	NS	12	2	14
	Wt	610.09	61.49	671.57
Het	Chi	36.97	0.16	37.20
Het	df	14	2	17
Het	P	***	N.S.	**
Fixed	RR	1.15	1.11	1.14
	RRl	1.06	0.86	1.06
	RRu	1.24	1.42	1.23
	P	+++	N.S.	+++
Random	RR	1.20	1.11	1.19
	RRl	1.03	0.86	1.04
	RRu	1.39	1.42	1.35
	P	+	N.S.	+
Between	Chi			0.07
Between	df			1
Between	P			N.S.

RR adjusted for ex-smoking or other ETS

		Yes	No	Total
	N	3	15	18
	NS	3	11	14
	Wt	86.79	584.79	671.57
Het	Chi	1.32	35.58	37.20
Het	df	2	14	17
Het	P	N.S.	**	**
Fixed	RR	1.21	1.13	1.14
	RRl	0.98	1.05	1.06
	RRu	1.49	1.23	1.23
	P	(+)	++	+++
Random	RR	1.21	1.18	1.19
	RRl	0.98	1.01	1.04
	RRu	1.49	1.38	1.35
	P	(+)	+	+
Between	Chi			0.30
Between	df			1
Between	P			N.S.

Appendix Table F1 - 3

IASTAD - Meta-analysis of Biochemical/Total/Household/Workplace Exposure (preferring earliest)
Lifetime/Current Asthma
Adjusted
RR adjusted for factor other than sex, age, other ETS

		Yes	No	Total
	N	15	3	18
	NS	12	2	14
	Wt	610.09	61.49	671.57
Het	Chi	36.97	0.16	37.20
Het	df	14	2	17
Het	P	***	N.S.	**
Fixed	RR	1.15	1.11	1.14
	RRl	1.06	0.86	1.06
	RRu	1.24	1.42	1.23
	P	+++	N.S.	+++
Random	RR	1.20	1.11	1.19
	RRl	1.03	0.86	1.04
	RRu	1.39	1.42	1.35
	P	+	N.S.	+
Between	Chi			0.07
Between	df			1
Between	P			N.S.

Derivation of RR/CI

		Original	Numbers	Sum/F&L	Total
	N	11	3	4	18
	NS	8	2	4	14
	Wt	521.67	61.49	88.42	671.57
Het	Chi	33.88	0.16	1.45	37.20
Het	df	10	2	3	17
Het	P	***	N.S.	N.S.	**
Fixed	RR	1.12	1.11	1.30	1.14
	RRl	1.03	0.86	1.06	1.06
	RRu	1.22	1.42	1.60	1.23
	P	++	N.S.	+	+++
Random	RR	1.17	1.11	1.30	1.19
	RRl	0.97	0.86	1.06	1.04
	RRu	1.41	1.42	1.60	1.35
	P	(+)	N.S.	+	+
Between	Chi				1.71
Between	df				2
Between	P				N.S.

Appendix Table F1 - 4

IASTAD - Meta-analysis of Biochemical/Total/Household/Workplace Exposure (preferring earliest)
Lifetime/Current Asthma
Unadjusted

REF	NRR	X	SEX	AST	SMOK	AGEL	AGEH	LOC	BEGYR	PUBYR	STTYP	ONS	ADJ	EXPOS	UNEXsrce	EXPOS-time	UNEXTI
BECKE2	1	x	b	l	Non	18	40	US:mul	1985	2001	Pr	prv	0	Cot	Low	current	non
BECKE2	3	x	b	l	Non	18	40	US:mul	1985	2001	Pr	ons	0	Cot	Low	current	non
JAAKK2	10	x	b	c	Never	21	63	Eu:Fin	1997	2003	CC	ons	0	Hh,Wk	None	lifetime	non
JANSON	1		b	c	<1yr	20	48	multi	1990	2001	CS	prv	9	Hh,Wk	None	current	non
JEDRYC	1		f	c	<1yr	65	99	Eu:Pol	*	1995	CS	prv	3	Hh	NoHhMemb	current	non
LARSS1	1	x	b	l	Never	15	69	Eu:Swe	1995	2001	CS	prv	0	Hh	NoHhMemb	childhood	non
LARSS2	4		b	l	Never	15	64	Eu:Est	1995	2003	CS	prv	5	Work	NotWork	current	non
MISHRA	1	x	m	c	NevReg	60	99	As:Ind	1998	2003	CS	prv	0	Hh	NoHhMemb	current	non
MISHRA	2	x	f	c	NevReg	60	99	As:Ind	1998	2003	CS	prv	0	Hh	NoHhMemb	current	non
NG	3	x	f	c	<1yr	20	74	As:Sin	*	1993	CS	prv	0	Hh	NoHhMemb	lifetime	non
NHANES	1		b	c	Non	17	99	US:nat	1988	2002	CS	prv	0	Hh	NoHhMemb	current	non
ORYSZC	1		m	c	NevReg	25	54	Eu:Fra	*	2000	CC	prv	0	Hh	NoHhMemb	current	non
ORYSZC	2		f	c	NevReg	25	54	Eu:Fra	*	2000	CC	prv	0	Hh	NoHhMemb	current	non
PILOTT	1		b	l	Non	18	99	Austra	1995	1999	CS	prv	3	Hh	NoHhMemb	unspec	non
ROBBIN	10		b	l	Non	25	99	US:Cal	1977	1993	Pr	ons	4	Hh,Wk	None	childhood	never
SAPALD	1	x	b	l	<20pks	18	60	Eu:Swi	1991	1994	CS	prv	0	Hh,Wk	None	current	non
THORN	1	x	b	l	Never	20	50	Eu:Swe	1994	2001	CC	prv	0	Hh	NoHhMemb	last6homes	non

Appendix Table F1 - 5

IASTAD - Meta-analysis of Biochemical/Total/Household/Workplace Exposure (preferring earliest)
Lifetime/Current Asthma
Unadjusted

```
                            Numbers
                            Numbers exposed Non-exposed
 REF     NRR      SEX ADJ    Case    Cont    Case    Cont     RR      95.00%CI
 BECKE2 1        b   0        63     799     215    2051     0.75 (  0.56-   1.01)
*BECKE2 3        b   0        54     799     141    2051     0.98 (  0.73-   1.33)
 Subtotal BECKE2                                            0.86 (  0.69-   1.06)
 JAAKK2 10       b   0       135     256     104     231     1.17 (  0.86-   1.60)
 JANSON 1        b   9        -       -       -       -      1.15 (  0.84-   1.58)
 JEDRYC 1        f   3        -       -       -       -      0.53 (  0.24-   1.14)
 LARSS1 1        b   0        85    1171      58    1470     1.84 (  1.31-   2.59)
 LARSS2 4        b   5        -       -       -       -      1.13 (  0.80-   1.59)
 MISHRA 1        m   0       242    1739     835    8047     1.34 (  1.15-   1.56)
 MISHRA 2        f   0       561    6037     829    9659     1.08 (  0.97-   1.21)
 Subtotal MISHRA                                            1.17 (  1.07-   1.28)
 NG      3       f   0        18     645      15     604     1.12 (  0.56-   2.25)
 NHANES 1        b   0        70    1481     370    8660     1.11 (  0.85-   1.44)
 ORYSZC 1        m   0         3       4      14      28     1.50 (  0.29-   7.65)
 ORYSZC 2        f   0         8      13      26      43     1.02 (  0.37-   2.78)
 Subtotal ORYSZC                                            1.13 (  0.48-   2.67)
 PILOTT 1        b   3        -       -       -       -      1.09 (  0.65-   1.82)
*ROBBIN 10       b   4        -       -       -       -      1.57 (  0.96-   2.58)
 SAPALD 1        b   0        96    1163     191    2747     1.19 (  0.92-   1.53)
 THORN  1        b   0        33     116      36     302     2.39 (  1.42-   4.01)
Partial Totals                1368   14223    2834   35893
*prospective study

 REF     NRR      SEX ADJ          Ys      Ws      Qs       Ps

 BECKE2 1        b   0          -0.28   44.92    8.36     0.0563
*BECKE2 3        b   0          -0.02   41.89    1.12     0.9121
 Subtotal BECKE2               -0.59   86.81    9.48
 JAAKK2 10       b   0           0.16   39.59    0.01     0.3198
 JANSON 1        b   9           0.14   38.50    0.00     0.3859
 JEDRYC 1        f   3          -0.63    6.33    3.86     0.1102
 LARSS1 1        b   0           0.61   32.74    7.02     0.0005
 LARSS2 4        b   5           0.12   32.57    0.02     0.4855
 MISHRA 1        m   0           0.29  165.86    3.58     0.0002
 MISHRA 2        f   0           0.08  306.94    1.38     0.1638
 Subtotal MISHRA                0.08  472.80    4.96
 NG      3       f   0           0.12    7.97    0.01     0.7419
 NHANES 1        b   0           0.10   56.25    0.12     0.4488
 ORYSZC 1        m   0           0.41    1.45    0.10     0.6256
 ORYSZC 2        f   0           0.02    3.79    0.06     0.9727
 Subtotal ORYSZC                0.13    5.24    0.16
 PILOTT 1        b   3           0.09   14.49    0.05     0.7428
*ROBBIN 10       b   4           0.45   15.72    1.46     0.0737
 SAPALD 1        b   0           0.17   59.26    0.04     0.1866
 THORN  1        b   0           0.87   14.28    7.47     0.0010
```

```
            N      17
            NS     14


            Wt     882.55
    Het Chi        34.66
    Het  df        16
    Het  P         **
    Fixed  RR      1.16
           RRl     1.08
           RRu     1.24
           P       +++
    Random RR      1.17
           RRl     1.04
           RRu     1.32
           P       ++
    Asymm  P       N.S.
```

Appendix Table F1 - 6

IASTAD - Meta-analysis of Biochemical/Total/Household/Workplace Exposure (preferring earliest)
Lifetime/Current Asthma
Unadjusted

```
         N       17
         NS      14


         Wt   882.55
  Het Chi  34.66
  Het  df      16
  Het  P       **
Fixed  RR    1.16
       RRl   1.08
       RRu   1.24
       P      +++
Random  RR   1.17
       RRl   1.04
       RRu   1.32
       P      ++
  Asymm  P   N.S.
```

| | Sex | | | |
	both	male	female	Total
N	11	2	4	17
NS	10	2	4	16
Wt	390.21	167.31	325.03	882.55
Het Chi	25.66	0.02	3.19	34.66
Het df	10	1	3	16
Het P	**	N.S.	N.S.	**
Fixed RR	1.16	1.34	1.07	1.16
RRl	1.05	1.15	0.96	1.08
RRu	1.28	1.56	1.19	1.24
P	++	+++	N.S.	+++
Random RR	1.20	1.34	1.05	1.17
RRl	1.02	1.15	0.88	1.04
RRu	1.42	1.56	1.24	1.32
P	+	+++	N.S.	++
Between Chi				5.79
Between df				2
Between P				(*)

| | Asthma definition (lifetime/current) | | |
	lifetime	current	Total
N	8	9	17
NS	7	7	14
Wt	255.87	626.68	882.55
Het Chi	25.48	9.09	34.66
Het df	7	8	16
Het P	***	N.S.	**
Fixed RR	1.18	1.15	1.16
RRl	1.04	1.06	1.08
RRu	1.33	1.24	1.24
P	++	+++	+++
Random RR	1.25	1.15	1.17
RRl	0.98	1.05	1.04
RRu	1.59	1.27	1.32
P	(+)	++	++
Between Chi			0.08
Between df			1
Between P			N.S.

Appendix Table F1 - 6

IASTAD - Meta-analysis of Biochemical/Total/Household/Workplace Exposure (preferring earliest)
Lifetime/Current Asthma
Unadjusted

| | | Continent | | | |
		NAmer	Europe	Oth/Mult	Total
	N	4	8	5	17
	NS	3	7	4	14
	Wt	158.78	190.01	533.76	882.55
Het	Chi	7.42	16.13	5.01	34.66
Het	df	3	7	4	16
Het	P	(*)	*	N.S.	**
Fixed	RR	1.00	1.30	1.16	1.16
	RRl	0.85	1.13	1.07	1.08
	RRu	1.16	1.50	1.27	1.24
	P	N.S.	+++	+++	+++
Random	RR	1.02	1.30	1.17	1.17
	RRl	0.79	1.01	1.05	1.04
	RRu	1.32	1.66	1.31	1.32
	P	N.S.	+	++	++
Between	Chi				6.09
Between	df				2
Between	P				*

| | | Start year of study | | | |
		<1990	1990-99	unknown	Total
	N	4	9	4	17
	NS	3	8	3	14
	Wt	158.78	704.23	19.54	882.55
Het	Chi	7.42	18.35	2.60	34.66
Het	df	3	8	3	16
Het	P	(*)	*	N.S.	**
Fixed	RR	1.00	1.21	0.88	1.16
	RRl	0.85	1.12	0.57	1.08
	RRu	1.16	1.30	1.38	1.24
	P	N.S.	+++	N.S.	+++
Random	RR	1.02	1.27	0.88	1.17
	RRl	0.79	1.11	0.57	1.04
	RRu	1.32	1.45	1.38	1.32
	P	N.S.	+++	N.S.	++
Between	Chi				6.28
Between	df				2
Between	P				*

| | | Study type | | | |
		CC	Pr	CS	Total
	N	4	3	10	17
	NS	3	2	9	14
	Wt	59.12	102.53	720.91	882.55
Het	Chi	5.71	6.45	15.92	34.66
Het	df	3	2	9	16
Het	P	N.S.	*	(*)	**
Fixed	RR	1.39	0.94	1.18	1.16
	RRl	1.07	0.77	1.09	1.08
	RRu	1.79	1.14	1.26	1.24
	P	+	N.S.	+++	+++
Random	RR	1.47	1.00	1.19	1.17
	RRl	0.94	0.70	1.06	1.04
	RRu	2.32	1.45	1.34	1.32
	P	(+)	N.S.	++	++
Between	Chi				6.57
Between	df				2
Between	P				*

Analysis run on 17-MAR-05

Appendix Table F1 - 6

IASTAD - Meta-analysis of Biochemical/Total/Household/Workplace Exposure (preferring earliest)
Lifetime/Current Asthma
Unadjusted

Ex smokers

		excluded	included	Total
	N	12	5	17
	NS	10	4	14
	Wt	709.28	173.27	882.55
Het	Chi	22.68	7.53	34.66
Het	df	11	4	16
Het	P	*	N.S.	**
Fixed	RR	1.20	1.00	1.16
	RRl	1.11	0.86	1.08
	RRu	1.29	1.16	1.24
	P	+++	N.S.	+++
Random	RR	1.24	1.02	1.17
	RRl	1.09	0.83	1.04
	RRu	1.42	1.27	1.32
	P	++	N.S.	++
Between	Chi			4.44
Between	df			1
Between	P			*

Appendix Table F1 - 7

IASTAD - Meta-analysis of Biochemical/Total/Household/Workplace Exposure (preferring earliest)
Lifetime/Current Asthma
Excluded studies (and stage at which they were excluded)


```
       1       2       3       4       5       6       7       8       9      10      11      12      13      14      15      16

3      KRONQV PLATTS
9      RAHERI
                                           Potentially overlapping studies
    REF| REFGP|PRINC|              OVERLAP|
 JANSON JANSON    p       JANSON/RAHERI


                                   Adjusted - insufficient data for metaanalysis
    REF|NRR|SEX|AST|   SMOK|AGEL|AGEH|   LOC|BEGYR|PUBYR|STTYP|ONS|ADJ|EXPOS|UNEXsrce| EXPOS-time|UNEXTI|      RR|SIG|
 KRONQV  1   b   l  Never   15   65 Eu:Swe 1996  1999   CS prv  4 Total    None    childhood   non        *    n
 LARSS2  5   b   l  Never   15   64 Eu:Est 1995  2003   CS prv  5   Hh NoHhMemb     current    non        *    n
 PLATTS  1   b   c    Non   15   55 US:Del 1988  1993   CC prv  0 Total    None      unspec    non        *    n
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Appendix Table F2 -

IASTAD - Meta-analysis of Biochemical/Total/Household/Workplace (preferring earliest) - Ex-smokers excluded
Lifetime/Current Asthma

This analysis is restricted to results for:
1) Biochemical, total, household (overall), parental, or workplace exposure
2) Ex-smokers excluded
3) Results not by amount of exposure
4) Results complete enough for use in metaanalysis

Within each study, results are then selected (in the following order of preference, within each sex) for:
5) ASTHMA : lifetime, current
6) EXPOS   : biochemical (cotinine), total, household, workplace
7) WHESMO : 3=childhood, 1=lifetime, 10=adult, 7=recent, 6=unspec, 2=current
8) WHOHOU : household overall, mother
9) UNEXTI : unexposed group never, non (i.e. not at time defined for exposed group)
10) For overlapping studies: principal rather than subsidiary studies
Finally for single sex results (m, f) in preference to results for both sexes combined (b).

Results adjusted for the most potential confounders are then chosen in Sections -1 to -3
and results adjusted for the least confounders in Sections -4 to -6. (Those least adjusted results which
actually differ from the most adjusted are marked 'x' in column X in Section -4)

Section -7 shows excluded studies, together with the stage (as above) at which no qualifying results
were found. It then lists the potentially overlapping studies which have been included (1=principal,
2=subsidiary), and any results which would have been included in preference except that they had data
not complete enough for use in metaanalysis. It also lists their significance (yes/no), if known.

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Appendix Table F2 - 1

IASTAD - Meta-analysis of Biochemical/Total/Household/Workplace (preferring earliest) - Ex-smokers excluded
Lifetime/Current Asthma
Adjusted

REF	NRR	SEX	AST	SMOK	AGEL	AGEH	LOC	BEGYR	PUBYR	STTYP	ONS	ADJ	EXPOS	UNEXsrce	EXPOS-time	UNEXTI
JAAKK2	34	b	c	Never	21	63	Eu:Fin	1997	2003	CC	ons	7	Hh,Wk	None	lifetime	non
JANSON	1	b	c	<1yr	20	48	multi	1990	2001	CS	prv	9	Hh,Wk	None	current	non
JEDRYC	1	f	c	<1yr	65	99	Eu:Pol	*	1995	CS	prv	3	Hh	NoHhMemb	current	non
LARSS1	2	b	l	Never	15	69	Eu:Swe	1995	2001	CS	prv	3	Hh	NoHhMemb	childhood	non
LARSS2	4	b	l	Never	15	64	Eu:Est	1995	2003	CS	prv	5	Work	NotWork	current	non
MISHRA	3	m	c	NevReg	60	99	As:Ind	1998	2003	CS	prv	12	Hh	NoHhMemb	current	non
MISHRA	4	f	c	NevReg	60	99	As:Ind	1998	2003	CS	prv	12	Hh	NoHhMemb	current	non
NG	6	f	c	<1yr	20	74	As:Sin	*	1993	CS	prv	6	Hh	NoHhMemb	lifetime	non
ORYSZC	1	m	c	NevReg	25	54	Eu:Fra	*	2000	CC	prv	0	Hh	NoHhMemb	current	non
ORYSZC	2	f	c	NevReg	25	54	Eu:Fra	*	2000	CC	prv	0	Hh	NoHhMemb	current	non
SAPALD	2	b	l	<20pks	18	60	Eu:Swi	1991	1994	CS	prv	8	Hh,Wk	None	current	non
THORN	2	m	l	Never	20	50	Eu:Swe	1994	2001	CC	prv	2	Hh	NoHhMemb	last6homes	non
THORN	3	f	l	Never	20	50	Eu:Swe	1994	2001	CC	prv	2	Hh	NoHhMemb	last6homes	non

Appendix Table F2 - 2

IASTAD - Meta-analysis of Biochemical/Total/Household/Workplace (preferring earliest) - Ex-smokers excluded
Lifetime/Current Asthma
Adjusted

				Numbers					
				Numbers exposed		Non-exposed			
REF	NRR	SEX	ADJ	Case	Cont	Case	Cont	RR	95.00%CI
JAAKK2	34	b	7	135	–	104	–	1.40 (	0.99– 1.96)
JANSON	1	b	9	–	–	–	–	1.15 (	0.84– 1.58)
JEDRYC	1	f	3	–	–	–	–	0.53 (	0.24– 1.14)
LARSS1	2	b	3	85	–	58	–	1.82 (	1.28– 2.58)
LARSS2	4	b	5	–	–	–	–	1.13 (	0.80– 1.59)
MISHRA	3	m	12	242	–	835	–	1.20 (	0.99– 1.46)
MISHRA	4	f	12	561	–	829	–	1.05 (	0.91– 1.21)
Subtotal MISHRA								1.10 (	0.98– 1.23)
NG	6	f	6	18	–	15	–	1.18 (	0.57– 2.46)
ORYSZC	1	m	0	3	4	14	28	1.50 (	0.29– 7.65)
ORYSZC	2	f	0	8	13	26	43	1.02 (	0.37– 2.78)
Subtotal ORYSZC								1.13 (	0.48– 2.67)
SAPALD	2	b	8	96	–	191	–	1.39 (	1.04– 1.86)
THORN	2	m	2	–	–	–	–	4.80 (	2.00– 11.60)
THORN	3	f	2	–	–	–	–	1.50 (	0.80– 3.10)
Subtotal THORN								2.31 (	1.35– 3.96)
Partial Totals				1148	17	2072	71		

*prospective study

REF	NRR	SEX	ADJ	Ys	Ws	Qs	Ps
JAAKK2	34	b	7	0.34	32.94	0.80	0.0535
JANSON	1	b	9	0.14	38.50	0.06	0.3859
JEDRYC	1	f	3	-0.63	6.33	4.21	0.1102
LARSS1	2	b	3	0.60	31.28	5.47	0.0008
LARSS2	4	b	5	0.12	32.57	0.11	0.4855
MISHRA	3	m	12	0.18	101.81	0.00	0.0658
MISHRA	4	f	12	0.05	189.27	3.28	0.5021
Subtotal MISHRA				-0.13	291.08	3.28	
NG	6	f	6	0.17	7.19	0.00	0.6573
ORYSZC	1	m	0	0.41	1.45	0.07	0.6256
ORYSZC	2	f	0	0.02	3.79	0.10	0.9727
Subtotal ORYSZC				0.06	5.24	0.17	
SAPALD	2	b	8	0.33	45.46	1.01	0.0264
THORN	2	m	2	1.57	4.97	9.58	0.0005
THORN	3	f	2	0.41	8.37	0.42	0.2406
Subtotal THORN				1.61	13.35	10.01	

N	13
NS	10
Wt	503.93
Het Chi	25.13
Het df	12
Het P	*
Fixed RR	1.20
RRl	1.10
RRu	1.31
P	+++
Random RR	1.27
RRl	1.09
RRu	1.49
P	++
Asymm P	N.S.

Appendix Table F2 - 3

IASTAD - Meta-analysis of Biochemical/Total/Household/Workplace (preferring earliest) - Ex-smokers excluded
Lifetime/Current Asthma
Adjusted

N	13
NS	10

Wt	503.93
Het Chi	25.13
Het df	12
Het P	*
Fixed RR	1.20
RRl	1.10
RRu	1.31
P	+++
Random RR	1.27
RRl	1.09
RRu	1.49
P	++
Asymm P	N.S.

	Sex			
	both	male	female	Total
N	5	3	5	13
NS	5	3	5	13
Wt	180.75	108.23	214.95	503.93
Het Chi	4.89	9.15	4.12	25.13
Het df	4	2	4	12
Het P	N.S.	*	N.S.	*
Fixed RR	1.35	1.28	1.05	1.20
RRl	1.17	1.06	0.92	1.10
RRu	1.56	1.55	1.20	1.31
P	+++	++	N.S.	+++
Random RR	1.35	2.02	1.05	1.27
RRl	1.15	0.73	0.89	1.09
RRu	1.59	5.56	1.23	1.49
P	+++	N.S.	N.S.	++
Between Chi				6.96
Between df				2
Between P				*

	Asthma definition (lifetime/current)		
	lifetime	current	Total
N	5	8	13
NS	4	6	10
Wt	122.66	381.27	503.93
Het Chi	10.77	6.66	25.13
Het df	4	7	12
Het P	*	N.S.	*
Fixed RR	1.49	1.12	1.20
RRl	1.25	1.01	1.10
RRu	1.78	1.23	1.31
P	+++	+	+++
Random RR	1.61	1.12	1.27
RRl	1.17	1.01	1.09
RRu	2.21	1.23	1.49
P	++	+	++
Between Chi			7.70
Between df			1
Between P			**

Appendix Table F2 - 3

IASTAD - Meta-analysis of Biochemical/Total/Household/Workplace (preferring earliest) - Ex-smokers excluded
Lifetime/Current Asthma
Adjusted

		Continent		
	NAmer	Europe	Oth/Mult	Total
N		9	4	13
NS		7	3	10
Wt		167.17	336.76	503.93
Het Chi		17.60	1.28	25.13
Het df		8	3	12
Het P		*	N.S.	*
Fixed RR		1.40	1.11	1.20
RRl		1.21	1.00	1.10
RRu		1.63	1.23	1.31
P		+++	(+)	+++
Random RR		1.40	1.11	1.27
RRl		1.08	1.00	1.09
RRu		1.82	1.23	1.49
P		++	(+)	++
Between Chi				6.25
Between df				1
Between P				*

	Start year of study			
	<1990	1990-99	unknown	Total
N		9	4	13
NS		7	3	10
Wt		485.17	18.76	503.93
Het Chi		20.68	2.74	25.13
Het df		8	3	12
Het P		**	N.S.	*
Fixed RR		1.21	0.89	1.20
RRl		1.11	0.57	1.10
RRu		1.32	1.40	1.31
P		+++	N.S.	+++
Random RR		1.32	0.89	1.27
RRl		1.12	0.57	1.09
RRu		1.56	1.40	1.49
P		+++	N.S.	++
Between Chi				1.71
Between df				1
Between P				N.S.

	Study type			
	CC	Pr	CS	Total
N	5		8	13
NS	3		7	10
Wt	51.53		452.40	503.93
Het Chi	7.37		13.74	25.13
Het df	4		7	12
Het P	N.S.		(*)	*
Fixed RR	1.56		1.16	1.20
RRl	1.19		1.06	1.10
RRu	2.05		1.27	1.31
P	++		++	+++
Random RR	1.69		1.20	1.27
RRl	1.06		1.03	1.09
RRu	2.69		1.39	1.49
P	+		+	++
Between Chi				4.02
Between df				1
Between P				*

Appendix Table F2 - 4

IASTAD - Meta-analysis of Biochemical/Total/Household/Workplace (preferring earliest) - Ex-smokers excluded
Lifetime/Current Asthma
Unadjusted

REF	NRR	X	SEX	AST	SMOK	AGEL	AGEH	LOC	BEGYR	PUBYR	STTYP	ONS	ADJ	EXPOS	UNEXsrce	EXPOS-time	UNEXTI
JAAKK2	10	x	b	c	Never	21	63	Eu:Fin	1997	2003	CC	ons	0	Hh,Wk	None	lifetime	non
JANSON	1		b	c	<1yr	20	48	multi	1990	2001	CS	prv	9	Hh,Wk	None	current	non
JEDRYC	1		f	c	<1yr	65	99	Eu:Pol	*	1995	CS	prv	3	Hh	NoHhMemb	current	non
LARSS1	1	x	b	l	Never	15	69	Eu:Swe	1995	2001	CS	prv	0	Hh	NoHhMemb	childhood	non
LARSS2	4		b	l	Never	15	64	Eu:Est	1995	2003	CS	prv	5	Work	NotWork	current	non
MISHRA	1	x	m	c	NevReg	60	99	As:Ind	1998	2003	CS	prv	0	Hh	NoHhMemb	current	non
MISHRA	2	x	f	c	NevReg	60	99	As:Ind	1998	2003	CS	prv	0	Hh	NoHhMemb	current	non
NG	3	x	f	c	<1yr	20	74	As:Sin	*	1993	CS	prv	0	Hh	NoHhMemb	lifetime	non
ORYSZC	1		m	c	NevReg	25	54	Eu:Fra	*	2000	CC	prv	0	Hh	NoHhMemb	current	non
ORYSZC	2		f	c	NevReg	25	54	Eu:Fra	*	2000	CC	prv	0	Hh	NoHhMemb	current	non
SAPALD	1	x	b	l	<20pks	18	60	Eu:Swi	1991	1994	CS	prv	0	Hh,Wk	None	current	non
THORN	1	x	b	l	Never	20	50	Eu:Swe	1994	2001	CC	prv	0	Hh	NoHhMemb	last6homes	non

Appendix Table F2 - 5

IASTAD - Meta-analysis of Biochemical/Total/Household/Workplace (preferring earliest) - Ex-smokers excluded
Lifetime/Current Asthma
Unadjusted

				Numbers	Numbers exposed	Non-exposed					
REF	NRR	SEX	ADJ	Case	Cont	Case	Cont	RR		95.00%CI	
JAAKK2	10	b	0	135	256	104	231	1.17 (	0.86-	1.60)
JANSON	1	b	9	-	-	-	-	1.15 (	0.84-	1.58)
JEDRYC	1	f	3	-	-	-	-	0.53 (	0.24-	1.14)
LARSS1	1	b	0	85	1171	58	1470	1.84 (	1.31-	2.59)
LARSS2	4	b	5	-	-	-	-	1.13 (	0.80-	1.59)
MISHRA	1	m	0	242	1739	835	8047	1.34 (	1.15-	1.56)
MISHRA	2	f	0	561	6037	829	9659	1.08 (	0.97-	1.21)
Subtotal MISHRA								1.17 (	1.07-	1.28)
NG	3	f	0	18	645	15	604	1.12 (	0.56-	2.25)
ORYSZC	1	m	0	3	4	14	28	1.50 (	0.29-	7.65)
ORYSZC	2	f	0	8	13	26	43	1.02 (	0.37-	2.78)
Subtotal ORYSZC								1.13 (	0.48-	2.67)
SAPALD	1	b	0	96	1163	191	2747	1.19 (	0.92-	1.53)
THORN	1	b	0	33	116	36	302	2.39 (	1.42-	4.01)
Partial Totals				1181	11144	2108	23131			

*prospective study

REF	NRR	SEX	ADJ	Ys	Ws	Qs	Ps
JAAKK2	10	b	0	0.16	39.59	0.02	0.3198
JANSON	1	b	9	0.14	38.50	0.07	0.3859
JEDRYC	1	f	3	-0.63	6.33	4.22	0.1102
LARSS1	1	b	0	0.61	32.74	6.00	0.0005
LARSS2	4	b	5	0.12	32.57	0.11	0.4855
MISHRA	1	m	0	0.29	165.86	2.08	0.0002
MISHRA	2	f	0	0.08	306.94	3.20	0.1638
Subtotal MISHRA				0.01	472.80	5.28	
NG	3	f	0	0.12	7.97	0.03	0.7419
ORYSZC	1	m	0	0.41	1.45	0.07	0.6256
ORYSZC	2	f	0	0.02	3.79	0.10	0.9727
Subtotal ORYSZC				0.06	5.24	0.17	
SAPALD	1	b	0	0.17	59.26	0.01	0.1866
THORN	1	b	0	0.87	14.28	6.77	0.0010

N		12
NS		10
Wt		709.28
Het Chi		22.68
Het df		11
Het P		*
Fixed	RR	1.20
	RRl	1.11
	RRu	1.29
	P	+++
Random	RR	1.24
	RRl	1.09
	RRu	1.42
	P	++
Asymm	P	N.S.

Appendix Table F2 - 6

IASTAD - Meta-analysis of Biochemical/Total/Household/Workplace (preferring earliest) - Ex-smokers excluded
Lifetime/Current Asthma
Unadjusted

N	12
NS	10

Wt	709.28
Het Chi	22.68
Het df	11
Het P	*
Fixed RR	1.20
RRl	1.11
RRu	1.29
P	+++
Random RR	1.24
RRl	1.09
RRu	1.42
P	++
Asymm P	N.S.

	Sex			
	both	male	female	Total
N	6	2	4	12
NS	6	2	4	12
Wt	216.94	167.31	325.03	709.28
Het Chi	11.35	0.02	3.19	22.68
Het df	5	1	3	11
Het P	*	N.S.	N.S.	*
Fixed RR	1.31	1.34	1.07	1.20
RRl	1.14	1.15	0.96	1.11
RRu	1.49	1.56	1.19	1.29
P	+++	+++	N.S.	+++
Random RR	1.35	1.34	1.05	1.24
RRl	1.10	1.15	0.88	1.09
RRu	1.66	1.56	1.24	1.42
P	++	+++	N.S.	++
Between Chi				8.12
Between df				2
Between P				*

	Asthma definition (lifetime/current)		
	lifetime	current	Total
N	4	8	12
NS	4	6	10
Wt	138.85	570.43	709.28
Het Chi	9.61	9.00	22.68
Het df	3	7	11
Het P	*	N.S.	*
Fixed RR	1.40	1.16	1.20
RRl	1.18	1.06	1.11
RRu	1.65	1.25	1.29
P	+++	+++	+++
Random RR	1.49	1.16	1.24
RRl	1.09	1.03	1.09
RRu	2.04	1.30	1.42
P	+	+	++
Between Chi			4.07
Between df			1
Between P			*

Appendix Table F2 - 6

IASTAD - Meta-analysis of Biochemical/Total/Household/Workplace (preferring earliest) - Ex-smokers excluded
Lifetime/Current Asthma
Unadjusted

	Continent			
	NAmer	Europe	Oth/Mult	Total
N		8	4	12
NS		7	3	10
Wt		190.01	519.27	709.28
Het Chi		16.13	4.95	22.68
Het df		7	3	11
Het P		*	N.S.	*
Fixed RR		1.30	1.17	1.20
RRl		1.13	1.07	1.11
RRu		1.50	1.27	1.29
P		+++	+++	+++
Random RR		1.30	1.18	1.24
RRl		1.01	1.03	1.09
RRu		1.66	1.35	1.42
P		+	+	++
Between Chi				1.60
Between df				1
Between P				N.S.

	Start year of study			
	<1990	1990-99	unknown	Total
N		8	4	12
NS		7	3	10
Wt		689.74	19.54	709.28
Het Chi		18.20	2.60	22.68
Het df		7	3	11
Het P		*	N.S.	*
Fixed RR		1.21	0.88	1.20
RRl		1.12	0.57	1.11
RRu		1.30	1.38	1.29
P		+++	N.S.	+++
Random RR		1.28	0.88	1.24
RRl		1.11	0.57	1.09
RRu		1.48	1.38	1.42
P		+++	N.S.	++
Between Chi				1.88
Between df				1
Between P				N.S.

	Study type			
	CC	Pr	CS	Total
N	4		8	12
NS	3		7	10
Wt	59.12		650.17	709.28
Het Chi	5.71		15.60	22.68
Het df	3		7	11
Het P	N.S.		*	*
Fixed RR	1.39		1.18	1.20
RRl	1.07		1.10	1.11
RRu	1.79		1.28	1.29
P	+		+++	+++
Random RR	1.47		1.21	1.24
RRl	0.94		1.05	1.09
RRu	2.32		1.39	1.42
P	(+)		+	++
Between Chi				1.37
Between df				1
Between P				N.S.

Appendix Table F2 - 7

<u>IASTAD - Meta-analysis of Biochemical/Total/Household/Workplace (preferring earliest) - Ex-smokers excluded</u>
Lifetime/Current Asthma
Excluded studies (and stage at which they were excluded)


```
         1       2       3       4       5       6       7       8       9      10      11      12      13      14      15      16

2       BECKE2 NHANES PILOTT PLATTS ROBBIN
4       KRONQV
10      RAHERI
```

Potentially overlapping studies

```
    REF| REFGP|PRINC|            OVERLAP|
 JANSON JANSON      p       JANSON/RAHERI
```


Adjusted - insufficient data for metaanalysis

```
    REF|NRR|SEX|AST|  SMOK|AGEL|AGEH|   LOC|BEGYR|PUBYR|STTYP|ONS|ADJ|EXPOS|UNEXsrce| EXPOS-time|UNEXTI|       RR|SIG|
 KRONQV  1   b   l  Never   15   65 Eu:Swe  1996  1999   CS prv   4 Total    None   childhood   non        *   n
 LARSS2  5   b   l  Never   15   64 Eu:Est  1995  2003   CS prv   5    Hh NoHhMemb    current   non        *   n
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Appendix Table F3 -

IASTAD - Meta-analysis of Biochemical/Total/Household/Workplace Exposure (preferring most recent)
Lifetime/Current Asthma

This analysis is restricted to results for:
1) Biochemical, total, household (overall), parental, or workplace exposure
2) Results not by amount of exposure
3) Results complete enough for use in metaanalysis

Within each study, results are then selected (in the following order of preference, within each sex) for:
4) ASTHMA : lifetime, current
5) EXPOS   : biochemical (cotinine), total, household, workplace
6) WHESMO : 2=current, 7=recent, 6=unspec, 10=adult, 1=lifetime, 3=childhood
7) WHOHOU : household overall, mother
8) UNEXTI : unexposed group never, non (i.e. not at time defined for exposed group)
9) For overlapping studies: principal rather than subsidiary studies
Finally for single sex results (m, f) in preference to results for both sexes combined (b).

Results adjusted for the most potential confounders are then chosen in Sections -1 to -3
(and those which actually differ from the adjusted results in Appendix Table F1 - 1 are marked 'x' in Section -1)
and results adjusted for the least confounders in Sections -4 to -6. (Those least adjusted results which
actually differ from the most adjusted are marked 'x' in column X in Section -4)

Section -7 shows excluded studies, together with the stage (as above) at which no qualifying results
were found. It then lists the potentially overlapping studies which have been included (1=principal,
2=subsidiary), and any results which would have been included in preference except that they had data
not complete enough for use in metaanalysis. It also lists their significance (yes/no), if known.

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Appendix Table F3 - 1

IASTAD - Meta-analysis of Biochemical/Total/Household/Workplace Exposure (preferring most recent)
Lifetime/Current Asthma
Adjusted

REF	NRR	CompF1	SEX	AST	SMOK	AGEL	AGEH	LOC	BEGYR	PUBYR	STTYP	ONS	ADJ	EXPOS	UNEXsrce	EXPOS-time	UNEXTI
BECKE2	2		b	l	Non	18	40	US:mul	1985	2001	Pr	prv	5	Cot	Low	current	non
BECKE2	4		b	l	Non	18	40	US:mul	1985	2001	Pr	ons	5	Cot	Low	current	non
JAAKK2	25	x	b	c	Never	21	63	Eu:Fin	1997	2003	CC	ons	7	Hh,Wk	None	current	non
JANSON	1		b	c	<1yr	20	48	multi	1990	2001	CS	prv	9	Hh,Wk	None	current	non
JEDRYC	1		f	c	<1yr	65	99	Eu:Pol	*	1995	CS	prv	3	Hh	NoHhMemb	current	non
LARSS1	2		b	l	Never	15	69	Eu:Swe	1995	2001	CS	prv	3	Hh	NoHhMemb	childhood	non
LARSS2	4		b	l	Never	15	64	Eu:Est	1995	2003	CS	prv	5	Work	NotWork	current	non
MISHRA	3		m	c	NevReg	60	99	As:Ind	1998	2003	CS	prv	12	Hh	NoHhMemb	current	non
MISHRA	4		f	c	NevReg	60	99	As:Ind	1998	2003	CS	prv	12	Hh	NoHhMemb	current	non
NG	6		f	c	<1yr	20	74	As:Sin	*	1993	CS	prv	6	Hh	NoHhMemb	lifetime	non
NHANES	1		b	c	Non	17	99	US:nat	1988	2002	CS	prv	0	Hh	NoHhMemb	current	non
ORYSZC	1		m	c	NevReg	25	54	Eu:Fra	*	2000	CC	prv	0	Hh	NoHhMemb	current	non
ORYSZC	2		f	c	NevReg	25	54	Eu:Fra	*	2000	CC	prv	0	Hh	NoHhMemb	current	non
PILOTT	1		b	l	Non	18	99	Austra	1995	1999	CS	prv	3	Hh	NoHhMemb	unspec	non
ROBBIN	11	x	b	l	Non	25	99	US:Cal	1977	1993	Pr	ons	4	Hh,Wk	None	adult	never
SAPALD	2		b	l	<20pks	18	60	Eu:Swi	1991	1994	CS	prv	8	Hh,Wk	None	current	non
THORN	2		m	l	Never	20	50	Eu:Swe	1994	2001	CC	prv	2	Hh	NoHhMemb	last6homes	non
THORN	3		f	l	Never	20	50	Eu:Swe	1994	2001	CC	prv	2	Hh	NoHhMemb	last6homes	non

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Appendix Table F3 - 2

<u>IASTAD - Meta-analysis of Biochemical/Total/Household/Workplace Exposure (preferring most recent)</u>
Lifetime/Current Asthma
Adjusted

REF	NRR	SEX	ADJ	Numbers Numbers exposed Non-exposed Case	Cont	Case	Cont	RR	95.00%CI
BECKE2	2	b	5	63	–	215	–	0.74 (	0.55- 1.00)
*BECKE2	4	b	5	54	–	141	–	0.96 (	0.70- 1.32)
Subtotal BECKE2								0.84 (	0.67- 1.04)
JAAKK2	25	b	7	38	–	196	–	1.97 (	1.19- 3.25)
JANSON	1	b	9	–	–	–	–	1.15 (	0.84- 1.58)
JEDRYC	1	f	3	–	–	–	–	0.53 (	0.24- 1.14)
LARSS1	2	b	3	85	–	58	–	1.82 (	1.28- 2.58)
LARSS2	4	b	5	–	–	–	–	1.13 (	0.80- 1.59)
MISHRA	3	m	12	242	–	835	–	1.20 (	0.99- 1.46)
MISHRA	4	f	12	561	–	829	–	1.05 (	0.91- 1.21)
Subtotal MISHRA								1.10 (	0.98- 1.23)
NG	6	f	6	18	–	15	–	1.18 (	0.57- 2.46)
NHANES	1	b	0	70	1481	370	8660	1.11 (	0.85- 1.44)
ORYSZC	1	m	0	3	4	14	28	1.50 (	0.29- 7.65)
ORYSZC	2	f	0	8	13	26	43	1.02 (	0.37- 2.78)
Subtotal ORYSZC								1.13 (	0.48- 2.67)
PILOTT	1	b	3	–	–	–	–	1.09 (	0.65- 1.82)
*ROBBIN	11	b	4	–	–	–	–	1.77 (	1.11- 2.83)
SAPALD	2	b	8	96	–	191	–	1.39 (	1.04- 1.86)
THORN	2	m	2	–	–	–	–	4.80 (	2.00- 11.60)
THORN	3	f	2	–	–	–	–	1.50 (	0.80- 3.10)
Subtotal THORN								2.31 (	1.35- 3.96)
Partial Totals				1238	1498	2890	8731		

*prospective study

REF	NRR	SEX	ADJ	Ys	Ws	Qs	Ps
BECKE2	2	b	5	-0.30	42.99	8.41	0.0483
*BECKE2	4	b	5	-0.04	38.19	1.27	0.8008
Subtotal BECKE2				-0.62	81.18	9.68	
JAAKK2	25	b	7	0.68	15.22	4.39	0.0082
JANSON	1	b	9	0.14	38.50	0.00	0.3859
JEDRYC	1	f	3	-0.63	6.33	3.81	0.1102
LARSS1	2	b	3	0.60	31.28	6.55	0.0008
LARSS2	4	b	5	0.12	32.57	0.01	0.4855
MISHRA	3	m	12	0.18	101.81	0.17	0.0658
MISHRA	4	f	12	0.05	189.27	1.62	0.5021
Subtotal MISHRA				-0.05	291.08	1.79	
NG	6	f	6	0.17	7.19	0.00	0.6573
NHANES	1	b	0	0.10	56.25	0.09	0.4488
ORYSZC	1	m	0	0.41	1.45	0.10	0.6256
ORYSZC	2	f	0	0.02	3.79	0.06	0.9727
Subtotal ORYSZC				0.14	5.24	0.16	
PILOTT	1	b	3	0.09	14.49	0.04	0.7428
*ROBBIN	11	b	4	0.57	17.54	3.24	0.0168
SAPALD	2	b	8	0.33	45.46	1.61	0.0264
THORN	2	m	2	1.57	4.97	10.13	0.0005
THORN	3	f	2	0.41	8.37	0.58	0.2406
Subtotal THORN				1.69	13.35	10.71	

Appendix Table F3 - 2

IASTAD - Meta-analysis of Biochemical/Total/Household/Workplace Exposure (preferring most recent)
Lifetime/Current Asthma
Adjusted

```
            N        18
           NS        14


           Wt    655.68
     Het  Chi     42.09
     Het   df        17
     Het    P       ***
   Fixed   RR      1.15
          RRl      1.07
          RRu      1.24
            P       +++
  Random   RR      1.21
          RRl      1.05
          RRu      1.40
            P        ++
   Asymm    P      N.S.
```

Appendix Table F3 - 3

IASTAD - Meta-analysis of Biochemical/Total/Household/Workplace Exposure (preferring most recent)
Lifetime/Current Asthma
Adjusted

```
            N       18
            NS      14


            Wt    655.68
    Het Chi  42.09
    Het  df     17
    Het  P     ***
  Fixed  RR    1.15
           RRl   1.07
           RRu   1.24
           P     +++
 Random  RR    1.21
           RRl   1.05
           RRu   1.40
           P      ++
  Asymm  P    N.S.
```

| | Sex | | | |
	both	male	female	Total
N	10	3	5	18
NS	9	3	5	17
Wt	332.49	108.23	214.95	655.68
Het Chi	25.37	9.15	4.12	42.09
Het df	9	2	4	17
Het P	**	*	N.S.	***
Fixed RR	1.18	1.28	1.05	1.15
RRl	1.06	1.06	0.92	1.07
RRu	1.32	1.55	1.20	1.24
P	++	++	N.S.	+++
Random RR	1.22	2.02	1.05	1.21
RRl	1.02	0.73	0.89	1.05
RRu	1.47	5.56	1.23	1.40
P	+	N.S.	N.S.	++
Between Chi				3.45
Between df				2
Between P				N.S.

| | Asthma definition (lifetime/current) | | |
	lifetime	current	Total
N	9	9	18
NS	7	7	14
Wt	235.88	419.80	655.68
Het Chi	31.20	9.88	42.09
Het df	8	8	17
Het P	***	N.S.	***
Fixed RR	1.21	1.12	1.15
RRl	1.07	1.02	1.07
RRu	1.38	1.23	1.24
P	++	+	+++
Random RR	1.33	1.13	1.21
RRl	1.02	1.00	1.05
RRu	1.73	1.28	1.40
P	+	+	++
Between Chi			1.00
Between df			1
Between P			N.S.

Appendix Table F3 - 3

IASTAD - Meta-analysis of Biochemical/Total/Household/Workplace Exposure (preferring most recent)
Lifetime/Current Asthma
Adjusted

		Continent		
	NAmer	Europe	Oth/Mult	Total
N	4	9	5	18
NS	3	7	4	14
Wt	154.97	149.45	351.26	655.68
Het Chi	10.25	19.17	1.28	42.09
Het df	3	8	4	17
Het P	*	*	N.S.	***
Fixed RR	1.01	1.45	1.11	1.15
RRl	0.86	1.24	1.00	1.07
RRu	1.18	1.71	1.23	1.24
P	N.S.	+++	(+)	+++
Random RR	1.05	1.47	1.11	1.21
RRl	0.78	1.10	1.00	1.05
RRu	1.42	1.96	1.23	1.40
P	N.S.	++	(+)	++
Between Chi				11.39
Between df				2
Between P				**

		Start year of study		
	<1990	1990-99	unknown	Total
N	4	10	4	18
NS	3	8	3	14
Wt	154.97	481.95	18.76	655.68
Het Chi	10.25	23.75	2.74	42.09
Het df	3	9	3	17
Het P	*	**	N.S.	***
Fixed RR	1.01	1.21	0.89	1.15
RRl	0.86	1.11	0.57	1.07
RRu	1.18	1.33	1.40	1.24
P	N.S.	+++	N.S.	+++
Random RR	1.05	1.34	0.89	1.21
RRl	0.78	1.13	0.57	1.05
RRu	1.42	1.59	1.40	1.40
P	N.S.	+++	N.S.	++
Between Chi				5.36
Between df				2
Between P				(*)

		Study type		
	CC	Pr	CS	Total
N	5	3	10	18
NS	3	2	9	14
Wt	33.81	98.72	523.14	655.68
Het Chi	6.31	9.48	13.91	42.09
Het df	4	2	9	17
Het P	N.S.	**	N.S.	***
Fixed RR	1.93	0.96	1.15	1.15
RRl	1.38	0.78	1.06	1.07
RRu	2.70	1.16	1.26	1.24
P	+++	N.S.	++	+++
Random RR	1.92	1.04	1.18	1.21
RRl	1.21	0.67	1.04	1.05
RRu	3.05	1.63	1.33	1.40
P	++	N.S.	++	++
Between Chi				12.39
Between df				2
Between P				**

Appendix Table F3 - 3

<u>IASTAD - Meta-analysis of Biochemical/Total/Household/Workplace Exposure (preferring most recent)</u>
Lifetime/Current Asthma
Adjusted

<u>Ex smokers</u>

		excluded	included	Total
	N	13	5	18
	NS	10	4	14
	Wt	486.21	169.47	655.68
Het	Chi	28.08	10.33	42.09
Het	df	12	4	17
Het	P	**	*	***
Fixed	RR	1.20	1.01	1.15
	RRl	1.10	0.87	1.07
	RRu	1.32	1.18	1.24
	P	+++	N.S.	+++
Random	RR	1.30	1.05	1.21
	RRl	1.10	0.81	1.05
	RRu	1.55	1.35	1.40
	P	++	N.S.	++
Between	Chi			3.68
Between	df			1
Between	P			(*)

<u>Exposed group : when Exposed</u>

		life	adult	child	current	unspec	Total
	N	1	3	1	12	1	18
	NS	1	2	1	9	1	14
	Wt	7.19	30.89	31.28	571.83	14.49	655.68
Het	Chi	0.00	4.76	0.00	19.91	0.00	42.09
Het	df	0	2	0	11	0	17
Het	P	N.S.	(*)	N.S.	*	N.S.	***
Fixed	RR	1.18	1.99	1.82	1.09	1.09	1.15
	RRl	0.57	1.40	1.28	1.01	0.65	1.07
	RRu	2.45	2.83	2.58	1.19	1.82	1.24
	P	N.S.	+++	+++	+	N.S.	+++
Random	RR	1.18	2.15	1.82	1.10	1.09	1.21
	RRl	0.57	1.20	1.28	0.96	0.65	1.05
	RRu	2.45	3.87	2.58	1.24	1.82	1.40
	P	N.S.	+	+++	N.S.	N.S.	++
Between	Chi						17.41
Between	df						4
Between	P						**

Appendix Table F3 - 4

IASTAD - Meta-analysis of Biochemical/Total/Household/Workplace Exposure (preferring most recent)
Lifetime/Current Asthma
Unadjusted

REF	NRR	X	SEX	AST	SMOK	AGEL	AGEH	LOC	BEGYR	PUBYR	STTYP	ONS	ADJ	EXPOS	UNEXsrce	EXPOS-time	UNEXTI
BECKE2	1	x	b	l	Non	18	40	US:mul	1985	2001	Pr	prv	0	Cot	Low	current	non
BECKE2	3	x	b	l	Non	18	40	US:mul	1985	2001	Pr	ons	0	Cot	Low	current	non
JAAKK2	1	x	b	c	Never	21	63	Eu:Fin	1997	2003	CC	ons	0	Hh,Wk	None	current	non
JANSON	1		b	c	<1yr	20	48	multi	1990	2001	CS	prv	9	Hh,Wk	None	current	non
JEDRYC	1		f	c	<1yr	65	99	Eu:Pol	*	1995	CS	prv	3	Hh	NoHhMemb	current	non
LARSS1	1	x	b	l	Never	15	69	Eu:Swe	1995	2001	CS	prv	0	Hh	NoHhMemb	childhood	non
LARSS2	4		b	l	Never	15	64	Eu:Est	1995	2003	CS	prv	5	Work	NotWork	current	non
MISHRA	1	x	m	c	NevReg	60	99	As:Ind	1998	2003	CS	prv	0	Hh	NoHhMemb	current	non
MISHRA	2	x	f	c	NevReg	60	99	As:Ind	1998	2003	CS	prv	0	Hh	NoHhMemb	current	non
NG	3	x	f	c	<1yr	20	74	As:Sin	*	1993	CS	prv	0	Hh	NoHhMemb	lifetime	non
NHANES	1		b	c	Non	17	99	US:nat	1988	2002	CS	prv	0	Hh	NoHhMemb	current	non
ORYSZC	1		m	c	NevReg	25	54	Eu:Fra	*	2000	CC	prv	0	Hh	NoHhMemb	current	non
ORYSZC	2		f	c	NevReg	25	54	Eu:Fra	*	2000	CC	prv	0	Hh	NoHhMemb	current	non
PILOTT	1		b	l	Non	18	99	Austra	1995	1999	CS	prv	3	Hh	NoHhMemb	unspec	non
ROBBIN	11		b	l	Non	25	99	US:Cal	1977	1993	Pr	ons	4	Hh,Wk	None	adult	never
SAPALD	1	x	b	l	<20pks	18	60	Eu:Swi	1991	1994	CS	prv	0	Hh,Wk	None	current	non
THORN	1	x	b	l	Never	20	50	Eu:Swe	1994	2001	CC	prv	0	Hh	NoHhMemb	last6homes	non

Appendix Table F3 - 5

IASTAD - Meta-analysis of Biochemical/Total/Household/Workplace Exposure (preferring most recent)
Lifetime/Current Asthma
Unadjusted

```
                                Numbers
                                Numbers exposed Non-exposed
 REF       NRR     SEX ADJ      Case    Cont    Case    Cont     RR       95.00%CI
 BECKE2 1        b   0           63     799     215    2051     0.75 ( 0.56-  1.01)
*BECKE2 3        b   0           54     799     141    2051     0.98 ( 0.73-  1.33)
 Subtotal BECKE2                                                0.86 ( 0.69-  1.06)
 JAAKK2 1        b   0           38      49     196     436     1.73 ( 1.09-  2.72)
 JANSON 1        b   9            -       -       -       -     1.15 ( 0.84-  1.58)
 JEDRYC 1        f   3            -       -       -       -     0.53 ( 0.24-  1.14)
 LARSS1 1        b   0           85    1171      58    1470     1.84 ( 1.31-  2.59)
 LARSS2 4        b   5            -       -       -       -     1.13 ( 0.80-  1.59)
 MISHRA 1        m   0          242    1739     835    8047     1.34 ( 1.15-  1.56)
 MISHRA 2        f   0          561    6037     829    9659     1.08 ( 0.97-  1.21)
 Subtotal MISHRA                                                1.17 ( 1.07-  1.28)
 NG     3        f   0           18     645      15     604     1.12 ( 0.56-  2.25)
 NHANES 1        b   0           70    1481     370    8660     1.11 ( 0.85-  1.44)
 ORYSZC 1        m   0            3       4      14      28     1.50 ( 0.29-  7.65)
 ORYSZC 2        f   0            8      13      26      43     1.02 ( 0.37-  2.78)
 Subtotal ORYSZC                                                1.13 ( 0.48-  2.67)
 PILOTT 1        b   3            -       -       -       -     1.09 ( 0.65-  1.82)
*ROBBIN 11       b   4            -       -       -       -     1.77 ( 1.11-  2.83)
 SAPALD 1        b   0           96    1163     191    2747     1.19 ( 0.92-  1.53)
 THORN  1        b   0           33     116      36     302     2.39 ( 1.42-  4.01)
Partial Totals                 1271   14016    2926   36098
*prospective study

 REF       NRR     SEX ADJ              Ys       Ws       Qs       Ps

 BECKE2 1        b   0                -0.28    44.92     8.79    0.0563
*BECKE2 3        b   0                -0.02    41.89     1.28    0.9121
 Subtotal BECKE2                      -0.62    86.81    10.07
 JAAKK2 1        b   0                 0.55    18.48     2.78    0.0191
 JANSON 1        b   9                 0.14    38.50     0.01    0.3859
 JEDRYC 1        f   3                -0.63     6.33     3.98    0.1102
 LARSS1 1        b   0                 0.61    32.74     6.69    0.0005
 LARSS2 4        b   5                 0.12    32.57     0.04    0.4855
 MISHRA 1        m   0                 0.29   165.86     3.06    0.0002
 MISHRA 2        f   0                 0.08   306.94     1.87    0.1638
 Subtotal MISHRA                       0.06   472.80     4.94
 NG     3        f   0                 0.12     7.97     0.01    0.7419
 NHANES 1        b   0                 0.10    56.25     0.18    0.4488
 ORYSZC 1        m   0                 0.41     1.45     0.09    0.6256
 ORYSZC 2        f   0                 0.02     3.79     0.07    0.9727
 Subtotal ORYSZC                       0.11     5.24     0.16
 PILOTT 1        b   3                 0.09    14.49     0.07    0.7428
*ROBBIN 11       b   4                 0.57    17.54     3.00    0.0168
 SAPALD 1        b   0                 0.17    59.26     0.01    0.1866
 THORN  1        b   0                 0.87    14.28     7.24    0.0010
```

```
              N     17
              NS    14


         Wt  863.26
    Het Chi  39.18
    Het  df     16
    Het  P     **
    Fixed RR   1.17
         RRl   1.10
         RRu   1.25
          P    +++
    Random RR  1.20
         RRl   1.06
         RRu   1.37
          P    ++
    Asymm P   N.S.
```

Appendix Table F3 - 6

IASTAD - Meta-analysis of Biochemical/Total/Household/Workplace Exposure (preferring most recent)
Lifetime/Current Asthma
Unadjusted

```
        N       17
        NS      14


        Wt   863.26
  Het Chi    39.18
  Het  df       16
  Het  P       **
Fixed  RR     1.17
       RRl    1.10
       RRu    1.25
       P      +++
Random RR     1.20
       RRl    1.06
       RRu    1.37
       P       ++
 Asymm P      N.S.
```

		Sex		
	both	male	female	Total
N	11	2	4	17
NS	10	2	4	16
Wt	370.92	167.31	325.03	863.26
Het Chi	29.97	0.02	3.19	39.18
Het df	10	1	3	16
Het P	***	N.S.	N.S.	**
Fixed RR	1.19	1.34	1.07	1.17
RRl	1.08	1.15	0.96	1.10
RRu	1.32	1.56	1.19	1.25
P	+++	+++	N.S.	+++
Random RR	1.26	1.34	1.05	1.20
RRl	1.05	1.15	0.88	1.06
RRu	1.51	1.56	1.24	1.37
P	+	+++	N.S.	++
Between Chi				6.01
Between df				2
Between P				*

	Asthma definition (lifetime/current)		
	lifetime	current	Total
N	8	9	17
NS	7	7	14
Wt	257.69	605.56	863.26
Het Chi	27.07	12.04	39.18
Het df	7	8	16
Het P	***	N.S.	**
Fixed RR	1.19	1.16	1.17
RRl	1.05	1.07	1.10
RRu	1.34	1.26	1.25
P	++	+++	+++
Random RR	1.27	1.18	1.20
RRl	0.99	1.03	1.06
RRu	1.62	1.34	1.37
P	(+)	+	++
Between Chi			0.07
Between df			1
Between P			N.S.

Appendix Table F3 - 6

IASTAD - Meta-analysis of Biochemical/Total/Household/Workplace Exposure (preferring most recent)
Lifetime/Current Asthma
Unadjusted

| | | Continent | | | |
		NAmer	Europe	Oth/Mult	Total
	N	4	8	5	17
	NS	3	7	4	14
	Wt	160.60	168.90	533.76	863.26
Het	Chi	9.92	16.71	5.01	39.18
Het	df	3	7	4	16
Het	P	*	*	N.S.	**
Fixed	RR	1.01	1.37	1.16	1.17
	RRl	0.87	1.18	1.07	1.10
	RRu	1.18	1.59	1.27	1.25
	P	N.S.	+++	+++	+++
Random	RR	1.06	1.38	1.17	1.20
	RRl	0.79	1.05	1.05	1.06
	RRu	1.41	1.80	1.31	1.37
	P	N.S.	+	++	++
Between	Chi				7.55
Between	df				2
Between	P				*

| | | Start year of study | | | |
		<1990	1990-99	unknown	Total
	N	4	9	4	17
	NS	3	8	3	14
	Wt	160.60	683.12	19.54	863.26
Het	Chi	9.92	20.59	2.60	39.18
Het	df	3	8	3	16
Het	P	*	**	N.S.	**
Fixed	RR	1.01	1.22	0.88	1.17
	RRl	0.87	1.13	0.57	1.10
	RRu	1.18	1.32	1.38	1.25
	P	N.S.	+++	N.S.	+++
Random	RR	1.06	1.31	0.88	1.20
	RRl	0.79	1.13	0.57	1.06
	RRu	1.41	1.52	1.38	1.37
	P	N.S.	+++	N.S.	++
Between	Chi				6.09
Between	df				2
Between	P				*

| | | Study type | | | |
		CC	Pr	CS	Total
	N	4	3	10	17
	NS	3	2	9	14
	Wt	38.00	104.35	720.91	863.26
Het	Chi	2.43	9.26	15.92	39.18
Het	df	3	2	9	16
Het	P	N.S.	**	(*)	**
Fixed	RR	1.84	0.97	1.18	1.17
	RRl	1.34	0.80	1.09	1.10
	RRu	2.53	1.17	1.26	1.25
	P	+++	N.S.	+++	+++
Random	RR	1.84	1.06	1.19	1.20
	RRl	1.34	0.69	1.06	1.06
	RRu	2.53	1.62	1.34	1.37
	P	+++	N.S.	++	++
Between	Chi				11.57
Between	df				2
Between	P				**

Analysis run on 17-MAR-05

Appendix Table F3 - 6

IASTAD - Meta-analysis of Biochemical/Total/Household/Workplace Exposure (preferring most recent)
Lifetime/Current Asthma
Unadjusted

		Ex smokers excluded	included	Total
	N	12	5	17
	NS	10	4	14
	Wt	688.17	175.09	863.26
Het	Chi	25.02	9.99	39.18
Het	df	11	4	16
Het	P	**	*	**
Fixed	RR	1.21	1.02	1.17
	RRl	1.13	0.88	1.10
	RRu	1.31	1.18	1.25
	P	+++	N.S.	+++
Random	RR	1.28	1.06	1.20
	RRl	1.11	0.83	1.06
	RRu	1.49	1.35	1.37
	P	++	N.S.	++
Between	Chi			4.18
Between	df			1
Between	P			*

Appendix Table F3 - 7

IASTAD - Meta-analysis of Biochemical/Total/Household/Workplace Exposure (preferring most recent)
Lifetime/Current Asthma
Excluded studies (and stage at which they were excluded)


```
        1       2      3      4      5      6      7      8      9     10     11     12     13     14     15     16

3      KRONQV PLATTS
9      RAHERI
                                              Potentially overlapping studies
   REF|  REFGP|PRINC|              OVERLAP|
 JANSON JANSON      p       JANSON/RAHERI


                              Adjusted - insufficient data for metaanalysis
   REF|NRR|SEX|AST|   SMOK|AGEL|AGEH|   LOC|BEGYR|PUBYR|STTYP|ONS|ADJ|EXPOS|UNEXsrce| EXPOS-time|UNEXTI|      RR|SIG|
 KRONQV  1   b   l  Never   15   65 Eu:Swe 1996  1999    CS prv   4 Total    None   childhood   non      *    n
 LARSS2  5   b   l  Never   15   64 Eu:Est 1995  2003    CS prv   5   Hh NoHhMemb    current    non      *    n
 PLATTS  1   b   c    Non   15   55 US:Del 1988  1993    CC prv   0 Total    None     unspec    non      *    n
```

_____

Appendix Table F4 -

IASTAD - Meta-analysis of Total/Household/Workplace Exposure in Childhood
Lifetime/Current Asthma

This analysis is restricted to results for:
1) Total, household (overall), parental, or workplace exposure
2) Childhood exposure
3) Results not by amount of exposure
4) Results complete enough for use in metaanalysis

Within each study, results are then selected (in the following order of preference, within each sex) for:
5) ASTHMA : lifetime, current
6) EXPOS   : biochemical (cotinine), total, household, workplace
7) WHOHOU : household overall, mother
8) UNEXTI : unexposed group never, non (i.e. not at time defined for exposed group)
9) For overlapping studies: principal rather than subsidiary studies
Finally for single sex results (m, f) in preference to results for both sexes combined (b).

Results adjusted for the most potential confounders are then chosen in Sections -1 to -3
(and those which actually differ from the adjusted results in Appendix Table F1 - 1 are marked 'x' in Section -1)
and results adjusted for the least confounders in Sections -4 to -6. (Those least adjusted results which
actually differ from the most adjusted are marked 'x' in column X in Section -4)

Section -7 shows excluded studies, together with the stage (as above) at which no qualifying results
were found. It then lists the potentially overlapping studies which have been included (1=principal,
2=subsidiary), and any results which would have been included in preference except that they had data
not complete enough for use in metaanalysis. It also lists their significance (yes/no), if known.

_____

Appendix Table F4 - 1

IASTAD - Meta-analysis of Total/Household/Workplace Exposure in Childhood
Lifetime/Current Asthma
Adjusted

REF	NRR	CompF1	SEX	AST	SMOK	AGEL	AGEH	LOC	BEGYR	PUBYR	STTYP	ONS	ADJ	EXPOS	UNEXsrce	EXPOS-time	UNEXTI
JANSON	9	x	m	c	<1yr	20	48	multi	1990	2001	CS	prv	6	Mothr	NotMoth	childhood	non
JANSON	10	x	f	c	<1yr	20	48	multi	1990	2001	CS	prv	6	Mothr	NotMoth	childhood	non
LARSS1	2		b	l	Never	15	69	Eu:Swe	1995	2001	CS	prv	3	Hh	NoHhMemb	childhood	non
ROBBIN	10		b	l	Non	25	99	US:Cal	1977	1993	Pr	ons	4	Hh,Wk	None	childhood	never

Appendix Table F4 - 2

IASTAD - Meta-analysis of Total/Household/Workplace Exposure in Childhood
Lifetime/Current Asthma
Adjusted

				Numbers Numbers exposed Non-exposed							
REF	NRR	SEX	ADJ	Case	Cont	Case	Cont	RR		95.00%CI	
JANSON 9		m	6	–	–	–	–	0.81 (	0.54–	1.23)	
JANSON 10		f	6	–	–	–	–	1.10 (	0.78–	1.55)	
Subtotal JANSON								0.97 (	0.75–	1.26)	
LARSS1 2		b	3	85	–	58	–	1.82 (	1.28–	2.58)	
*ROBBIN 10		b	4	–	–	–	–	1.57 (	0.96–	2.58)	
Partial Totals				85	0	58	0				

*prospective study

REF	NRR	SEX	ADJ	Ys	Ws	Qs	Ps
JANSON 9		m	6	-0.21	22.67	4.53	0.3157
JANSON 10		f	6	0.10	32.58	0.65	0.5864
Subtotal JANSON				-0.59	55.26	5.17	
LARSS1 2		b	3	0.60	31.28	4.11	0.0008
*ROBBIN 10		b	4	0.45	15.72	0.73	0.0737

```
          N      4
          NS     3


          Wt   102.26
     Het Chi   10.01
     Het  df      3
     Het  P       *
   Fixed RR    1.27
         RRl   1.04
         RRu   1.54
           P     +
  Random RR    1.26
         RRl   0.88
         RRu   1.81
           P   N.S.
   Asymm P    N.S.
```

Appendix Table F4 - 3

IASTAD - Meta-analysis of Total/Household/Workplace Exposure in Childhood
Lifetime/Current Asthma
Adjusted

```
           N      4
          NS      3


          Wt  102.26
    Het Chi   10.01
    Het  df       3
    Het  P        *
  Fixed RR     1.27
        RRl    1.04
        RRu    1.54
          P      +
 Random RR     1.26
        RRl    0.88
        RRu    1.81
          P    N.S.
  Asymm  P     N.S.
```

	Sex			
	both	male	female	Total
N	2	1	1	4
NS	2	1	1	3
Wt	47.00	22.67	32.58	102.26
Het Chi	0.23	0.00	0.00	10.01
Het df	1	0	0	3
Het P	N.S.	N.S.	N.S.	*
Fixed RR	1.73	0.81	1.10	1.27
RRl	1.30	0.54	0.78	1.04
RRu	2.31	1.22	1.55	1.54
P	+++	N.S.	N.S.	+
Random RR	1.73	0.81	1.10	1.26
RRl	1.30	0.54	0.78	0.88
RRu	2.31	1.22	1.55	1.81
P	+++	N.S.	N.S.	N.S.
Between Chi				9.79
Between df				2
Between P				**

	Asthma definition (lifetime/current)		
	lifetime	current	Total
N	2	2	4
NS	2	1	3
Wt	47.00	55.26	102.26
Het Chi	0.23	1.25	10.01
Het df	1	1	3
Het P	N.S.	N.S.	*
Fixed RR	1.73	0.97	1.27
RRl	1.30	0.75	1.04
RRu	2.31	1.26	1.54
P	+++	N.S.	+
Random RR	1.73	0.96	1.26
RRl	1.30	0.72	0.88
RRu	2.31	1.30	1.81
P	+++	N.S.	N.S.
Between Chi			8.53
Between df			1
Between P			**

Appendix Table F4 - 3

IASTAD - Meta-analysis of Total/Household/Workplace Exposure in Childhood
Lifetime/Current Asthma
Adjusted

	Continent			
	NAmer	Europe	Oth/Mult	Total
N	1	1	2	4
NS	1	1	1	3
Wt	15.72	31.28	55.26	102.26
Het Chi	0.00	0.00	1.25	10.01
Het df	0	0	1	3
Het P	N.S.	N.S.	N.S.	*
Fixed RR	1.57	1.82	0.97	1.27
RRl	0.96	1.28	0.75	1.04
RRu	2.57	2.58	1.26	1.54
P	(+)	+++	N.S.	+
Random RR	1.57	1.82	0.96	1.26
RRl	0.96	1.28	0.72	0.88
RRu	2.57	2.58	1.30	1.81
P	(+)	+++	N.S.	N.S.
Between Chi				8.76
Between df				2
Between P				*

	Start year of study			
	<1990	1990-99	unknown	Total
N	1	3		4
NS	1	2		3
Wt	15.72	86.53		102.26
Het Chi	0.00	9.16		10.01
Het df	0	2		3
Het P	N.S.	*		*
Fixed RR	1.57	1.22		1.27
RRl	0.96	0.99		1.04
RRu	2.57	1.50		1.54
P	(+)	(+)		+
Random RR	1.57	1.19		1.26
RRl	0.96	0.75		0.88
RRu	2.57	1.87		1.81
P	(+)	N.S.		N.S.
Between Chi				0.86
Between df				1
Between P				N.S.

	Study type			
	CC	Pr	CS	Total
N		1	3	4
NS		1	2	3
Wt		15.72	86.53	102.26
Het Chi		0.00	9.16	10.01
Het df		0	2	3
Het P		N.S.	*	*
Fixed RR		1.57	1.22	1.27
RRl		0.96	0.99	1.04
RRu		2.57	1.50	1.54
P		(+)	(+)	+
Random RR		1.57	1.19	1.26
RRl		0.96	0.75	0.88
RRu		2.57	1.87	1.81
P		(+)	N.S.	N.S.
Between Chi				0.86
Between df				1
Between P				N.S.

Analysis run on 17-MAR-05

Appendix Table F4 - 3

IASTAD - Meta-analysis of Total/Household/Workplace Exposure in Childhood
Lifetime/Current Asthma
Adjusted

Ex smokers

		excluded	included	Total
	N	3	1	4
	NS	2	1	3
	Wt	86.53	15.72	102.26
Het	Chi	9.16	0.00	10.01
Het	df	2	0	3
Het	P	*	N.S.	*
Fixed	RR	1.22	1.57	1.27
	RRl	0.99	0.96	1.04
	RRu	1.50	2.57	1.54
	P	(+)	(+)	+
Random	RR	1.19	1.57	1.26
	RRl	0.75	0.96	0.88
	RRu	1.87	2.57	1.81
	P	N.S.	(+)	N.S.
Between	Chi			0.86
Between	df			1
Between	P			N.S.

Appendix Table F4 - 4

IASTAD - Meta-analysis of Total/Household/Workplace Exposure in Childhood
Lifetime/Current Asthma
Unadjusted

REF	NRR	X	SEX	AST		SMOK	AGEL	AGEH		LOC	BEGYR	PUBYR	STTYP	ONS	ADJ	EXPOS	UNEXsrce		EXPOS-time	UNEXTI	
JANSON	9		m	c	<1yr	20	48	multi	1990	2001	CS	prv	6	Mothr	NotMoth	childhood	non
JANSON	10		f	c	<1yr	20	48	multi	1990	2001	CS	prv	6	Mothr	NotMoth	childhood	non
LARSS1	1	x	b	l	Never	15	69	Eu:Swe	1995	2001	CS	prv	0	Hh	NoHhMemb	childhood	non
ROBBIN	10		b	l	Non	25	99	US:Cal	1977	1993	Pr	ons	4	Hh,Wk	None	childhood	never

Appendix Table F4 - 5

IASTAD - Meta-analysis of Total/Household/Workplace Exposure in Childhood
Lifetime/Current Asthma
Unadjusted

```
                                 Numbers
                                 Numbers exposed Non-exposed
REF     NRR      SEX ADJ         Case    Cont    Case    Cont    RR        95.00%CI
 JANSON 9        m   6            -       -       -       -      0.81 ( 0.54-  1.23)
 JANSON 10       f   6            -       -       -       -      1.10 ( 0.78-  1.55)
 Subtotal JANSON                                                0.97 ( 0.75-  1.26)
 LARSS1 1        b   0           85      1171    58      1470   1.84 ( 1.31-  2.59)
*ROBBIN 10       b   4            -       -       -       -      1.57 ( 0.96-  2.58)
Partial Totals                  85      1171    58      1470
*prospective study

REF     NRR      SEX ADJ                 Ys      Ws      Qs      Ps

 JANSON 9        m   6                  -0.21   22.67   4.70    0.3157
 JANSON 10       f   6                   0.10   32.58   0.73    0.5864
 Subtotal JANSON                       -0.60   55.26   5.43
 LARSS1 1        b   0                   0.61   32.74   4.36    0.0005
*ROBBIN 10       b   4                   0.45   15.72   0.67    0.0737
```

```
           N      4
           NS     3


           Wt   103.72
      Het Chi    10.46
      Het  df        3
      Het  P         *
    Fixed  RR     1.28
           RRl    1.05
           RRu    1.55
             P      +
   Random   RR     1.27
           RRl    0.88
           RRu    1.83
             P    N.S.
   Asymm    P    N.S.
```

Appendix Table F4 - 6

IASTAD - Meta-analysis of Total/Household/Workplace Exposure in Childhood
Lifetime/Current Asthma
Unadjusted

N	4	
NS	3	

Wt	103.72
Het Chi	10.46
Het df	3
Het P	*
Fixed RR	1.28
RRl	1.05
RRu	1.55
P	+
Random RR	1.27
RRl	0.88
RRu	1.83
P	N.S.
Asymm P	N.S.

	Sex			
	both	male	female	Total
N	2	1	1	4
NS	2	1	1	3
Wt	48.47	22.67	32.58	103.72
Het Chi	0.27	0.00	0.00	10.46
Het df	1	0	0	3
Het P	N.S.	N.S.	N.S.	*
Fixed RR	1.75	0.81	1.10	1.28
RRl	1.32	0.54	0.78	1.05
RRu	2.32	1.22	1.55	1.55
P	+++	N.S.	N.S.	+
Random RR	1.75	0.81	1.10	1.27
RRl	1.32	0.54	0.78	0.88
RRu	2.32	1.22	1.55	1.83
P	+++	N.S.	N.S.	N.S.
Between Chi				10.19
Between df				2
Between P				**

	Asthma definition (lifetime/current)		
	lifetime	current	Total
N	2	2	4
NS	2	1	3
Wt	48.47	55.26	103.72
Het Chi	0.27	1.25	10.46
Het df	1	1	3
Het P	N.S.	N.S.	*
Fixed RR	1.75	0.97	1.28
RRl	1.32	0.75	1.05
RRu	2.32	1.26	1.55
P	+++	N.S.	+
Random RR	1.75	0.96	1.27
RRl	1.32	0.72	0.88
RRu	2.32	1.30	1.83
P	+++	N.S.	N.S.
Between Chi			8.94
Between df			1
Between P			**

Appendix Table F4 - 6

IASTAD - Meta-analysis of Total/Household/Workplace Exposure in Childhood
Lifetime/Current Asthma
Unadjusted

	Continent			
	NAmer	Europe	Oth/Mult	Total
N	1	1	2	4
NS	1	1	1	3
Wt	15.72	32.74	55.26	103.72
Het Chi	0.00	0.00	1.25	10.46
Het df	0	0	1	3
Het P	N.S.	N.S.	N.S.	*
Fixed RR	1.57	1.84	0.97	1.28
RRl	0.96	1.31	0.75	1.05
RRu	2.57	2.59	1.26	1.55
P	(+)	+++	N.S.	+
Random RR	1.57	1.84	0.96	1.27
RRl	0.96	1.31	0.72	0.88
RRu	2.57	2.59	1.30	1.83
P	(+)	+++	N.S.	N.S.
Between Chi				9.21
Between df				2
Between P				*

	Start year of study			
	<1990	1990-99	unknown	Total
N	1	3		4
NS	1	2		3
Wt	15.72	88.00		103.72
Het Chi	0.00	9.67		10.46
Het df	0	2		3
Het P	N.S.	**		*
Fixed RR	1.57	1.23		1.28
RRl	0.96	1.00		1.05
RRu	2.57	1.52		1.55
P	(+)	(+)		+
Random RR	1.57	1.19		1.27
RRl	0.96	0.75		0.88
RRu	2.57	1.89		1.83
P	(+)	N.S.		N.S.
Between Chi				0.79
Between df				1
Between P				N.S.

	Study type			
	CC	Pr	CS	Total
N		1	3	4
NS		1	2	3
Wt		15.72	88.00	103.72
Het Chi		0.00	9.67	10.46
Het df		0	2	3
Het P		N.S.	**	*
Fixed RR		1.57	1.23	1.28
RRl		0.96	1.00	1.05
RRu		2.57	1.52	1.55
P		(+)	(+)	+
Random RR		1.57	1.19	1.27
RRl		0.96	0.75	0.88
RRu		2.57	1.89	1.83
P		(+)	N.S.	N.S.
Between Chi				0.79
Between df				1
Between P				N.S.

Analysis run on 17-MAR-05

Appendix Table F4 - 6

IASTAD - Meta-analysis of Total/Household/Workplace Exposure in Childhood
Lifetime/Current Asthma
Unadjusted

Ex smokers

		excluded	included	Total
	N	3	1	4
	NS	2	1	3
	Wt	88.00	15.72	103.72
Het	Chi	9.67	0.00	10.46
Het	df	2	0	3
Het	P	**	N.S.	*
Fixed	RR	1.23	1.57	1.28
	RRl	1.00	0.96	1.05
	RRu	1.52	2.57	1.55
	P	(+)	(+)	+
Random	RR	1.19	1.57	1.27
	RRl	0.75	0.96	0.88
	RRu	1.89	2.57	1.83
	P	N.S.	(+)	N.S.
Between	Chi			0.79
Between	df			1
Between	P			N.S.

Appendix Table F4 - 7

IASTAD - Meta-analysis of Total/Household/Workplace Exposure in Childhood
Lifetime/Current Asthma
Excluded studies (and stage at which they were excluded)


```
      1      2      3      4      5      6      7      8      9     10     11     12     13     14     15     16

2      BECKE2 JAAKK2 JEDRYC LARSS2 MISHRA        NG NHANES ORYSZC PILOTT PLATTS SAPALD  THORN
4      KRONQV
9      RAHERI
```
Potentially overlapping studies
```
   REF|  REFGP|PRINC|             OVERLAP|
 JANSON JANSON     p       JANSON/RAHERI
```

Adjusted - insufficient data for metaanalysis
```
   REF|NRR|SEX|AST|  SMOK|AGEL|AGEH|   LOC|BEGYR|PUBYR|STTYP|ONS|ADJ|EXPOS|UNEXsrce| EXPOS-time|UNEXTI|     RR|SIG|
 KRONQV  1   b   l Never   15   65 Eu:Swe 1996  1999   CS prv   4 Total    None   childhood    non       *   n
```

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Appendix Table F5 -

IASTAD - Meta-analysis of Total/Household/Workplace Exposure in Childhood (preferring father)
Lifetime/Current Asthma

This analysis is restricted to results for:
1) Total, household (overall), parental, or workplace exposure
2) Childhood exposure
3) Results not by amount of exposure
4) Results complete enough for use in metaanalysis

Within each study, results are then selected (in the following order of preference, within each sex) for:
5) ASTHMA : lifetime, current
6) EXPOS   : biochemical (cotinine), total, household, workplace
7) WHOHOU : household overall, father
8) UNEXTI : unexposed group never, non (i.e. not at time defined for exposed group)
9) For overlapping studies: principal rather than subsidiary studies
Finally for single sex results (m, f) in preference to results for both sexes combined (b).

Results adjusted for the most potential confounders are then chosen in Sections -1 to -3
(and those which actually differ from the adjusted results in Appendix Table F4 - 1 are marked 'x' in Section -1)
and results adjusted for the least confounders in Sections -4 to -6. (Those least adjusted results which
actually differ from the most adjusted are marked 'x' in column X in Section -4)

Section -7 shows excluded studies, together with the stage (as above) at which no qualifying results
were found. It then lists the potentially overlapping studies which have been included (1=principal,
2=subsidiary), and any results which would have been included in preference except that they had data
not complete enough for use in metaanalysis. It also lists their significance (yes/no), if known.

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Appendix Table F5 - 1

IASTAD - Meta-analysis of Total/Household/Workplace Exposure in Childhood (preferring father)
Lifetime/Current Asthma
Adjusted

REF	NRR	CompF4	SEX	AST	SMOK	AGEL	AGEH	LOC	BEGYR	PUBYR	STTYP	ONS	ADJ	EXPOS	UNEXsrce	EXPOS-time	UNEXTI
JANSON	7	x	m	c	<1yr	20	48	multi	1990	2001	CS	prv	6	Fathr	NotFathr	childhood	non
JANSON	8	x	f	c	<1yr	20	48	multi	1990	2001	CS	prv	6	Fathr	NotFathr	childhood	non
LARSS1	2		b	l	Never	15	69	Eu:Swe	1995	2001	CS	prv	3	Hh	NoHhMemb	childhood	non
ROBBIN	10		b	l	Non	25	99	US:Cal	1977	1993	Pr	ons	4	Hh,Wk	None	childhood	never

_____

Appendix Table F5 - 2

IASTAD - Meta-analysis of Total/Household/Workplace Exposure in Childhood (preferring father)
Lifetime/Current Asthma
Adjusted

```
                                   Numbers
                                   Numbers exposed  Non-exposed
REF      NRR      SEX ADJ          Case    Cont    Case    Cont      RR        95.00%CI
 JANSON 7          m   6            -       -       -       -       1.08 ( 0.76-  1.54)
 JANSON 8          f   6            -       -       -       -       0.67 ( 0.49-  0.91)
 Subtotal JANSON                                                   0.82 ( 0.65-  1.04)
 LARSS1 2          b   3           85       -      58       -       1.82 ( 1.28-  2.58)
*ROBBIN 10         b   4            -       -       -       -       1.57 ( 0.96-  2.58)
 Partial Totals                    85       0      58       0
*prospective study

REF      NRR      SEX ADJ                  Ys      Ws      Qs       Ps

 JANSON 7          m   6                   0.08    30.81    0.02    0.6692
 JANSON 8          f   6                  -0.40    40.10   10.16    0.0112
 Subtotal JANSON                          -0.53    70.91   10.18
 LARSS1 2          b   3                   0.60    31.28    7.69    0.0008
*ROBBIN 10         b   4                   0.45    15.72    1.91    0.0737
```

```
              N       4
              NS      3


             Wt   117.90
         Het Chi   19.78
         Het  df      3
         Het  P     ***
      Fixed  RR    1.11
             RRl   0.93
             RRu   1.33
               P   N.S.
     Random  RR    1.18
             RRl   0.74
             RRu   1.90
               P   N.S.
      Asymm  P     N.S.
```

Appendix Table F5 - 3

IASTAD - Meta-analysis of Total/Household/Workplace Exposure in Childhood (preferring father)
Lifetime/Current Asthma
Adjusted

N	4
NS	3

Wt	117.90
Het Chi	19.78
Het df	3
Het P	***
Fixed RR	1.11
RRl	0.93
RRu	1.33
P	N.S.
Random RR	1.18
RRl	0.74
RRu	1.90
P	N.S.
Asymm P	N.S.

	Sex			
	both	male	female	Total
N	2	1	1	4
NS	2	1	1	3
Wt	47.00	30.81	40.10	117.90
Het Chi	0.23	0.00	0.00	19.78
Het df	1	0	0	3
Het P	N.S.	N.S.	N.S.	***
Fixed RR	1.73	1.08	0.67	1.11
RRl	1.30	0.76	0.49	0.93
RRu	2.31	1.54	0.91	1.33
P	+++	N.S.	−	N.S.
Random RR	1.73	1.08	0.67	1.18
RRl	1.30	0.76	0.49	0.74
RRu	2.31	1.54	0.91	1.90
P	+++	N.S.	−	N.S.
Between Chi				19.55
Between df				2
Between P				***

	Asthma definition (lifetime/current)		
	lifetime	current	Total
N	2	2	4
NS	2	1	3
Wt	47.00	70.91	117.90
Het Chi	0.23	3.97	19.78
Het df	1	1	3
Het P	N.S.	*	***
Fixed RR	1.73	0.82	1.11
RRl	1.30	0.65	0.93
RRu	2.31	1.04	1.33
P	+++	N.S.	N.S.
Random RR	1.73	0.84	1.18
RRl	1.30	0.53	0.74
RRu	2.31	1.35	1.90
P	+++	N.S.	N.S.
Between Chi			15.58
Between df			1
Between P			***

Appendix Table F5 - 3

IASTAD - Meta-analysis of Total/Household/Workplace Exposure in Childhood (preferring father)
Lifetime/Current Asthma
Adjusted

		Continent			
		NAmer	Europe	Oth/Mult	Total
N		1	1	2	4
NS		1	1	1	3
	Wt	15.72	31.28	70.91	117.90
Het	Chi	0.00	0.00	3.97	19.78
Het	df	0	0	1	3
Het	P	N.S.	N.S.	*	***
Fixed	RR	1.57	1.82	0.82	1.11
	RRl	0.96	1.28	0.65	0.93
	RRu	2.57	2.58	1.04	1.33
	P	(+)	+++	N.S.	N.S.
Random	RR	1.57	1.82	0.84	1.18
	RRl	0.96	1.28	0.53	0.74
	RRu	2.57	2.58	1.35	1.90
	P	(+)	+++	N.S.	N.S.
Between	Chi				15.81
Between	df				2
Between	P				***

		Start year of study			
		<1990	1990-99	unknown	Total
N		1	3		4
NS		1	2		3
	Wt	15.72	102.18		117.90
Het	Chi	0.00	17.58		19.78
Het	df	0	2		3
Het	P	N.S.	***		***
Fixed	RR	1.57	1.05		1.11
	RRl	0.96	0.87		0.93
	RRu	2.57	1.28		1.33
	P	(+)	N.S.		N.S.
Random	RR	1.57	1.09		1.18
	RRl	0.96	0.61		0.74
	RRu	2.57	1.94		1.90
	P	(+)	N.S.		N.S.
Between	Chi				2.20
Between	df				1
Between	P				N.S.

		Study type			
		CC	Pr	CS	Total
N			1	3	4
NS			1	2	3
	Wt		15.72	102.18	117.90
Het	Chi		0.00	17.58	19.78
Het	df		0	2	3
Het	P		N.S.	***	***
Fixed	RR		1.57	1.05	1.11
	RRl		0.96	0.87	0.93
	RRu		2.57	1.28	1.33
	P		(+)	N.S.	N.S.
Random	RR		1.57	1.09	1.18
	RRl		0.96	0.61	0.74
	RRu		2.57	1.94	1.90
	P		(+)	N.S.	N.S.
Between	Chi				2.20
Between	df				1
Between	P				N.S.

Analysis run on 17-MAR-05

Appendix Table F5 - 3

IASTAD - Meta-analysis of Total/Household/Workplace Exposure in Childhood (preferring father)
Lifetime/Current Asthma
Adjusted

Ex smokers

		excluded	included	Total
	N	3	1	4
	NS	2	1	3
	Wt	102.18	15.72	117.90
Het	Chi	17.58	0.00	19.78
Het	df	2	0	3
Het	P	***	N.S.	***
Fixed	RR	1.05	1.57	1.11
	RRl	0.87	0.96	0.93
	RRu	1.28	2.57	1.33
	P	N.S.	(+)	N.S.
Random	RR	1.09	1.57	1.18
	RRl	0.61	0.96	0.74
	RRu	1.94	2.57	1.90
	P	N.S.	(+)	N.S.
Between	Chi			2.20
Between	df			1
Between	P			N.S.

Appendix Table F5 - 4

IASTAD - Meta-analysis of Total/Household/Workplace Exposure in Childhood (preferring father)
Lifetime/Current Asthma
Unadjusted

REF	NRR	X	SEX	AST	SMOK	AGEL	AGEH	LOC	BEGYR	PUBYR	STTYP	ONS	ADJ	EXPOS	UNEXsrce	EXPOS-time	UNEXTI
JANSON	7		m	c	<1yr	20	48	multi	1990	2001	CS	prv	6	Fathr	NotFathr	childhood	non
JANSON	8		f	c	<1yr	20	48	multi	1990	2001	CS	prv	6	Fathr	NotFathr	childhood	non
LARSS1	1	x	b	l	Never	15	69	Eu:Swe	1995	2001	CS	prv	0	Hh	NoHhMemb	childhood	non
ROBBIN	10		b	l	Non	25	99	US:Cal	1977	1993	Pr	ons	4	Hh,Wk	None	childhood	never

Appendix Table F5 - 5

IASTAD - Meta-analysis of Total/Household/Workplace Exposure in Childhood (preferring father)
Lifetime/Current Asthma
Unadjusted

```
                               Numbers
                               Numbers exposed Non-exposed
 REF      NRR     SEX ADJ       Case    Cont    Case    Cont     RR        95.00%CI
 JANSON 7        m   6           -       -       -       -      1.08 ( 0.76-   1.54)
 JANSON 8        f   6           -       -       -       -      0.67 ( 0.49-   0.91)
 Subtotal JANSON                                                0.82 ( 0.65-   1.04)
 LARSS1 1        b   0          85     1171      58    1470     1.84 ( 1.31-   2.59)
*ROBBIN 10       b   4           -       -       -       -      1.57 ( 0.96-   2.58)
 Partial Totals                 85     1171      58    1470
*prospective study

 REF      NRR     SEX ADJ               Ys      Ws      Qs      Ps

 JANSON 7        m   6                 0.08   30.81    0.04    0.6692
 JANSON 8        f   6                -0.40   40.10   10.53    0.0112
 Subtotal JANSON                      -0.55   70.91   10.57
 LARSS1 1        b   0                 0.61   32.74    8.11    0.0005
*ROBBIN 10       b   4                 0.45   15.72    1.81    0.0737
```

```
                N      4
                NS     3


               Wt  119.37
          Het Chi   20.48
          Het  df       3
          Het  P      ***
        Fixed RR     1.12
              RRl    0.93
              RRu    1.34
               P    N.S.
       Random RR     1.19
              RRl    0.74
              RRu    1.92
               P    N.S.
        Asymm P     N.S.
```

Appendix Table F5 - 6

IASTAD - Meta-analysis of Total/Household/Workplace Exposure in Childhood (preferring father)
Lifetime/Current Asthma
Unadjusted

N	4	
NS	3	

Wt	119.37	
Het Chi	20.48	
Het df	3	
Het P	***	
Fixed RR	1.12	
RRl	0.93	
RRu	1.34	
P	N.S.	
Random RR	1.19	
RRl	0.74	
RRu	1.92	
P	N.S.	
Asymm P	N.S.	

	Sex			
	both	male	female	Total
N	2	1	1	4
NS	2	1	1	3
Wt	48.47	30.81	40.10	119.37
Het Chi	0.27	0.00	0.00	20.48
Het df	1	0	0	3
Het P	N.S.	N.S.	N.S.	***
Fixed RR	1.75	1.08	0.67	1.12
RRl	1.32	0.76	0.49	0.93
RRu	2.32	1.54	0.91	1.34
P	+++	N.S.	−	N.S.
Random RR	1.75	1.08	0.67	1.19
RRl	1.32	0.76	0.49	0.74
RRu	2.32	1.54	0.91	1.92
P	+++	N.S.	−	N.S.
Between Chi				20.22
Between df				2
Between P				***

	Asthma definition (lifetime/current)		
	lifetime	current	Total
N	2	2	4
NS	2	1	3
Wt	48.47	70.91	119.37
Het Chi	0.27	3.97	20.48
Het df	1	1	3
Het P	N.S.	*	***
Fixed RR	1.75	0.82	1.12
RRl	1.32	0.65	0.93
RRu	2.32	1.04	1.34
P	+++	N.S.	N.S.
Random RR	1.75	0.84	1.19
RRl	1.32	0.53	0.74
RRu	2.32	1.35	1.92
P	+++	N.S.	N.S.
Between Chi			16.25
Between df			1
Between P			***

Appendix Table F5 - 6

IASTAD - Meta-analysis of Total/Household/Workplace Exposure in Childhood (preferring father)
Lifetime/Current Asthma
Unadjusted

		Continent			
		NAmer	Europe	Oth/Mult	Total
N		1	1	2	4
NS		1	1	1	3
	Wt	15.72	32.74	70.91	119.37
Het	Chi	0.00	0.00	3.97	20.48
Het	df	0	0	1	3
Het	P	N.S.	N.S.	*	***
Fixed	RR	1.57	1.84	0.82	1.12
	RRl	0.96	1.31	0.65	0.93
	RRu	2.57	2.59	1.04	1.34
	P	(+)	+++	N.S.	N.S.
Random	RR	1.57	1.84	0.84	1.19
	RRl	0.96	1.31	0.53	0.74
	RRu	2.57	2.59	1.35	1.92
	P	(+)	+++	N.S.	N.S.
Between	Chi				16.51
Between	df				2
Between	P				***

		Start year of study			
		<1990	1990-99	unknown	Total
N		1	3		4
NS		1	2		3
	Wt	15.72	103.65		119.37
Het	Chi	0.00	18.40		20.48
Het	df	0	2		3
Het	P	N.S.	***		***
Fixed	RR	1.57	1.06		1.12
	RRl	0.96	0.88		0.93
	RRu	2.57	1.29		1.34
	P	(+)	N.S.		N.S.
Random	RR	1.57	1.10		1.19
	RRl	0.96	0.61		0.74
	RRu	2.57	1.97		1.92
	P	(+)	N.S.		N.S.
Between	Chi				2.08
Between	df				1
Between	P				N.S.

		Study type			
		CC	Pr	CS	Total
N			1	3	4
NS			1	2	3
	Wt		15.72	103.65	119.37
Het	Chi		0.00	18.40	20.48
Het	df		0	2	3
Het	P		N.S.	***	***
Fixed	RR		1.57	1.06	1.12
	RRl		0.96	0.88	0.93
	RRu		2.57	1.29	1.34
	P		(+)	N.S.	N.S.
Random	RR		1.57	1.10	1.19
	RRl		0.96	0.61	0.74
	RRu		2.57	1.97	1.92
	P		(+)	N.S.	N.S.
Between	Chi				2.08
Between	df				1
Between	P				N.S.

Appendix Table F5 - 6

IASTAD - Meta-analysis of Total/Household/Workplace Exposure in Childhood (preferring father)
Lifetime/Current Asthma
Unadjusted

		Ex smokers excluded	included	Total
	N	3	1	4
	NS	2	1	3
	Wt	103.65	15.72	119.37
Het	Chi	18.40	0.00	20.48
Het	df	2	0	3
Het	P	***	N.S.	***
Fixed	RR	1.06	1.57	1.12
	RRl	0.88	0.96	0.93
	RRu	1.29	2.57	1.34
	P	N.S.	(+)	N.S.
Random	RR	1.10	1.57	1.19
	RRl	0.61	0.96	0.74
	RRu	1.97	2.57	1.92
	P	N.S.	(+)	N.S.
Between	Chi			2.08
Between	df			1
Between	P			N.S.

Appendix Table F5 - 7

IASTAD - Meta-analysis of Total/Household/Workplace Exposure in Childhood (preferring father)
Lifetime/Current Asthma
Excluded studies (and stage at which they were excluded)


```
         1       2       3       4       5       6       7       8       9      10      11      12      13      14      15      16

2       BECKE2 JAAKK2 JEDRYC LARSS2 MISHRA        NG NHANES ORYSZC PILOTT PLATTS SAPALD  THORN
4       KRONQV
9       RAHERI
```
                                        Potentially overlapping studies
```
    REF| REFGP|PRINC|              OVERLAP|
 JANSON JANSON      p       JANSON/RAHERI
```

                                Adjusted - insufficient data for metaanalysis
```
    REF|NRR|SEX|AST|  SMOK|AGEL|AGEH|   LOC|BEGYR|PUBYR|STTYP|ONS|ADJ|EXPOS|UNEXsrce| EXPOS-time|UNEXTI|     RR|SIG|
 KRONQV  1   b   l  Never  15   65 Eu:Swe 1996  1999   CS prv   4 Total    None   childhood    non        *   n
```

_____

Appendix Table F6 -

IASTAD - Meta-analysis of Biochemical/Total/Household/Workplace (preferring earliest, and preferring current asthma)
Current/Lifetime Asthma

This analysis is restricted to results for:
1) Biochemical, total, household (overall), parental, or workplace exposure
2) Results not by amount of exposure
3) Results complete enough for use in metaanalysis

Within each study, results are then selected (in the following order of preference, within each sex) for:
4) ASTHMA : current, lifetime
5) EXPOS   : biochemical (cotinine), total, household, workplace
6) WHESMO : 3=childhood, 1=lifetime, 10=adult, 7=recent, 6=unspec, 2=current
7) WHOHOU : household overall, mother
8) UNEXTI : unexposed group never, non (i.e. not at time defined for exposed group)
9) For overlapping studies: principal rather than subsidiary studies
Finally for single sex results (m, f) in preference to results for both sexes combined (b).

Results adjusted for the most potential confounders are then chosen in Sections -1 to -3
(and those which actually differ from the adjusted results in Appendix Table F1 - 1 are marked 'x' in Section -1)
and results adjusted for the least confounders in Sections -4 to -6. (Those least adjusted results which
actually differ from the most adjusted are marked 'x' in column X in Section -4)

Section -7 shows excluded studies, together with the stage (as above) at which no qualifying results
were found. It then lists the potentially overlapping studies which have been included (1=principal,
2=subsidiary), and any results which would have been included in preference except that they had data
not complete enough for use in metaanalysis. It also lists their significance (yes/no), if known.

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Appendix Table F6 - 1

IASTAD - Meta-analysis of Biochemical/Total/Household/Workplace (preferring earliest, and preferring current asthma)
Current/Lifetime Asthma
Adjusted

REF	NRR	CompF1	SEX	AST	SMOK	AGEL	AGEH	LOC	BEGYR	PUBYR	STTYP	ONS	ADJ	EXPOS	UNEXsrce	EXPOS-time	UNEXTI
BECKE2	2		b	l	Non	18	40	US:mul	1985	2001	Pr	prv	5	Cot	Low	current	non
BECKE2	4		b	l	Non	18	40	US:mul	1985	2001	Pr	ons	5	Cot	Low	current	non
JAAKK2	34		b	c	Never	21	63	Eu:Fin	1997	2003	CC	ons	7	Hh,Wk	None	lifetime	non
JANSON	1		b	c	<1yr	20	48	multi	1990	2001	CS	prv	9	Hh,Wk	None	current	non
JEDRYC	1		f	c	<1yr	65	99	Eu:Pol	*	1995	CS	prv	3	Hh	NoHhMemb	current	non
LARSS1	2		b	l	Never	15	69	Eu:Swe	1995	2001	CS	prv	3	Hh	NoHhMemb	childhood	non
LARSS2	4		b	l	Never	15	64	Eu:Est	1995	2003	CS	prv	5	Work	NotWork	current	non
MISHRA	3		m	c	NevReg	60	99	As:Ind	1998	2003	CS	prv	12	Hh	NoHhMemb	current	non
MISHRA	4		f	c	NevReg	60	99	As:Ind	1998	2003	CS	prv	12	Hh	NoHhMemb	current	non
NG	6		f	c	<1yr	20	74	As:Sin	*	1993	CS	prv	6	Hh	NoHhMemb	lifetime	non
NHANES	1		b	c	Non	17	99	US:nat	1988	2002	CS	prv	0	Hh	NoHhMemb	current	non
ORYSZC	1		m	c	NevReg	25	54	Eu:Fra	*	2000	CC	prv	0	Hh	NoHhMemb	current	non
ORYSZC	2		f	c	NevReg	25	54	Eu:Fra	*	2000	CC	prv	0	Hh	NoHhMemb	current	non
PILOTT	1		b	l	Non	18	99	Austra	1995	1999	CS	prv	3	Hh	NoHhMemb	unspec	non
ROBBIN	10		b	l	Non	25	99	US:Cal	1977	1993	Pr	ons	4	Hh,Wk	None	childhood	never
SAPALD	7	x	b	c	<20pks	18	60	Eu:Swi	1991	1994	CS	prv	8	Hh,Wk	None	current	non
THORN	2		m	l	Never	20	50	Eu:Swe	1994	2001	CC	prv	2	Hh	NoHhMemb	last6homes	non
THORN	3		f	l	Never	20	50	Eu:Swe	1994	2001	CC	prv	2	Hh	NoHhMemb	last6homes	non

Appendix Table F6 - 2

IASTAD - Meta-analysis of Biochemical/Total/Household/Workplace (preferring earliest, and preferring current asthma)
Current/Lifetime Asthma
Adjusted

```
                             Numbers
                             Numbers exposed Non-exposed
 REF      NRR     SEX ADJ    Case    Cont    Case    Cont      RR        95.00%CI
 BECKE2 2        b   5        63      -       215     -       0.74 (  0.55-   1.00)
*BECKE2 4        b   5        54      -       141     -       0.96 (  0.70-   1.32)
 Subtotal BECKE2                                              0.84 (  0.67-   1.04)
 JAAKK2 34       b   7       135      -       104     -       1.40 (  0.99-   1.96)
 JANSON 1        b   9        -       -        -      -       1.15 (  0.84-   1.58)
 JEDRYC 1        f   3        -       -        -      -       0.53 (  0.24-   1.14)
 LARSS1 2        b   3        85      -        58     -       1.82 (  1.28-   2.58)
 LARSS2 4        b   5        -       -        -      -       1.13 (  0.80-   1.59)
 MISHRA 3        m  12       242      -       835     -       1.20 (  0.99-   1.46)
 MISHRA 4        f  12       561      -       829     -       1.05 (  0.91-   1.21)
 Subtotal MISHRA                                             1.10 (  0.98-   1.23)
 NG     6        f   6        18      -        15     -       1.18 (  0.57-   2.46)
 NHANES 1        b   0        70     1481      370    8660    1.11 (  0.85-   1.44)
 ORYSZC 1        m   0         3      4        14     28      1.50 (  0.29-   7.65)
 ORYSZC 2        f   0         8      13       26     43      1.02 (  0.37-   2.78)
 Subtotal ORYSZC                                             1.13 (  0.48-   2.67)
 PILOTT 1        b   3        -       -        -      -       1.09 (  0.65-   1.82)
*ROBBIN 10       b   4        -       -        -      -       1.57 (  0.96-   2.58)
 SAPALD 7        b   8        -       -        -      -       1.62 (  1.10-   2.37)
 THORN  2        m   2        -       -        -      -       4.80 (  2.00-  11.60)
 THORN  3        f   2        -       -        -      -       1.50 (  0.80-   3.10)
 Subtotal THORN                                             2.31 (  1.35-   3.96)
Partial Totals              1239    1498     2607    8731
*prospective study

 REF      NRR     SEX ADJ            Ys      Ws      Qs      Ps

 BECKE2 2        b   5             -0.30    42.99    8.18    0.0483
*BECKE2 4        b   5             -0.04    38.19    1.18    0.8008
 Subtotal BECKE2                   -0.61    81.18    9.36
 JAAKK2 34       b   7              0.34    32.94    1.34    0.0535
 JANSON 1        b   9              0.14    38.50    0.00    0.3859
 JEDRYC 1        f   3             -0.63     6.33    3.75    0.1102
 LARSS1 2        b   3              0.60    31.28    6.73    0.0008
 LARSS2 4        b   5              0.12    32.57    0.01    0.4855
 MISHRA 3        m  12              0.18   101.81    0.23    0.0658
 MISHRA 4        f  12              0.05   189.27    1.41    0.5021
 Subtotal MISHRA                   -0.04   291.08    1.64
 NG     6        f   6              0.17     7.19    0.01    0.6573
 NHANES 1        b   0              0.10    56.25    0.07    0.4488
 ORYSZC 1        m   0              0.41     1.45    0.11    0.6256
 ORYSZC 2        f   0              0.02     3.79    0.05    0.9727
 Subtotal ORYSZC                    0.15     5.24    0.16
 PILOTT 1        b   3              0.09    14.49    0.03    0.7428
*ROBBIN 10       b   4              0.45    15.72    1.57    0.0737
 SAPALD 7        b   8              0.48    26.08    3.15    0.0138
 THORN  2        m   2              1.57     4.97   10.22    0.0005
 THORN  3        f   2              0.41     8.37    0.61    0.2406
 Subtotal THORN                     1.70    13.35   10.83
```

Appendix Table F6 - 2

IASTAD - Meta-analysis of Biochemical/Total/Household/Workplace (preferring earliest, and preferring current asthma)
Current/Lifetime Asthma
Adjusted

```
            N      18
           NS      14


           Wt  652.19
   Het Chi   38.63
   Het  df      17
   Het  P       **
Fixed  RR    1.14
        RRl    1.06
        RRu    1.24
         P      +++
Random  RR    1.20
        RRl    1.04
        RRu    1.37
         P       ++
Asymm  P     N.S.
```

Appendix Table F6 - 3

IASTAD - Meta-analysis of Biochemical/Total/Household/Workplace (preferring earliest, and preferring current asthma)
Current/Lifetime Asthma
Adjusted

```
        N       18
        NS      14


        Wt     652.19
  Het  Chi     38.63
  Het   df        17
  Het    P        **
Fixed   RR      1.14
        RRl     1.06
        RRu     1.24
         P      +++
Random  RR      1.20
        RRl     1.04
        RRu     1.37
         P       ++
Asymm    P      N.S.
```

		Sex		
	both	male	female	Total
N	10	3	5	18
NS	9	3	5	17
Wt	329.01	108.23	214.95	652.19
Het Chi	22.10	9.15	4.12	38.63
Het df	9	2	4	17
Het P	**	*	N.S.	**
Fixed RR	1.17	1.28	1.05	1.14
RRl	1.05	1.06	0.92	1.06
RRu	1.30	1.55	1.20	1.24
P	++	++	N.S.	+++
Random RR	1.20	2.02	1.05	1.20
RRl	1.01	0.73	0.89	1.04
RRu	1.42	5.56	1.23	1.37
P	+	N.S.	N.S.	++
Between Chi				3.26
Between df				2
Between P				N.S.

	Asthma definition (lifetime/current)		
	lifetime	current	Total
N	8	10	18
NS	6	8	14
Wt	188.59	463.60	652.19
Het Chi	28.50	10.09	38.63
Het df	7	9	17
Het P	***	N.S.	**
Fixed RR	1.16	1.14	1.14
RRl	1.00	1.04	1.06
RRu	1.34	1.25	1.24
P	+	++	+++
Random RR	1.31	1.15	1.20
RRl	0.96	1.04	1.04
RRu	1.78	1.28	1.37
P	(+)	++	++
Between Chi			0.04
Between df			1
Between P			N.S.

Appendix Table F6 - 3

IASTAD - Meta-analysis of Biochemical/Total/Household/Workplace (preferring earliest, and preferring current asthma)
Current/Lifetime Asthma
Adjusted

		Continent			
		NAmer	Europe	Oth/Mult	Total
	N	4	9	5	18
	NS	3	7	4	14
	Wt	153.15	147.78	351.26	652.19
Het	Chi	7.71	18.02	1.28	38.63
Het	df	3	8	4	17
Het	P	(*)	*	N.S.	**
Fixed	RR	0.99	1.44	1.11	1.14
	RRl	0.84	1.23	1.00	1.06
	RRu	1.16	1.70	1.23	1.24
	P	N.S.	+++	(+)	+++
Random	RR	1.01	1.44	1.11	1.20
	RRl	0.78	1.09	1.00	1.04
	RRu	1.32	1.89	1.23	1.37
	P	N.S.	++	(+)	++
Between	Chi				11.62
Between	df				2
Between	P				**

		Start year of study			
		<1990	1990-99	unknown	Total
	N	4	10	4	18
	NS	3	8	3	14
	Wt	153.15	480.28	18.76	652.19
Het	Chi	7.71	22.19	2.74	38.63
Het	df	3	9	3	17
Het	P	(*)	**	N.S.	**
Fixed	RR	0.99	1.21	0.89	1.14
	RRl	0.84	1.11	0.57	1.06
	RRu	1.16	1.32	1.40	1.24
	P	N.S.	+++	N.S.	+++
Random	RR	1.01	1.33	0.89	1.20
	RRl	0.78	1.12	0.57	1.04
	RRu	1.32	1.56	1.40	1.37
	P	N.S.	+++	N.S.	++
Between	Chi				6.00
Between	df				2
Between	P				*

		Study type			
		CC	Pr	CS	Total
	N	5	3	10	18
	NS	3	2	9	14
	Wt	51.53	96.90	503.76	652.19
Het	Chi	7.37	6.59	15.33	38.63
Het	df	4	2	9	17
Het	P	N.S.	*	(*)	**
Fixed	RR	1.56	0.93	1.15	1.14
	RRl	1.19	0.76	1.06	1.06
	RRu	2.05	1.13	1.26	1.24
	P	++	N.S.	++	+++
Random	RR	1.69	0.99	1.19	1.20
	RRl	1.06	0.68	1.04	1.04
	RRu	2.69	1.45	1.35	1.37
	P	+	N.S.	+	++
Between	Chi				9.33
Between	df				2
Between	P				**

Appendix Table F6 - 3

IASTAD - Meta-analysis of Biochemical/Total/Household/Workplace (preferring earliest, and preferring current asthma)
Current/Lifetime Asthma
Adjusted

<u>Ex smokers</u>

		excluded	included	Total
	N	13	5	18
	NS	10	4	14
	Wt	484.55	167.65	652.19
Het	Chi	26.50	7.84	38.63
Het	df	12	4	17
Het	P	**	(*)	**
Fixed	RR	1.20	1.00	1.14
	RRl	1.10	0.86	1.06
	RRu	1.31	1.16	1.24
	P	+++	N.S.	+++
Random	RR	1.29	1.02	1.20
	RRl	1.09	0.82	1.04
	RRu	1.52	1.27	1.37
	P	++	N.S.	++
Between	Chi			4.29
Between	df			1
Between	P			*

Appendix Table F6 - 4

IASTAD - Meta-analysis of Biochemical/Total/Household/Workplace (preferring earliest, and preferring current asthma)
Current/Lifetime Asthma
Unadjusted

REF	NRR	X	SEX	AST	SMOK	AGEL	AGEH	LOC	BEGYR	PUBYR	STTYP	ONS	ADJ	EXPOS	UNEXsrce	EXPOS-time	UNEXTI
BECKE2	1	x	b	l	Non	18	40	US:mul	1985	2001	Pr	prv	0	Cot	Low	current	non
BECKE2	3	x	b	l	Non	18	40	US:mul	1985	2001	Pr	ons	0	Cot	Low	current	non
JAAKK2	10	x	b	c	Never	21	63	Eu:Fin	1997	2003	CC	ons	0	Hh,Wk	None	lifetime	non
JANSON	1		b	c	<1yr	20	48	multi	1990	2001	CS	prv	9	Hh,Wk	None	current	non
JEDRYC	1		f	c	<1yr	65	99	Eu:Pol	*	1995	CS	prv	3	Hh	NoHhMemb	current	non
LARSS1	1	x	b	l	Never	15	69	Eu:Swe	1995	2001	CS	prv	0	Hh	NoHhMemb	childhood	non
LARSS2	4		b	l	Never	15	64	Eu:Est	1995	2003	CS	prv	5	Work	NotWork	current	non
MISHRA	1	x	m	c	NevReg	60	99	As:Ind	1998	2003	CS	prv	0	Hh	NoHhMemb	current	non
MISHRA	2	x	f	c	NevReg	60	99	As:Ind	1998	2003	CS	prv	0	Hh	NoHhMemb	current	non
NG	3	x	f	c	<1yr	20	74	As:Sin	*	1993	CS	prv	0	Hh	NoHhMemb	lifetime	non
NHANES	1		b	c	Non	17	99	US:nat	1988	2002	CS	prv	0	Hh	NoHhMemb	current	non
ORYSZC	1		m	c	NevReg	25	54	Eu:Fra	*	2000	CC	prv	0	Hh	NoHhMemb	current	non
ORYSZC	2		f	c	NevReg	25	54	Eu:Fra	*	2000	CC	prv	0	Hh	NoHhMemb	current	non
PILOTT	1		b	l	Non	18	99	Austra	1995	1999	CS	prv	3	Hh	NoHhMemb	unspec	non
ROBBIN	10		b	l	Non	25	99	US:Cal	1977	1993	Pr	ons	4	Hh,Wk	None	childhood	never
SAPALD	7		b	c	<20pks	18	60	Eu:Swi	1991	1994	CS	prv	8	Hh,Wk	None	current	non
THORN	1	x	b	l	Never	20	50	Eu:Swe	1994	2001	CC	prv	0	Hh	NoHhMemb	last6homes	non

Appendix Table F6 - 5

IASTAD - Meta-analysis of Biochemical/Total/Household/Workplace (preferring earliest, and preferring current asthma)
Current/Lifetime Asthma
Unadjusted

```
                           Numbers
                           Numbers exposed Non-exposed
 REF     NRR    SEX ADJ    Case    Cont   Case    Cont     RR      95.00%CI
 BECKE2 1       b   0        63     799    215    2051    0.75 ( 0.56-  1.01)
*BECKE2 3       b   0        54     799    141    2051    0.98 ( 0.73-  1.33)
 Subtotal BECKE2                                          0.86 ( 0.69-  1.06)
 JAAKK2 10      b   0       135     256    104     231    1.17 ( 0.86-  1.60)
 JANSON 1       b   9        -       -      -       -     1.15 ( 0.84-  1.58)
 JEDRYC 1       f   3        -       -      -       -     0.53 ( 0.24-  1.14)
 LARSS1 1       b   0        85    1171     58    1470    1.84 ( 1.31-  2.59)
 LARSS2 4       b   5        -       -      -       -     1.13 ( 0.80-  1.59)
 MISHRA 1       m   0       242    1739    835    8047    1.34 ( 1.15-  1.56)
 MISHRA 2       f   0       561    6037    829    9659    1.08 ( 0.97-  1.21)
 Subtotal MISHRA                                          1.17 ( 1.07-  1.28)
 NG     3       f   0        18     645     15     604    1.12 ( 0.56-  2.25)
 NHANES 1       b   0        70    1481    370    8660    1.11 ( 0.85-  1.44)
 ORYSZC 1       m   0         3       4     14      28    1.50 ( 0.29-  7.65)
 ORYSZC 2       f   0         8      13     26      43    1.02 ( 0.37-  2.78)
 Subtotal ORYSZC                                          1.13 ( 0.48-  2.67)
 PILOTT 1       b   3        -       -      -       -     1.09 ( 0.65-  1.82)
*ROBBIN 10      b   4        -       -      -       -     1.57 ( 0.96-  2.58)
 SAPALD 7       b   8        -       -      -       -     1.62 ( 1.10-  2.37)
 THORN  1       b   0        33     116     36     302    2.39 ( 1.42-  4.01)
Partial Totals             1272   13060   2643   33146
*prospective study

 REF     NRR    SEX ADJ            Ys      Ws      Qs      Ps

 BECKE2 1       b   0            -0.28   44.92    8.69    0.0563
*BECKE2 3       b   0            -0.02   41.89    1.24    0.9121
 Subtotal BECKE2                -0.61   86.81    9.93
 JAAKK2 10      b   0             0.16   39.59    0.00    0.3198
 JANSON 1       b   9             0.14   38.50    0.01    0.3859
 JEDRYC 1       f   3            -0.63    6.33    3.95    0.1102
 LARSS1 1       b   0             0.61   32.74    6.76    0.0005
 LARSS2 4       b   5             0.12   32.57    0.04    0.4855
 MISHRA 1       m   0             0.29  165.86    3.18    0.0002
 MISHRA 2       f   0             0.08  306.94    1.76    0.1638
 Subtotal MISHRA                 0.06  472.80    4.93
 NG     3       f   0             0.12    7.97    0.01    0.7419
 NHANES 1       b   0             0.10   56.25    0.16    0.4488
 ORYSZC 1       m   0             0.41    1.45    0.09    0.6256
 ORYSZC 2       f   0             0.02    3.79    0.07    0.9727
 Subtotal ORYSZC                 0.11    5.24    0.16
 PILOTT 1       b   3             0.09   14.49    0.07    0.7428
*ROBBIN 10      b   4             0.45   15.72    1.38    0.0737
 SAPALD 7       b   8             0.48   26.08    2.79    0.0138
 THORN  1       b   0             0.87   14.28    7.30    0.0010
```

```
              N      17
              NS     14


              Wt    849.38
          Het Chi    37.50
          Het  df     16
          Het  P      **
         Fixed RR    1.17
               RRl   1.09
               RRu   1.25
               P     +++
         Random RR   1.19
               RRl   1.05
               RRu   1.35
               P     ++
         Asymm  P    N.S.
```

Appendix Table F6 - 6

IASTAD - Meta-analysis of Biochemical/Total/Household/Workplace (preferring earliest, and preferring current asthma)
Current/Lifetime Asthma
Unadjusted

N	17	
NS	14	
Wt	849.38	
Het Chi	37.50	
Het df	16	
Het P	**	
Fixed RR	1.17	
RRl	1.09	
RRu	1.25	
P	+++	
Random RR	1.19	
RRl	1.05	
RRu	1.35	
P	++	
Asymm P	N.S.	

Sex

	both	male	female	Total
N	11	2	4	17
NS	10	2	4	16
Wt	357.03	167.31	325.03	849.38
Het Chi	28.35	0.02	3.19	37.50
Het df	10	1	3	16
Het P	**	N.S.	N.S.	**
Fixed RR	1.19	1.34	1.07	1.17
RRl	1.07	1.15	0.96	1.09
RRu	1.32	1.56	1.19	1.25
P	++	+++	N.S.	+++
Random RR	1.24	1.34	1.05	1.19
RRl	1.04	1.15	0.88	1.05
RRu	1.48	1.56	1.24	1.35
P	+	+++	N.S.	++
Between Chi				5.94
Between df				2
Between P				(*)

Asthma definition (lifetime/current)

	lifetime	current	Total
N	7	10	17
NS	6	8	14
Wt	196.62	652.76	849.38
Het Chi	25.47	12.02	37.50
Het df	6	9	16
Het P	***	N.S.	**
Fixed RR	1.17	1.17	1.17
RRl	1.02	1.08	1.09
RRu	1.35	1.26	1.25
P	+	+++	+++
Random RR	1.27	1.18	1.19
RRl	0.94	1.06	1.05
RRu	1.71	1.31	1.35
P	N.S.	++	++
Between Chi			0.00
Between df			1
Between P			N.S.

Appendix Table F6 - 6

IASTAD - Meta-analysis of Biochemical/Total/Household/Workplace (preferring earliest, and preferring current asthma)
Current/Lifetime Asthma
Unadjusted

		Continent		
	NAmer	Europe	Oth/Mult	Total
N	4	8	5	17
NS	3	7	4	14
Wt	158.78	156.84	533.76	849.38
Het Chi	7.42	16.17	5.01	37.50
Het df	3	7	4	16
Het P	(*)	*	N.S.	**
Fixed RR	1.00	1.39	1.16	1.17
RRl	0.85	1.19	1.07	1.09
RRu	1.16	1.63	1.27	1.25
P	N.S.	+++	+++	+++
Random RR	1.02	1.37	1.17	1.19
RRl	0.79	1.05	1.05	1.05
RRu	1.32	1.78	1.31	1.35
P	N.S.	+	++	++
Between Chi				8.89
Between df				2
Between P				*

		Start year of study		
	<1990	1990-99	unknown	Total
N	4	9	4	17
NS	3	8	3	14
Wt	158.78	671.06	19.54	849.38
Het Chi	7.42	20.48	2.60	37.50
Het df	3	8	3	16
Het P	(*)	**	N.S.	**
Fixed RR	1.00	1.22	0.88	1.17
RRl	0.85	1.13	0.57	1.09
RRu	1.16	1.32	1.38	1.25
P	N.S.	+++	N.S.	+++
Random RR	1.02	1.31	0.88	1.19
RRl	0.79	1.13	0.57	1.05
RRu	1.32	1.52	1.38	1.35
P	N.S.	+++	N.S.	++
Between Chi				7.00
Between df				2
Between P				*

		Study type		
	CC	Pr	CS	Total
N	4	3	10	17
NS	3	2	9	14
Wt	59.12	102.53	687.73	849.38
Het Chi	5.71	6.45	18.51	37.50
Het df	3	2	9	16
Het P	N.S.	*	*	**
Fixed RR	1.39	0.94	1.19	1.17
RRl	1.07	0.77	1.10	1.09
RRu	1.79	1.14	1.28	1.25
P	+	N.S.	+++	+++
Random RR	1.47	1.00	1.22	1.19
RRl	0.94	0.70	1.07	1.05
RRu	2.32	1.45	1.39	1.35
P	(+)	N.S.	++	++
Between Chi				6.82
Between df				2
Between P				*

Appendix Table F6 - 6

IASTAD - Meta-analysis of Biochemical/Total/Household/Workplace (preferring earliest, and preferring current asthma)
Current/Lifetime Asthma
Unadjusted

Ex smokers

		excluded	included	Total
	N	12	5	17
	NS	10	4	14
	Wt	676.11	173.27	849.38
Het	Chi	24.93	7.53	37.50
Het	df	11	4	16
Het	P	**	N.S.	**
Fixed	RR	1.21	1.00	1.17
	RRl	1.13	0.86	1.09
	RRu	1.31	1.16	1.25
	P	+++	N.S.	+++
Random	RR	1.28	1.02	1.19
	RRl	1.10	0.83	1.05
	RRu	1.49	1.27	1.35
	P	++	N.S.	++
Between	Chi			5.04
Between	df			1
Between	P			*

Appendix Table F6 - 7

IASTAD - Meta-analysis of Biochemical/Total/Household/Workplace (preferring earliest, and preferring current asthma)
Current/Lifetime Asthma
Excluded studies (and stage at which they were excluded)

```
         1       2       3       4       5       6       7       8       9      10      11      12      13      14      15      16

3       KRONQV PLATTS
9       RAHERI
```
                                        Potentially overlapping studies
```
   REF| REFGP|PRINC|              OVERLAP|
JANSON JANSON      p       JANSON/RAHERI
```

                          Adjusted - insufficient data for metaanalysis
```
   REF|NRR|SEX|AST|  SMOK|AGEL|AGEH|    LOC|BEGYR|PUBYR|STTYP|ONS|ADJ|EXPOS|UNEXsrce| EXPOS-time|UNEXTI|      RR|SIG|
KRONQV   1   b   l  Never   15   65 Eu:Swe  1996  1999   CS prv   4 Total    None    childhood   non        *    n
LARSS2   5   b   l  Never   15   64 Eu:Est  1995  2003   CS prv   5    Hh NoHhMemb     current   non        *    n
PLATTS   1   b   c    Non   15   55 US:Del  1988  1993   CC prv   0 Total    None      unspec   non        *    n
```

_____

Appendix Table F7 -

IASTAD - Meta-analysis of Household exposure (preferring earliest)
Lifetime/Current Asthma

This analysis is restricted to results for:
1) Household (overall) or parental exposure
2) Results not by amount of exposure
3) Results complete enough for use in metaanalysis

Within each study, results are then selected (in the following order of preference, within each sex) for:
4) ASTHMA : lifetime, current
5) WHESMO : 3=childhood, 1=lifetime, 10=adult, 7=recent, 6=unspec, 2=current
6) WHOHOU : household overall, mother
7) UNEXTI : unexposed group never, non (i.e. not at time defined for exposed group)
8) For overlapping studies: principal rather than subsidiary studies
Finally for single sex results (m, f) in preference to results for both sexes combined (b).

Results adjusted for the most potential confounders are then chosen in Sections -1 to -3
(and those which actually differ from the adjusted results in Appendix Table F1 - 1 are marked 'x' in Section -1)
and results adjusted for the least confounders in Sections -4 to -6. (Those least adjusted results which
actually differ from the most adjusted are marked 'x' in column X in Section -4)

Section -7 shows excluded studies, together with the stage (as above) at which no qualifying results
were found. It then lists the potentially overlapping studies which have been included (1=principal,
2=subsidiary), and any results which would have been included in preference except that they had data
not complete enough for use in metaanalysis. It also lists their significance (yes/no), if known.

_____

Appendix Table F7 - 1

IASTAD - Meta-analysis of Household exposure (preferring earliest)
Lifetime/Current Asthma
Adjusted

REF	NRR	CompF1	SEX	AST	SMOK	AGEL	AGEH	LOC	BEGYR	PUBYR	STTYP	ONS	ADJ	EXPOS	UNEXsrce	EXPOS-time	UNEXTI
JAAKK2	44	x	b	c	Never	21	63	Eu:Fin	1997	2003	CC	ons	8	Hh	NoHhMemb	lifetime	non
JANSON	9	x	m	c	<1yr	20	48	multi	1990	2001	CS	prv	6	Mothr	NotMoth	childhood	non
JANSON	10	x	f	c	<1yr	20	48	multi	1990	2001	CS	prv	6	Mothr	NotMoth	childhood	non
JEDRYC	1		f	c	<1yr	65	99	Eu:Pol	*	1995	CS	prv	3	Hh	NoHhMemb	current	non
LARSS1	2		b	l	Never	15	69	Eu:Swe	1995	2001	CS	prv	3	Hh	NoHhMemb	childhood	non
MISHRA	3		m	c	NevReg	60	99	As:Ind	1998	2003	CS	prv	12	Hh	NoHhMemb	current	non
MISHRA	4		f	c	NevReg	60	99	As:Ind	1998	2003	CS	prv	12	Hh	NoHhMemb	current	non
NG	6		f	c	<1yr	20	74	As:Sin	*	1993	CS	prv	6	Hh	NoHhMemb	lifetime	non
NHANES	1		b	c	Non	17	99	US:nat	1988	2002	CS	prv	0	Hh	NoHhMemb	current	non
ORYSZC	1		m	c	NevReg	25	54	Eu:Fra	*	2000	CC	prv	0	Hh	NoHhMemb	current	non
ORYSZC	2		f	c	NevReg	25	54	Eu:Fra	*	2000	CC	prv	0	Hh	NoHhMemb	current	non
PILOTT	1		b	l	Non	18	99	Austra	1995	1999	CS	prv	3	Hh	NoHhMemb	unspec	non
THORN	2		m	l	Never	20	50	Eu:Swe	1994	2001	CC	prv	2	Hh	NoHhMemb	last6homes	non
THORN	3		f	l	Never	20	50	Eu:Swe	1994	2001	CC	prv	2	Hh	NoHhMemb	last6homes	non

Appendix Table F7 - 2

IASTAD - Meta-analysis of Household exposure (preferring earliest)
Lifetime/Current Asthma
Adjusted

```
                              Numbers
                              Numbers exposed Non-exposed
REF      NRR     SEX ADJ      Case    Cont    Case    Cont      RR        95.00%CI
JAAKK2 44        b   8         99      -       140     -       1.09 (  0.77-   1.53)
JANSON 9         m   6         -       -       -       -       0.81 (  0.54-   1.23)
JANSON 10        f   6         -       -       -       -       1.10 (  0.78-   1.55)
Subtotal JANSON                                                1.01 (  0.82-   1.25)
JEDRYC 1         f   3         -       -       -       -       0.53 (  0.24-   1.14)
LARSS1 2         b   3         85      -       58      -       1.82 (  1.28-   2.58)
MISHRA 3         m   12        242     -       835     -       1.20 (  0.99-   1.46)
MISHRA 4         f   12        561     -       829     -       1.05 (  0.91-   1.21)
Subtotal MISHRA                                                1.10 (  0.98-   1.23)
NG     6         f   6         18      -       15      -       1.18 (  0.57-   2.46)
NHANES 1         b   0         70      1481    370     8660    1.11 (  0.85-   1.44)
ORYSZC 1         m   0         3       4       14      28      1.50 (  0.29-   7.65)
ORYSZC 2         f   0         8       13      26      43      1.02 (  0.37-   2.78)
Subtotal ORYSZC                                                1.13 (  0.48-   2.67)
PILOTT 1         b   3         -       -       -       -       1.09 (  0.65-   1.82)
THORN  2         m   2         -       -       -       -       4.80 (  2.00-  11.60)
THORN  3         f   2         -       -       -       -       1.50 (  0.80-   3.10)
Subtotal THORN                                                 2.31 (  1.35-   3.96)
Partial Totals                 1086    1498    2287    8731
*prospective study

REF      NRR     SEX ADJ               Ys      Ws      Qs      Ps

JAAKK2 44        b   8                 0.09    32.59   0.05    0.6227
JANSON 9         m   6                -0.21    22.67   2.54    0.3157
JANSON 10        f   6                 0.10    32.58   0.03    0.5864
Subtotal JANSON                       -0.36    55.26   2.57
JEDRYC 1         f   3                -0.63    6.33    3.64    0.1102
LARSS1 2         b   3                 0.60    31.28   7.05    0.0008
MISHRA 3         m   12                0.18    101.81  0.35    0.0658
MISHRA 4         f   12                0.05    189.27  1.07    0.5021
Subtotal MISHRA                       -0.02    291.08  1.42
NG     6         f   6                 0.17    7.19    0.01    0.6573
NHANES 1         b   0                 0.10    56.25   0.03    0.4488
ORYSZC 1         m   0                 0.41    1.45    0.11    0.6256
ORYSZC 2         f   0                 0.02    3.79    0.04    0.9727
Subtotal ORYSZC                        0.18    5.24    0.16
PILOTT 1         b   3                 0.09    14.49   0.02    0.7428
THORN  2         m   2                 1.57    4.97    10.38   0.0005
THORN  3         f   2                 0.41    8.37    0.66    0.2406
Subtotal THORN                         1.73    13.35   11.04
```

```
         N      14
         NS     10


         Wt     513.05
   Het Chi      25.99
   Het  df      13
   Het  P       *
  Fixed RR      1.13
         RRl    1.04
         RRu    1.23
         P      ++
 Random RR      1.16
         RRl    1.00
         RRu    1.35
         P      +
  Asymm P       N.S.
```

Appendix Table F7 - 3

IASTAD - Meta-analysis of Household exposure (preferring earliest)
Lifetime/Current Asthma
Adjusted

```
            N      14
           NS      10


           Wt  513.05
      Het Chi   25.99
      Het  df      13
      Het  P        *
    Fixed  RR    1.13
          RRl    1.04
          RRu    1.23
            P      ++
   Random  RR    1.16
          RRl    1.00
          RRu    1.35
            P       +
    Asymm  P     N.S.
```

		Sex		
	both	male	female	Total
N	4	4	6	14
NS	4	4	6	14
Wt	134.61	130.91	247.53	513.05
Het Chi	6.12	13.11	4.19	25.99
Het df	3	3	5	13
Het P	N.S.	**	N.S.	*
Fixed RR	1.24	1.18	1.05	1.13
RRl	1.04	1.00	0.93	1.04
RRu	1.46	1.41	1.19	1.23
P	+	(+)	N.S.	++
Random RR	1.25	1.43	1.05	1.16
RRl	0.97	0.81	0.93	1.00
RRu	1.60	2.52	1.19	1.35
P	(+)	N.S.	N.S.	+
Between Chi				2.57
Between df				2
Between P				N.S.

	Asthma definition (lifetime/current)		
	lifetime	current	Total
N	4	10	14
NS	3	7	10
Wt	59.12	453.93	513.05
Het Chi	8.50	6.62	25.99
Het df	3	9	13
Het P	*	N.S.	*
Fixed RR	1.69	1.07	1.13
RRl	1.31	0.98	1.04
RRu	2.19	1.18	1.23
P	+++	N.S.	++
Random RR	1.79	1.07	1.16
RRl	1.11	0.98	1.00
RRu	2.88	1.18	1.35
P	+	N.S.	+
Between Chi			10.87
Between df			1
Between P			***

Appendix Table F7 - 3

IASTAD - Meta-analysis of Household exposure (preferring earliest)
Lifetime/Current Asthma
Adjusted

	Continent			
	NAmer	Europe	Oth/Mult	Total
N	1	7	6	14
NS	1	5	4	10
Wt	56.25	88.79	368.02	513.05
Het Chi	0.00	18.15	3.23	25.99
Het df	0	6	5	13
Het P	N.S.	**	N.S.	*
Fixed RR	1.11	1.39	1.08	1.13
RRl	0.85	1.13	0.98	1.04
RRu	1.44	1.71	1.20	1.23
P	N.S.	++	N.S.	++
Random RR	1.11	1.40	1.08	1.16
RRl	0.85	0.91	0.98	1.00
RRu	1.44	2.15	1.20	1.35
P	N.S.	N.S.	N.S.	+
Between Chi				4.62
Between df				2
Between P				(*)

	Start year of study			
	<1990	1990-99	unknown	Total
N	1	9	4	14
NS	1	6	3	10
Wt	56.25	438.05	18.76	513.05
Het Chi	0.00	22.07	2.74	25.99
Het df	0	8	3	13
Het P	N.S.	**	N.S.	*
Fixed RR	1.11	1.15	0.89	1.13
RRl	0.85	1.04	0.57	1.04
RRu	1.44	1.26	1.40	1.23
P	N.S.	++	N.S.	++
Random RR	1.11	1.22	0.89	1.16
RRl	0.85	1.01	0.57	1.00
RRu	1.44	1.47	1.40	1.35
P	N.S.	+	N.S.	+
Between Chi				1.19
Between df				2
Between P				N.S.

	Study type			
	CC	Pr	CS	Total
N	5		9	14
NS	3		7	10
Wt	51.18		461.87	513.05
Het Chi	9.90		14.59	25.99
Het df	4		8	13
Het P	*		(*)	*
Fixed RR	1.33		1.11	1.13
RRl	1.01		1.01	1.04
RRu	1.75		1.22	1.23
P	+		+	++
Random RR	1.58		1.12	1.16
RRl	0.92		0.96	1.00
RRu	2.73		1.29	1.35
P	(+)		N.S.	+
Between Chi				1.50
Between df				1
Between P				N.S.

Appendix Table F7 - 3

IASTAD - Meta-analysis of Household exposure (preferring earliest)
Lifetime/Current Asthma
Adjusted

Ex smokers

		excluded	included	Total
	N	12	2	14
	NS	8	2	10
	Wt	442.31	70.74	513.05
Het	Chi	25.93	0.00	25.99
Het	df	11	1	13
Het	P	**	N.S.	*
Fixed	RR	1.14	1.10	1.13
	RRl	1.04	0.87	1.04
	RRu	1.25	1.39	1.23
	P	++	N.S.	++
Random	RR	1.19	1.10	1.16
	RRl	0.99	0.87	1.00
	RRu	1.42	1.39	1.35
	P	(+)	N.S.	+
Between	Chi			0.06
Between	df			1
Between	P			N.S.

Exposed group : when Exposed

		life	adult	child	current	unspec	Total
	N	2	2	3	6	1	14
	NS	2	1	2	4	1	10
	Wt	39.78	13.35	86.53	358.90	14.49	513.05
Het	Chi	0.04	4.22	9.16	4.67	0.00	25.99
Het	df	1	1	2	5	0	13
Het	P	N.S.	*	*	N.S.	N.S.	*
Fixed	RR	1.11	2.31	1.22	1.09	1.09	1.13
	RRl	0.81	1.35	0.99	0.98	0.65	1.04
	RRu	1.51	3.96	1.50	1.21	1.82	1.23
	P	N.S.	++	(+)	N.S.	N.S.	++
Random	RR	1.11	2.59	1.19	1.09	1.09	1.16
	RRl	0.81	0.83	0.75	0.98	0.65	1.00
	RRu	1.51	8.08	1.87	1.21	1.82	1.35
	P	N.S.	N.S.	N.S.	N.S.	N.S.	+
Between	Chi						7.90
Between	df						4
Between	P						(*)

Appendix Table F7 - 4

IASTAD - Meta-analysis of Household exposure (preferring earliest)
Lifetime/Current Asthma
Unadjusted

REF	NRR	X	SEX	AST	SMOK	AGEL	AGEH	LOC	BEGYR	PUBYR	STTYP	ONS	ADJ	EXPOS	UNEXsrce	EXPOS-time	UNEXTI
JAAKK2	20	x	b	c	Never	21	63	Eu:Fin	1997	2003	CC	ons	0	Hh	NoHhMemb	lifetime	non
JANSON	9		m	c	<1yr	20	48	multi	1990	2001	CS	prv	6	Mothr	NotMoth	childhood	non
JANSON	10		f	c	<1yr	20	48	multi	1990	2001	CS	prv	6	Mothr	NotMoth	childhood	non
JEDRYC	1		f	c	<1yr	65	99	Eu:Pol	*	1995	CS	prv	3	Hh	NoHhMemb	current	non
LARSS1	1	x	b	l	Never	15	69	Eu:Swe	1995	2001	CS	prv	0	Hh	NoHhMemb	childhood	non
MISHRA	1	x	m	c	NevReg	60	99	As:Ind	1998	2003	CS	prv	0	Hh	NoHhMemb	current	non
MISHRA	2	x	f	c	NevReg	60	99	As:Ind	1998	2003	CS	prv	0	Hh	NoHhMemb	current	non
NG	3	x	f	c	<1yr	20	74	As:Sin	*	1993	CS	prv	0	Hh	NoHhMemb	lifetime	non
NHANES	1		b	c	Non	17	99	US:nat	1988	2002	CS	prv	0	Hh	NoHhMemb	current	non
ORYSZC	1		m	c	NevReg	25	54	Eu:Fra	*	2000	CC	prv	0	Hh	NoHhMemb	current	non
ORYSZC	2		f	c	NevReg	25	54	Eu:Fra	*	2000	CC	prv	0	Hh	NoHhMemb	current	non
PILOTT	1		b	l	Non	18	99	Austra	1995	1999	CS	prv	3	Hh	NoHhMemb	unspec	non
THORN	1	x	b	l	Never	20	50	Eu:Swe	1994	2001	CC	prv	0	Hh	NoHhMemb	last6homes	non

Appendix Table F7 - 5

IASTAD - Meta-analysis of Household exposure (preferring earliest)
Lifetime/Current Asthma
Unadjusted

```
                         Numbers
                         Numbers exposed Non-exposed
REF      NRR     SEX ADJ   Case    Cont    Case    Cont    RR        95.00%CI
JAAKK2 20        b   0       99     194     140     293    1.07 (  0.78-   1.46)
JANSON 9         m   6        -       -       -       -    0.81 (  0.54-   1.23)
JANSON 10        f   6        -       -       -       -    1.10 (  0.78-   1.55)
Subtotal JANSON                                           1.01 (  0.82-   1.24)
JEDRYC 1         f   3        -       -       -       -    0.53 (  0.24-   1.14)
LARSS1 1         b   0       85    1171      58    1470    1.84 (  1.31-   2.59)
MISHRA 1         m   0      242    1739     835    8047    1.34 (  1.15-   1.56)
MISHRA 2         f   0      561    6037     829    9659    1.08 (  0.97-   1.21)
Subtotal MISHRA                                           1.17 (  1.07-   1.28)
NG     3         f   0       18     645      15     604    1.12 (  0.56-   2.25)
NHANES 1         b   0       70    1481     370    8660    1.11 (  0.85-   1.44)
ORYSZC 1         m   0        3       4      14      28    1.50 (  0.29-   7.65)
ORYSZC 2         f   0        8      13      26      43    1.02 (  0.37-   2.78)
Subtotal ORYSZC                                           1.13 (  0.48-   2.67)
PILOTT 1         b   3        -       -       -       -    1.09 (  0.65-   1.82)
THORN  1         b   0       33     116      36     302    2.39 (  1.42-   4.01)
Partial Totals             1119   11400    2323   29106
*prospective study

REF      NRR     SEX ADJ           Ys       Ws       Qs       Ps

JAAKK2 20        b   0            0.07    38.74     0.33    0.6822
JANSON 9         m   6           -0.21    22.67     3.07    0.3157
JANSON 10        f   6            0.10    32.58     0.13    0.5864
Subtotal JANSON                 -0.43    55.26     3.20
JEDRYC 1         f   3           -0.63     6.33     3.97    0.1102
LARSS1 1         b   0            0.61    32.74     6.70    0.0005
MISHRA 1         m   0            0.29   165.86     3.07    0.0002
MISHRA 2         f   0            0.08   306.94     1.86    0.1638
Subtotal MISHRA                  0.06   472.80     4.94
NG     3         f   0            0.12     7.97     0.01    0.7419
NHANES 1         b   0            0.10    56.25     0.18    0.4488
ORYSZC 1         m   0            0.41     1.45     0.09    0.6256
ORYSZC 2         f   0            0.02     3.79     0.07    0.9727
Subtotal ORYSZC                  0.11     5.24     0.16
PILOTT 1         b   3            0.09    14.49     0.07    0.7428
THORN  1         b   0            0.87    14.28     7.25    0.0010
```

```
              N       13
              NS      10


              Wt   704.11
         Het Chi    26.81
         Het  df    12
         Het  P     **
       Fixed  RR    1.17
              RRl   1.09
              RRu   1.26
              P     +++
      Random  RR    1.18
              RRl   1.02
              RRu   1.37
              P     +
       Asymm  P     N.S.
```

Appendix Table F7 - 6

IASTAD - Meta-analysis of Household exposure (preferring earliest)
Lifetime/Current Asthma
Unadjusted

```
            N       13
            NS      10


            Wt    704.11
      Het Chi    26.81
      Het  df       12
      Het  P        **
    Fixed  RR     1.17
             RR1   1.09
             RRu   1.26
             P     +++
   Random  RR     1.18
             RR1   1.02
             RRu   1.37
             P       +
    Asymm  P      N.S.
```

		Sex			
		both	male	female	Total
N		5	3	5	13
NS		5	3	5	13
Wt		156.51	189.98	357.62	704.11
Het	Chi	12.63	5.11	3.22	26.81
Het	df	4	2	4	12
Het	P	*	(*)	N.S.	**
Fixed	RR	1.31	1.26	1.07	1.17
	RR1	1.12	1.10	0.97	1.09
	RRu	1.53	1.46	1.19	1.26
	P	+++	++	N.S.	+++
Random	RR	1.38	1.11	1.07	1.18
	RR1	1.03	0.74	0.97	1.02
	RRu	1.85	1.69	1.19	1.37
	P	+	N.S.	N.S.	+
Between	Chi				5.85
Between	df				2
Between	P				(*)

		Asthma definition (lifetime/current)		
		lifetime	current	Total
N		3	10	13
NS		3	7	10
Wt		61.52	642.59	704.11
Het	Chi	4.69	11.89	26.81
Het	df	2	9	12
Het	P	(*)	N.S.	**
Fixed	RR	1.73	1.13	1.17
	RR1	1.35	1.04	1.09
	RRu	2.22	1.22	1.26
	P	+++	++	+++
Random	RR	1.70	1.11	1.18
	RR1	1.14	1.00	1.02
	RRu	2.54	1.24	1.37
	P	++	(+)	+
Between	Chi			10.22
Between	df			1
Between	P			**

Appendix Table F7 - 6

IASTAD - Meta-analysis of Household exposure (preferring earliest)
Lifetime/Current Asthma
Unadjusted

		Continent		
	NAmer	Europe	Oth/Mult	Total
N	1	6	6	13
NS	1	5	4	10
Wt	56.25	97.34	550.53	704.11
Het Chi	0.00	15.69	7.91	26.81
Het df	0	5	5	12
Het P	N.S.	**	N.S.	**
Fixed RR	1.11	1.38	1.14	1.17
RRl	0.85	1.13	1.05	1.09
RRu	1.44	1.69	1.24	1.26
P	N.S.	++	++	+++
Random RR	1.11	1.31	1.13	1.18
RRl	0.85	0.86	0.99	1.02
RRu	1.44	1.99	1.30	1.37
P	N.S.	N.S.	(+)	+
Between Chi				3.20
Between df				2
Between P				N.S.

		Start year of study		
	<1990	1990-99	unknown	Total
N	1	8	4	13
NS	1	6	3	10
Wt	56.25	628.32	19.54	704.11
Het Chi	0.00	22.36	2.60	26.81
Het df	0	7	3	12
Het P	N.S.	**	N.S.	**
Fixed RR	1.11	1.19	0.88	1.17
RRl	0.85	1.10	0.57	1.09
RRu	1.44	1.28	1.38	1.26
P	N.S.	+++	N.S.	+++
Random RR	1.11	1.24	0.88	1.18
RRl	0.85	1.04	0.57	1.02
RRu	1.44	1.47	1.38	1.37
P	N.S.	+	N.S.	+
Between Chi				1.85
Between df				2
Between P				N.S.

		Study type		
	CC	Pr	CS	Total
N	4		9	13
NS	3		7	10
Wt	58.27		645.84	704.11
Het Chi	7.02		19.00	26.81
Het df	3		8	12
Het P	(*)		*	**
Fixed RR	1.31		1.16	1.17
RRl	1.01		1.07	1.09
RRu	1.69		1.25	1.26
P	+		+++	+++
Random RR	1.42		1.15	1.18
RRl	0.85		0.99	1.02
RRu	2.38		1.34	1.37
P	N.S.		(+)	+
Between Chi				0.78
Between df				1
Between P				N.S.

Analysis run on 17-MAR-05

Appendix Table F7 - 6

IASTAD - Meta-analysis of Household exposure (preferring earliest)
Lifetime/Current Asthma
Unadjusted

Ex smokers

	excluded	included	Total
N	11	2	13
NS	8	2	10
Wt	633.37	70.74	704.11
Het Chi	26.53	0.00	26.81
Het df	10	1	12
Het P	**	N.S.	**
Fixed RR	1.18	1.10	1.17
RRl	1.09	0.87	1.09
RRu	1.27	1.39	1.26
P	+++	N.S.	+++
Random RR	1.20	1.10	1.18
RRl	1.01	0.87	1.02
RRu	1.43	1.39	1.37
P	+	N.S.	+
Between Chi			0.28
Between df			1
Between P			N.S.

```
                              Appendix Table F7 - 7

                  IASTAD - Meta-analysis of Household exposure (preferring earliest)
                                   Lifetime/Current Asthma
                      Excluded studies (and stage at which they were excluded)


           1      2      3      4      5      6      7      8      9     10     11     12     13     14     15     16

1      BECKE2 PLATTS RAHERI SAPALD
2      ROBBIN
3      KRONQV LARSS2
                                     Potentially overlapping studies
        REF| REFGP|PRINC|              OVERLAP|
     JANSON JANSON     p        JANSON/RAHERI


                                Adjusted - insufficient data for metaanalysis
        REF|NRR|SEX|AST|  SMOK|AGEL|AGEH|    LOC|BEGYR|PUBYR|STTYP|ONS|ADJ|EXPOS|UNEXsrce| EXPOS-time|UNEXTI|      RR|SIG|
     KRONQV   2   b   l  Never   15   65 Eu:Swe  1996  1999    CS prv   4   Hh NoHhMemb    current   non       *    n
     LARSS2   5   b   l  Never   15   64 Eu:Est  1995  2003    CS prv   5   Hh NoHhMemb    current   non       *    n
```

_____

Appendix Table F8 -

IASTAD - Meta-analysis of Household exposure (preferring most recent)
Lifetime/Current Asthma

This analysis is restricted to results for:
1) Household (overall) or parental exposure
2) Results not by amount of exposure
3) Results complete enough for use in metaanalysis

Within each study, results are then selected (in the following order of preference, within each sex) for:
4) ASTHMA : lifetime, current
5) WHESMO : 2=current, 7=recent, 6=unspec, 10=adult, 1=lifetime, 3=childhood
6) WHOHOU : household overall, mother
7) UNEXTI : unexposed group never, non (i.e. not at time defined for exposed group)
8) For overlapping studies: principal rather than subsidiary studies
Finally for single sex results (m, f) in preference to results for both sexes combined (b).

Results adjusted for the most potential confounders are then chosen in Sections -1 to -3
(and those which actually differ from the adjusted results in Appendix Table F7 - 1 are marked 'x' in Section -1)
and results adjusted for the least confounders in Sections -4 to -6. (Those least adjusted results which
actually differ from the most adjusted are marked 'x' in column X in Section -4)

Section -7 shows excluded studies, together with the stage (as above) at which no qualifying results
were found. It then lists the potentially overlapping studies which have been included (1=principal,
2=subsidiary), and any results which would have been included in preference except that they had data
not complete enough for use in metaanalysis. It also lists their significance (yes/no), if known.

_____

Appendix Table F8 - 1

IASTAD - Meta-analysis of Household exposure (preferring most recent)
Lifetime/Current Asthma
Adjusted

REF	NRR	CompF7	SEX	AST	SMOK	AGEL	AGEH	LOC	BEGYR	PUBYR	STTYP	ONS	ADJ	EXPOS	UNEXsrce	EXPOS-time	UNEXTI
JAAKK2	31	x	b	c	Never	21	63	Eu:Fin	1997	2003	CC	ons	8	Hh	NoHhMemb	current	non
JANSON	2	x	b	c	<1yr	20	48	multi	1990	2001	CS	prv	10	Hh	NoHhMemb	current	non
JEDRYC	1		f	c	<1yr	65	99	Eu:Pol	*	1995	CS	prv	3	Hh	NoHhMemb	current	non
LARSS1	2		b	l	Never	15	69	Eu:Swe	1995	2001	CS	prv	3	Hh	NoHhMemb	childhood	non
MISHRA	3		m	c	NevReg	60	99	As:Ind	1998	2003	CS	prv	12	Hh	NoHhMemb	current	non
MISHRA	4		f	c	NevReg	60	99	As:Ind	1998	2003	CS	prv	12	Hh	NoHhMemb	current	non
NG	6		f	c	<1yr	20	74	As:Sin	*	1993	CS	prv	6	Hh	NoHhMemb	lifetime	non
NHANES	1		b	c	Non	17	99	US:nat	1988	2002	CS	prv	0	Hh	NoHhMemb	current	non
ORYSZC	1		m	c	NevReg	25	54	Eu:Fra	*	2000	CC	prv	0	Hh	NoHhMemb	current	non
ORYSZC	2		f	c	NevReg	25	54	Eu:Fra	*	2000	CC	prv	0	Hh	NoHhMemb	current	non
PILOTT	1		b	l	Non	18	99	Austra	1995	1999	CS	prv	3	Hh	NoHhMemb	unspec	non
THORN	2		m	l	Never	20	50	Eu:Swe	1994	2001	CC	prv	2	Hh	NoHhMemb	last6homes	non
THORN	3		f	l	Never	20	50	Eu:Swe	1994	2001	CC	prv	2	Hh	NoHhMemb	last6homes	non

Appendix Table F8 - 2

IASTAD - Meta-analysis of Household exposure (preferring most recent)
Lifetime/Current Asthma
Adjusted

```
                              Numbers
                              Numbers exposed Non-exposed
REF      NRR     SEX ADJ      Case    Cont    Case    Cont      RR        95.00%CI
JAAKK2 31        b   8          7       -     224       -     4.77 (  1.29-  17.70)
JANSON 2         b   10         -       -       -       -     1.14 (  0.68-   1.90)
JEDRYC 1         f   3          -       -       -       -     0.53 (  0.24-   1.14)
LARSS1 2         b   3         85       -      58       -     1.82 (  1.28-   2.58)
MISHRA 3         m   12       242       -     835       -     1.20 (  0.99-   1.46)
MISHRA 4         f   12       561       -     829       -     1.05 (  0.91-   1.21)
Subtotal MISHRA                                              1.10 (  0.98-   1.23)
NG     6         f   6         18       -      15       -     1.18 (  0.57-   2.46)
NHANES 1         b   0         70    1481     370    8660     1.11 (  0.85-   1.44)
ORYSZC 1         m   0          3       4      14      28     1.50 (  0.29-   7.65)
ORYSZC 2         f   0          8      13      26      43     1.02 (  0.37-   2.78)
Subtotal ORYSZC                                              1.13 (  0.48-   2.67)
PILOTT 1         b   3          -       -       -       -     1.09 (  0.65-   1.82)
THORN  2         m   2          -       -       -       -     4.80 (  2.00-  11.60)
THORN  3         f   2          -       -       -       -     1.50 (  0.80-   3.10)
Subtotal THORN                                              2.31 (  1.35-   3.96)
Partial Totals                994    1498    2371    8731
*prospective study

REF      NRR     SEX ADJ              Ys      Ws      Qs       Ps

JAAKK2 31        b   8              1.56    2.24    4.45    0.0194
JANSON 2         b   10            0.13   14.55    0.01    0.6172
JEDRYC 1         f   3            -0.63    6.33    3.93    0.1102
LARSS1 2         b   3             0.60   31.28    6.20    0.0008
MISHRA 3         m   12            0.18  101.81    0.08    0.0658
MISHRA 4         f   12            0.05  189.27    2.08    0.5021
Subtotal MISHRA                  -0.08  291.08    2.16
NG     6         f   6             0.17    7.19    0.00    0.6573
NHANES 1         b   0             0.10   56.25    0.16    0.4488
ORYSZC 1         m   0             0.41    1.45    0.09    0.6256
ORYSZC 2         f   0             0.02    3.79    0.07    0.9727
Subtotal ORYSZC                   0.12    5.24    0.16
PILOTT 1         b   3             0.09   14.49    0.07    0.7428
THORN  2         m   2             1.57    4.97    9.96    0.0005
THORN  3         f   2             0.41    8.37    0.53    0.2406
Subtotal THORN                    1.67   13.35   10.49
```

```
              N      13
              NS     10


             Wt     441.99
         Het Chi     27.62
         Het  df      12
         Het  P       **
       Fixed  RR     1.17
              RRl    1.06
              RRu    1.28
              P       ++
       Random RR     1.26
              RRl    1.05
              RRu    1.53
              P        +
        Asymm P     N.S.
```

Appendix Table F8 - 3

IASTAD - Meta-analysis of Household exposure (preferring most recent)
Lifetime/Current Asthma
Adjusted

```
           N        13
           NS       10


           Wt    441.99
   Het Chi   27.62
   Het  df      12
   Het  P       **
 Fixed  RR     1.17
        RRl    1.06
        RRu    1.28
        P       ++
 Random RR     1.26
        RRl    1.05
        RRu    1.53
        P        +
 Asymm  P      N.S.
```

	Sex			
	both	male	female	Total
N	5	3	5	13
NS	5	3	5	13
Wt	118.81	108.23	214.95	441.99
Het Chi	9.49	9.15	4.12	27.62
Het df	4	2	4	12
Het P	*	*	N.S.	**
Fixed RR	1.30	1.28	1.05	1.17
RRl	1.09	1.06	0.92	1.06
RRu	1.55	1.55	1.20	1.28
P	++	++	N.S.	++
Random RR	1.36	2.02	1.05	1.26
RRl	0.99	0.73	0.89	1.05
RRu	1.87	5.56	1.23	1.53
P	(+)	N.S.	N.S.	+
Between Chi				4.86
Between df				2
Between P				(*)

	Asthma definition (lifetime/current)		
	lifetime	current	Total
N	4	9	13
NS	3	7	10
Wt	59.12	382.88	441.99
Het Chi	8.50	9.59	27.62
Het df	3	8	12
Het P	*	N.S.	**
Fixed RR	1.69	1.10	1.17
RRl	1.31	1.00	1.06
RRu	2.19	1.22	1.28
P	+++	(+)	++
Random RR	1.79	1.11	1.26
RRl	1.11	0.97	1.05
RRu	2.88	1.26	1.53
P	+	N.S.	+
Between Chi			9.53
Between df			1
Between P			**

Appendix Table F8 - 3

IASTAD - Meta-analysis of Household exposure (preferring most recent)
Lifetime/Current Asthma
Adjusted

		Continent		
	NAmer	Europe	Oth/Mult	Total
N	1	7	5	13
NS	1	5	4	10
Wt	56.25	58.43	327.31	441.99
Het Chi	0.00	17.62	1.23	27.62
Het df	0	6	4	12
Het P	N.S.	**	N.S.	**
Fixed RR	1.11	1.67	1.10	1.17
RRl	0.85	1.29	0.99	1.06
RRu	1.44	2.16	1.23	1.28
P	N.S.	+++	(+)	++
Random RR	1.11	1.67	1.10	1.26
RRl	0.85	0.99	0.99	1.05
RRu	1.44	2.84	1.23	1.53
P	N.S.	(+)	(+)	+
Between Chi				8.77
Between df				2
Between P				*

		Start year of study		
	<1990	1990-99	unknown	Total
N	1	8	4	13
NS	1	6	3	10
Wt	56.25	366.99	18.76	441.99
Het Chi	0.00	23.20	2.74	27.62
Het df	0	7	3	12
Het P	N.S.	**	N.S.	**
Fixed RR	1.11	1.19	0.89	1.17
RRl	0.85	1.08	0.57	1.06
RRu	1.44	1.32	1.40	1.28
P	N.S.	+++	N.S.	++
Random RR	1.11	1.42	0.89	1.26
RRl	0.85	1.10	0.57	1.05
RRu	1.44	1.82	1.40	1.53
P	N.S.	++	N.S.	+
Between Chi				1.69
Between df				2
Between P				N.S.

		Study type		
	CC	Pr	CS	Total
N	5		8	13
NS	3		7	10
Wt	20.83		421.17	441.99
Het Chi	8.01		12.18	27.62
Het df	4		7	12
Het P	(*)		(*)	**
Fixed RR	2.09		1.13	1.17
RRl	1.36		1.03	1.06
RRu	3.21		1.25	1.28
P	+++		+	++
Random RR	2.18		1.16	1.26
RRl	1.14		0.99	1.05
RRu	4.17		1.35	1.53
P	+		(+)	+
Between Chi				7.44
Between df				1
Between P				**

Appendix Table F8 - 3

IASTAD - Meta-analysis of Household exposure (preferring most recent)
Lifetime/Current Asthma
Adjusted

Ex smokers

	excluded	included	Total
N	11	2	13
NS	8	2	10
Wt	371.25	70.74	441.99
Het Chi	27.36	0.00	27.62
Het df	10	1	12
Het P	**	N.S.	**
Fixed RR	1.18	1.10	1.17
RRl	1.06	0.87	1.06
RRu	1.30	1.39	1.28
P	++	N.S.	++
Random RR	1.33	1.10	1.26
RRl	1.05	0.87	1.05
RRu	1.70	1.39	1.53
P	+	N.S.	+
Between Chi			0.26
Between df			1
Between P			N.S.

Exposed group : when Exposed

	life	adult	child	current	unspec	Total
N	1	2	1	8	1	13
NS	1	1	1	6	1	10
Wt	7.19	13.35	31.28	375.69	14.49	441.99
Het Chi	0.00	4.22	0.00	9.56	0.00	27.62
Het df	0	1	0	7	0	12
Het P	N.S.	*	N.S.	N.S.	N.S.	**
Fixed RR	1.18	2.31	1.82	1.10	1.09	1.17
RRl	0.57	1.35	1.28	0.99	0.65	1.06
RRu	2.45	3.96	2.58	1.22	1.82	1.28
P	N.S.	++	+++	(+)	N.S.	++
Random RR	1.18	2.59	1.82	1.11	1.09	1.26
RRl	0.57	0.83	1.28	0.95	0.65	1.05
RRu	2.45	8.08	2.58	1.28	1.82	1.53
P	N.S.	N.S.	+++	N.S.	N.S.	+
Between Chi						13.84
Between df						4
Between P						**

Appendix Table F8 - 4

IASTAD - Meta-analysis of Household exposure (preferring most recent)
Lifetime/Current Asthma
Unadjusted

REF	NRR	X	SEX	AST	SMOK	AGEL	AGEH	LOC	BEGYR	PUBYR	STTYP	ONS	ADJ	EXPOS	UNEXsrce	EXPOS-time	UNEXTI
JAAKK2	7	x	b	c	Never	21	63	Eu:Fin	1997	2003	CC	ons	0	Hh	NoHhMemb	current	non
JANSON	2		b	c	<1yr	20	48	multi	1990	2001	CS	prv	10	Hh	NoHhMemb	current	non
JEDRYC	1		f	c	<1yr	65	99	Eu:Pol	*	1995	CS	prv	3	Hh	NoHhMemb	current	non
LARSS1	1	x	b	l	Never	15	69	Eu:Swe	1995	2001	CS	prv	0	Hh	NoHhMemb	childhood	non
MISHRA	1	x	m	c	NevReg	60	99	As:Ind	1998	2003	CS	prv	0	Hh	NoHhMemb	current	non
MISHRA	2	x	f	c	NevReg	60	99	As:Ind	1998	2003	CS	prv	0	Hh	NoHhMemb	current	non
NG	3	x	f	c	<1yr	20	74	As:Sin	*	1993	CS	prv	0	Hh	NoHhMemb	lifetime	non
NHANES	1		b	c	Non	17	99	US:nat	1988	2002	CS	prv	0	Hh	NoHhMemb	current	non
ORYSZC	1		m	c	NevReg	25	54	Eu:Fra	*	2000	CC	prv	0	Hh	NoHhMemb	current	non
ORYSZC	2		f	c	NevReg	25	54	Eu:Fra	*	2000	CC	prv	0	Hh	NoHhMemb	current	non
PILOTT	1		b	l	Non	18	99	Austra	1995	1999	CS	prv	3	Hh	NoHhMemb	unspec	non
THORN	1	x	b	l	Never	20	50	Eu:Swe	1994	2001	CC	prv	0	Hh	NoHhMemb	last6homes	non

Appendix Table F8 - 5

IASTAD - Meta-analysis of Household exposure (preferring most recent)
Lifetime/Current Asthma
Unadjusted

```
                           Numbers
                           Numbers exposed Non-exposed
REF      NRR     SEX ADJ    Case    Cont    Case    Cont    RR       95.00%CI
JAAKK2 7         b   0        7       8     224     475    1.86 (  0.66-   5.18)
JANSON 2         b   10       -       -       -       -    1.14 (  0.68-   1.90)
JEDRYC 1         f   3        -       -       -       -    0.53 (  0.24-   1.14)
LARSS1 1         b   0       85    1171      58    1470    1.84 (  1.31-   2.59)
MISHRA 1         m   0      242    1739     835    8047    1.34 (  1.15-   1.56)
MISHRA 2         f   0      561    6037     829    9659    1.08 (  0.97-   1.21)
Subtotal MISHRA                                           1.17 (  1.07-   1.28)
NG     3         f   0       18     645      15     604    1.12 (  0.56-   2.25)
NHANES 1         b   0       70    1481     370    8660    1.11 (  0.85-   1.44)
ORYSZC 1         m   0        3       4      14      28    1.50 (  0.29-   7.65)
ORYSZC 2         f   0        8      13      26      43    1.02 (  0.37-   2.78)
Subtotal ORYSZC                                           1.13 (  0.48-   2.67)
PILOTT 1         b   3        -       -       -       -    1.09 (  0.65-   1.82)
THORN  1         b   0       33     116      36     302    2.39 (  1.42-   4.01)
Partial Totals             1027   11214    2407   29288
*prospective study

REF      NRR     SEX ADJ            Ys      Ws      Qs      Ps

JAAKK2 7         b   0            0.62    3.64    0.69    0.2380
JANSON 2         b   10           0.13   14.55    0.04    0.6172
JEDRYC 1         f   3           -0.63    6.33    4.22    0.1102
LARSS1 1         b   0            0.61   32.74    6.00    0.0005
MISHRA 1         m   0            0.29  165.86    2.08    0.0002
MISHRA 2         f   0            0.08  306.94    3.20    0.1638
Subtotal MISHRA                  0.01  472.80    5.28
NG     3         f   0            0.12    7.97    0.03    0.7419
NHANES 1         b   0            0.10   56.25    0.37    0.4488
ORYSZC 1         m   0            0.41    1.45    0.07    0.6256
ORYSZC 2         f   0            0.02    3.79    0.10    0.9727
Subtotal ORYSZC                  0.06    5.24    0.17
PILOTT 1         b   3            0.09   14.49    0.13    0.7428
THORN  1         b   0            0.87   14.28    6.76    0.0010
```

```
            N        12
            NS       10


            Wt     628.31
       Het Chi     23.70
       Het  df        11
       Het   P         *
     Fixed  RR      1.20
            RRl     1.11
            RRu     1.30
              P     +++
    Random  RR      1.26
            RRl     1.07
            RRu     1.48
              P      ++
     Asymm   P      N.S.
```

Appendix Table F8 - 6

<u>IASTAD - Meta-analysis of Household exposure (preferring most recent)</u>
Lifetime/Current Asthma
Unadjusted

```
         N      12
         NS     10


         Wt  628.31
   Het Chi   23.70
   Het  df      11
   Het  P        *
 Fixed  RR    1.20
        RRl   1.11
        RRu   1.30
        P     +++
Random  RR    1.26
        RRl   1.07
        RRu   1.48
        P      ++
 Asymm  P     N.S.
```

		<u>Sex</u>		
	both	male	female	Total
N	6	2	4	12
NS	6	2	4	12
Wt	135.96	167.31	325.03	628.31
Het Chi	11.40	0.02	3.19	23.70
Het df	5	1	3	11
Het P	*	N.S.	N.S.	*
Fixed RR	1.38	1.34	1.07	1.20
RRl	1.16	1.15	0.96	1.11
RRu	1.63	1.56	1.19	1.30
P	+++	+++	N.S.	+++
Random RR	1.44	1.34	1.05	1.26
RRl	1.09	1.15	0.88	1.07
RRu	1.91	1.56	1.24	1.48
P	+	+++	N.S.	++
Between Chi				9.09
Between df				2
Between P				*

	<u>Asthma definition (lifetime/current)</u>		
	lifetime	current	Total
N	3	9	12
NS	3	7	10
Wt	61.52	566.79	628.31
Het Chi	4.69	9.91	23.70
Het df	2	8	11
Het P	(*)	N.S.	*
Fixed RR	1.73	1.15	1.20
RRl	1.35	1.06	1.11
RRu	2.22	1.25	1.30
P	+++	+++	+++
Random RR	1.70	1.16	1.26
RRl	1.14	1.03	1.07
RRu	2.54	1.30	1.48
P	++	+	++
Between Chi			9.09
Between df			1
Between P			**

Appendix Table F8 - 6

IASTAD - Meta-analysis of Household exposure (preferring most recent)
Lifetime/Current Asthma
Unadjusted

| | | Continent | | | |
		NAmer	Europe	Oth/Mult	Total
	N	1	6	5	12
	NS	1	5	4	10
	Wt	56.25	62.24	509.82	628.31
Het	Chi	0.00	11.44	5.01	23.70
Het	df	0	5	4	11
Het	P	N.S.	*	N.S.	*
Fixed	RR	1.11	1.65	1.16	1.20
	RRl	0.85	1.29	1.07	1.11
	RRu	1.44	2.12	1.27	1.30
	P	N.S.	+++	+++	+++
Random	RR	1.11	1.45	1.18	1.26
	RRl	0.85	0.92	1.05	1.07
	RRu	1.44	2.29	1.32	1.48
	P	N.S.	N.S.	++	++
Between	Chi				7.24
Between	df				2
Between	P				*

| | | Start year of study | | | |
		<1990	1990-99	unknown	Total
	N	1	7	4	12
	NS	1	6	3	10
	Wt	56.25	552.52	19.54	628.31
Het	Chi	0.00	18.70	2.60	23.70
Het	df	0	6	3	11
Het	P	N.S.	**	N.S.	*
Fixed	RR	1.11	1.22	0.88	1.20
	RRl	0.85	1.12	0.57	1.11
	RRu	1.44	1.33	1.38	1.30
	P	N.S.	+++	N.S.	+++
Random	RR	1.11	1.38	0.88	1.26
	RRl	0.85	1.12	0.57	1.07
	RRu	1.44	1.69	1.38	1.48
	P	N.S.	++	N.S.	++
Between	Chi				2.40
Between	df				2
Between	P				N.S.

| | | Study type | | | |
		CC	Pr	CS	Total
	N	4		8	12
	NS	3		7	10
	Wt	23.17		605.14	628.31
Het	Chi	2.29		15.86	23.70
Het	df	3		7	11
Het	P	N.S.		*	*
Fixed	RR	1.94		1.18	1.20
	RRl	1.29		1.09	1.11
	RRu	2.91		1.27	1.30
	P	++		+++	+++
Random	RR	1.94		1.19	1.26
	RRl	1.29		1.02	1.07
	RRu	2.91		1.40	1.48
	P	++		+	++
Between	Chi				5.54
Between	df				1
Between	P				*

Analysis run on 17-MAR-05

Appendix Table F8 - 6

IASTAD - Meta-analysis of Household exposure (preferring most recent)
Lifetime/Current Asthma
Unadjusted

Ex smokers

		excluded	included	Total
	N	10	2	12
	NS	8	2	10
	Wt	557.57	70.74	628.31
Het	Chi	23.14	0.00	23.70
Het	df	9	1	11
Het	P	**	N.S.	*
Fixed	RR	1.21	1.10	1.20
	RRl	1.12	0.87	1.11
	RRu	1.32	1.39	1.30
	P	+++	N.S.	+++
Random	RR	1.31	1.10	1.26
	RRl	1.07	0.87	1.07
	RRu	1.61	1.39	1.48
	P	++	N.S.	++
Between	Chi			0.56
Between	df			1
Between	P			N.S.

Appendix Table F8 - 7

IASTAD - Meta-analysis of Household exposure (preferring most recent)
Lifetime/Current Asthma
Excluded studies (and stage at which they were excluded)


```
         1       2       3       4       5       6       7       8       9      10      11      12      13      14      15      16

1     BECKE2 PLATTS RAHERI SAPALD
2     ROBBIN
3     KRONQV LARSS2
```

Potentially overlapping studies

```
    REF| REFGP|PRINC|              OVERLAP|
 JANSON JANSON     p      JANSON/RAHERI
```

Adjusted - insufficient data for metaanalysis

REF	NRR	SEX	AST	SMOK	AGEL	AGEH	LOC	BEGYR	PUBYR	STTYP	ONS	ADJ	EXPOS	UNEXsrce	EXPOS-time	UNEXTI	RR	SIG
KRONQV	2	b	l	Never	15	65	Eu:Swe	1996	1999	CS	prv	4	Hh	NoHhMemb	current	non	*	n
LARSS2	5	b	l	Never	15	64	Eu:Est	1995	2003	CS	prv	5	Hh	NoHhMemb	current	non	*	n

_____

Appendix Table F9 -

IASTAD - Meta-analysis of Workplace Exposure (preferring earliest)
Lifetime/Current Asthma

This analysis is restricted to results for:
1) Workplace exposure
2) Results not by amount of exposure
3) Results complete enough for use in metaanalysis

Within each study, results are then selected (in the following order of preference, within each sex) for:
4) ASTHMA : lifetime, current
5) WHESMO : 3=childhood, 1=lifetime, 10=adult, 7=recent, 6=unspec, 2=current
6) WHOHOU : household overall, mother
7) UNEXTI : unexposed group never, non (i.e. not at time defined for exposed group)
8) For overlapping studies: principal rather than subsidiary studies
Finally for single sex results (m, f) in preference to results for both sexes combined (b).

Results adjusted for the most potential confounders are then chosen in Sections -1 to -3
(and those which actually differ from the adjusted results in Appendix Table F1 - 1 are marked 'x' in Section -1)
and results adjusted for the least confounders in Sections -4 to -6. (Those least adjusted results which
actually differ from the most adjusted are marked 'x' in column X in Section -4)

Section -7 shows excluded studies, together with the stage (as above) at which no qualifying results
were found. It then lists the potentially overlapping studies which have been included (1=principal,
2=subsidiary), and any results which would have been included in preference except that they had data
not complete enough for use in metaanalysis. It also lists their significance (yes/no), if known.

_____

Appendix Table F9 - 1

IASTAD - Meta-analysis of Workplace Exposure (preferring earliest)
Lifetime/Current Asthma
Adjusted

```
   REF|NRR|CompF1|SEX|AST|   SMOK|AGEL|AGEH|    LOC|BEGYR|PUBYR|STTYP|ONS|ADJ|EXPOS|UNEXsrce| EXPOS-time|UNEXTI|

JAAKK2  39      x   b   c  Never   21   63 Eu:Fin 1997  2003   CC ons   8  Work  NotWork   lifetime    non
JANSON   3      x   b   c   <1yr   20   48  multi 1990  2001   CS prv  10  Work  NotWork   current     non
LARSS2   4          b   l  Never   15   64 Eu:Est 1995  2003   CS prv   5  Work  NotWork   current     non
NHANES   2      x   b   c    Non   17   99 US:nat 1988  2002   CS prv   0  Work  NotWork   current     non
ORYSZC   3      x   m   c NevReg   25   54 Eu:Fra    * 2000   CC prv   0  Work  NotWork   current     non
ORYSZC   4      x   f   c NevReg   25   54 Eu:Fra    * 2000   CC prv   0  Work  NotWork   current     non
```

Appendix Table F9 - 2

IASTAD - Meta-analysis of Workplace Exposure (preferring earliest)
Lifetime/Current Asthma
Adjusted

```
                              Numbers
                              Numbers exposed Non-exposed
REF      NRR      SEX ADJ     Case    Cont    Case    Cont      RR        95.00%CI
JAAKK2 39         b   8        76       -      163      -      1.55 ( 1.06-  2.25)
JANSON 3          b   10        -       -       -       -      1.90 ( 1.25-  2.88)
LARSS2 4          b   5         -       -       -       -      1.13 ( 0.80-  1.59)
NHANES 2          b   0       114     2069     326     8072    1.36 ( 1.10-  1.70)
ORYSZC 3          m   0         3       7       13      24     0.79 ( 0.17-  3.59)
ORYSZC 4          f   0         4       13      30       42    0.43 ( 0.13-  1.45)
Subtotal ORYSZC                                                0.55 ( 0.21-  1.41)
Partial Totals                197     2089     532     8138
*prospective study

REF      NRR      SEX ADJ                Ys      Ws      Qs       Ps

JAAKK2 39         b   8                 0.44    27.12   0.41    0.0225
JANSON 3          b   10                0.64    22.06   2.36    0.0026
LARSS2 4          b   5                 0.12    32.57   1.21    0.4855
NHANES 2          b   0                 0.31    80.34   0.00    0.0054
ORYSZC 3          m   0                -0.23     1.68   0.51    0.7614
ORYSZC 4          f   0                -0.84     2.60   3.49    0.1742
Subtotal ORYSZC                        -1.71     4.29   3.99
```

```
           N       6
           NS      5


           Wt   166.38
     Het Chi    7.97
     Het df      5
     Het P      N.S.
   Fixed RR     1.37
         RRl    1.18
         RRu    1.59
         P      +++
  Random RR     1.36
         RRl    1.09
         RRu    1.70
         P      ++
   Asymm P      N.S.
```

Appendix Table F9 - 3

IASTAD - Meta-analysis of Workplace Exposure (preferring earliest)
Lifetime/Current Asthma
Adjusted

```
        N       6
        NS      5


        Wt    166.38
   Het Chi     7.97
   Het  df        5
   Het  P      N.S.
 Fixed  RR     1.37
        RRl    1.18
        RRu    1.59
        P      +++
Random  RR     1.36
        RRl    1.09
        RRu    1.70
        P       ++
 Asymm  P      N.S.
```

| | Sex | | | |
	both	male	female	Total
N	4	1	1	6
NS	4	1	1	5
Wt	162.09	1.68	2.60	166.38
Het Chi	3.89	0.00	0.00	7.97
Het df	3	0	0	5
Het P	N.S.	N.S.	N.S.	N.S.
Fixed RR	1.40	0.79	0.43	1.37
RRl	1.20	0.17	0.13	1.18
RRu	1.64	3.59	1.45	1.59
P	+++	N.S.	N.S.	+++
Random RR	1.41	0.79	0.43	1.36
RRl	1.18	0.17	0.13	1.09
RRu	1.70	3.59	1.45	1.70
P	+++	N.S.	N.S.	++
Between Chi				4.09
Between df				2
Between P				N.S.

| | Asthma definition (lifetime/current) | | |
	lifetime	current	Total
N	1	5	6
NS	1	4	5
Wt	32.57	133.81	166.38
Het Chi	0.00	6.47	7.97
Het df	0	4	5
Het P	N.S.	N.S.	N.S.
Fixed RR	1.13	1.44	1.37
RRl	0.80	1.21	1.18
RRu	1.59	1.70	1.59
P	N.S.	+++	+++
Random RR	1.13	1.43	1.36
RRl	0.80	1.09	1.09
RRu	1.59	1.87	1.70
P	N.S.	++	++
Between Chi			1.50
Between df			1
Between P			N.S.

Appendix Table F9 - 3

IASTAD - Meta-analysis of Workplace Exposure (preferring earliest)
Lifetime/Current Asthma
Adjusted

Continent

	NAmer	Europe	Oth/Mult	Total
N	1	4	1	6
NS	1	3	1	5
Wt	80.34	63.98	22.06	166.38
Het Chi	0.00	4.88	0.00	7.97
Het df	0	3	0	5
Het P	N.S.	N.S.	N.S.	N.S.
Fixed RR	1.36	1.23	1.90	1.37
RRl	1.10	0.96	1.25	1.18
RRu	1.70	1.57	2.88	1.59
P	++	(+)	++	+++
Random RR	1.36	1.16	1.90	1.36
RRl	1.10	0.80	1.25	1.09
RRu	1.70	1.70	2.88	1.70
P	++	N.S.	++	++
Between Chi				3.10
Between df				2
Between P				N.S.

Start year of study

	<1990	1990-99	unknown	Total
N	1	3	2	6
NS	1	3	1	5
Wt	80.34	81.75	4.29	166.38
Het Chi	0.00	3.76	0.38	7.97
Het df	0	2	1	5
Het P	N.S.	N.S.	N.S.	N.S.
Fixed RR	1.36	1.44	0.55	1.37
RRl	1.10	1.16	0.21	1.18
RRu	1.70	1.79	1.41	1.59
P	++	+++	N.S.	+++
Random RR	1.36	1.47	0.55	1.36
RRl	1.10	1.09	0.21	1.09
RRu	1.70	1.98	1.41	1.70
P	++	+	N.S.	++
Between Chi				3.84
Between df				2
Between P				N.S.

Study type

	CC	Pr	CS	Total
N	3		3	6
NS	2		3	5
Wt	31.41		134.97	166.38
Het Chi	4.39		3.57	7.97
Het df	2		2	5
Het P	N.S.		N.S.	N.S.
Fixed RR	1.34		1.38	1.37
RRl	0.95		1.16	1.18
RRu	1.91		1.63	1.59
P	(+)		+++	+++
Random RR	0.96		1.39	1.36
RRl	0.41		1.09	1.09
RRu	2.23		1.78	1.70
P	N.S.		++	++
Between Chi				0.01
Between df				1
Between P				N.S.

Appendix Table F9 - 3

IASTAD - Meta-analysis of Workplace Exposure (preferring earliest)
Lifetime/Current Asthma
Adjusted

Ex smokers

	excluded	included	Total
N	5	1	6
NS	4	1	5
Wt	86.03	80.34	166.38
Het Chi	7.97	0.00	7.97
Het df	4	0	5
Het P	(*)	N.S.	N.S.
Fixed RR	1.38	1.36	1.37
RRl	1.11	1.10	1.18
RRu	1.70	1.70	1.59
P	++	++	+++
Random RR	1.32	1.36	1.36
RRl	0.93	1.10	1.09
RRu	1.86	1.70	1.70
P	N.S.	++	++
Between Chi			0.00
Between df			1
Between P			N.S.

Exposed group : when Exposed

	life	adult	child	current	unspec	Total
N	1			5		6
NS	1			4		5
Wt	27.12			139.25		166.38
Het Chi	0.00			7.48		7.97
Het df	0			4		5
Het P	N.S.			N.S.		N.S.
Fixed RR	1.55			1.34		1.37
RRl	1.06			1.13		1.18
RRu	2.26			1.58		1.59
P	+			+++		+++
Random RR	1.55			1.30		1.36
RRl	1.06			0.98		1.09
RRu	2.26			1.73		1.70
P	+			(+)		++
Between Chi						0.49
Between df						1
Between P						N.S.

Appendix Table F9 - 4

IASTAD - Meta-analysis of Workplace Exposure (preferring earliest)
Lifetime/Current Asthma
Unadjusted

REF	NRR	X	SEX	AST	SMOK	AGEL	AGEH	LOC	BEGYR	PUBYR	STTYP	ONS	ADJ	EXPOS	UNEXsrce	EXPOS-time	UNEXTI
JAAKK2	15	x	b	c	Never	21	63	Eu:Fin	1997	2003	CC	ons	0	Work	NotWork	lifetime	non
JANSON	3		b	c	<1yr	20	48	multi	1990	2001	CS	prv	10	Work	NotWork	current	non
LARSS2	4		b	l	Never	15	64	Eu:Est	1995	2003	CS	prv	5	Work	NotWork	current	non
NHANES	2		b	c	Non	17	99	US:nat	1988	2002	CS	prv	0	Work	NotWork	current	non
ORYSZC	3		m	c	NevReg	25	54	Eu:Fra	*	2000	CC	prv	0	Work	NotWork	current	non
ORYSZC	4		f	c	NevReg	25	54	Eu:Fra	*	2000	CC	prv	0	Work	NotWork	current	non

Appendix Table F9 - 5

IASTAD - Meta-analysis of Workplace Exposure (preferring earliest)
Lifetime/Current Asthma
Unadjusted

```
                                 Numbers
                                 Numbers exposed Non-exposed
REF     NRR     SEX ADJ          Case    Cont    Case    Cont    RR          95.00%CI
JAAKK2 15       b   0            76      132     163     355     1.25 (  0.89-   1.76)
JANSON 3        b   10           -       -       -       -       1.90 (  1.25-   2.88)
LARSS2 4        b   5            -       -       -       -       1.13 (  0.80-   1.59)
NHANES 2        b   0            114     2069    326     8072    1.36 (  1.10-   1.70)
ORYSZC 3        m   0            3       7       13      24      0.79 (  0.17-   3.59)
ORYSZC 4        f   0            4       13      30      42      0.43 (  0.13-   1.45)
 Subtotal ORYSZC                                                 0.55 (  0.21-   1.41)
Partial Totals                   197     2221    532     8493
*prospective study

REF     NRR     SEX ADJ                  Ys      Ws      Qs      Ps

JAAKK2 15       b   0                     0.23    33.69   0.09    0.1890
JANSON 3        b   10                    0.64    22.06   2.92    0.0026
LARSS2 4        b   5                     0.12    32.57   0.79    0.4855
NHANES 2        b   0                     0.31    80.34   0.08    0.0054
ORYSZC 3        m   0                    -0.23    1.68    0.44    0.7614
ORYSZC 4        f   0                    -0.84    2.60    3.27    0.1742
 Subtotal ORYSZC                         -1.63    4.29    3.71
```

```
                N       6
                NS      5


                Wt    172.94
         Het Chi     7.59
         Het  df        5
         Het  P      N.S.
       Fixed  RR     1.32
              RRl    1.14
              RRu    1.53
              P      +++
      Random  RR     1.30
              RRl    1.06
              RRu    1.61
              P       +
       Asymm  P      N.S.
```

Appendix Table F9 - 6

IASTAD - Meta-analysis of Workplace Exposure (preferring earliest)
Lifetime/Current Asthma
Unadjusted

```
           N      6
          NS      5


          Wt  172.94
   Het Chi    7.59
   Het  df       5
   Het  P     N.S.
 Fixed  RR    1.32
        RRl   1.14
        RRu   1.53
        P      +++
Random  RR    1.30
        RRl   1.06
        RRu   1.61
        P        +
 Asymm  P     N.S.
```

		Sex		
	both	male	female	Total
N	4	1	1	6
NS	4	1	1	5
Wt	168.66	1.68	2.60	172.94
Het Chi	3.80	0.00	0.00	7.59
Het df	3	0	0	5
Het P	N.S.	N.S.	N.S.	N.S.
Fixed RR	1.35	0.79	0.43	1.32
RRl	1.16	0.17	0.13	1.14
RRu	1.57	3.59	1.45	1.53
P	+++	N.S.	N.S.	+++
Random RR	1.35	0.79	0.43	1.30
RRl	1.14	0.17	0.13	1.06
RRu	1.61	3.59	1.45	1.61
P	+++	N.S.	N.S.	+
Between Chi				3.80
Between df				2
Between P				N.S.

	Asthma definition (lifetime/current)		
	lifetime	current	Total
N	1	5	6
NS	1	4	5
Wt	32.57	140.37	172.94
Het Chi	0.00	6.62	7.59
Het df	0	4	5
Het P	N.S.	N.S.	N.S.
Fixed RR	1.13	1.37	1.32
RRl	0.80	1.16	1.14
RRu	1.59	1.62	1.53
P	N.S.	+++	+++
Random RR	1.13	1.35	1.30
RRl	0.80	1.04	1.06
RRu	1.59	1.75	1.61
P	N.S.	+	+
Between Chi			0.98
Between df			1
Between P			N.S.

Appendix Table F9 - 6

IASTAD - Meta-analysis of Workplace Exposure (preferring earliest)
Lifetime/Current Asthma
Unadjusted

		Continent		
	NAmer	Europe	Oth/Mult	Total
N	1	4	1	6
NS	1	3	1	5
Wt	80.34	70.54	22.06	172.94
Het Chi	0.00	3.00	0.00	7.59
Het df	0	3	0	5
Het P	N.S.	N.S.	N.S.	N.S.
Fixed RR	1.36	1.14	1.90	1.32
RRl	1.10	0.90	1.25	1.14
RRu	1.70	1.44	2.88	1.53
P	++	N.S.	++	+++
Random RR	1.36	1.14	1.90	1.30
RRl	1.10	0.90	1.25	1.06
RRu	1.70	1.44	2.88	1.61
P	++	N.S.	++	+
Between Chi				4.60
Between df				2
Between P				N.S.

		Start year of study		
	<1990	1990-99	unknown	Total
N	1	3	2	6
NS	1	3	1	5
Wt	80.34	88.31	4.29	172.94
Het Chi	0.00	3.78	0.38	7.59
Het df	0	2	1	5
Het P	N.S.	N.S.	N.S.	N.S.
Fixed RR	1.36	1.34	0.55	1.32
RRl	1.10	1.09	0.21	1.14
RRu	1.70	1.65	1.41	1.53
P	++	++	N.S.	+++
Random RR	1.36	1.36	0.55	1.30
RRl	1.10	1.02	0.21	1.06
RRu	1.70	1.82	1.41	1.61
P	++	+	N.S.	+
Between Chi				3.43
Between df				2
Between P				N.S.

		Study type		
	CC	Pr	CS	Total
N	3		3	6
NS	2		3	5
Wt	37.97		134.97	172.94
Het Chi	3.00		3.57	7.59
Het df	2		2	5
Het P	N.S.		N.S.	N.S.
Fixed RR	1.14		1.38	1.32
RRl	0.83		1.16	1.14
RRu	1.57		1.63	1.53
P	N.S.		+++	+++
Random RR	0.95		1.39	1.30
RRl	0.51		1.09	1.06
RRu	1.78		1.78	1.61
P	N.S.		++	+
Between Chi				1.03
Between df				1
Between P				N.S.

Appendix Table F9 - 6

IASTAD - Meta-analysis of Workplace Exposure (preferring earliest)
Lifetime/Current Asthma
Unadjusted

Ex smokers

		excluded	included	Total
	N	5	1	6
	NS	4	1	5
	Wt	92.60	80.34	172.94
Het	Chi	7.44	0.00	7.59
Het	df	4	0	5
Het	P	N.S.	N.S.	N.S.
Fixed	RR	1.28	1.36	1.32
	RRl	1.05	1.10	1.14
	RRu	1.57	1.70	1.53
	P	+	++	+++
Random	RR	1.25	1.36	1.30
	RRl	0.91	1.10	1.06
	RRu	1.72	1.70	1.61
	P	N.S.	++	+
Between	Chi			0.16
Between	df			1
Between	P			N.S.

Appendix Table F9 - 7

IASTAD - Meta-analysis of Workplace Exposure (preferring earliest)
Lifetime/Current Asthma
Excluded studies (and stage at which they were excluded)


```
       1      2      3      4      5      6      7      8      9     10     11     12     13     14     15     16

1    BECKE2 JEDRYC LARSS1 MISHRA    NG PILOTT PLATTS RAHERI  THORN
2    ROBBIN
3    KRONQV SAPALD
```
                              Potentially overlapping studies
```
    REF| REFGP|PRINC|            OVERLAP|
 JANSON JANSON    p      JANSON/RAHERI
```

                         Adjusted - insufficient data for metaanalysis
```
    REF|NRR|SEX|AST|  SMOK|AGEL|AGEH|   LOC|BEGYR|PUBYR|STTYP|ONS|ADJ|EXPOS|UNEXsrce| EXPOS-time|UNEXTI|    RR|SIG|
 KRONQV  3   b   l  Never   15   65 Eu:Swe 1996 1999   CS prv   4 Work NotWork   current   non       *   n
 SAPALD  6   b   l <20pks   18   60 Eu:Swi 1991 1994   CS prv   8 Work   None    current   non       *   n
```

_____

Appendix Table F10 -

IASTAD - Meta-analysis of Workplace Exposure (preferring most recent)
Lifetime/Current Asthma

This analysis is restricted to results for:
1) Workplace exposure
2) Results not by amount of exposure
3) Results complete enough for use in metaanalysis

Within each study, results are then selected (in the following order of preference, within each sex) for:
4) ASTHMA : lifetime, current
5) WHESMO : 2=current, 7=recent, 6=unspec, 10=adult, 1=lifetime, 3=childhood
6) UNEXTI : unexposed group never, non (i.e. not at time defined for exposed group)
7) For overlapping studies: principal rather than subsidiary studies
Finally for single sex results (m, f) in preference to results for both sexes combined (b).

Results adjusted for the most potential confounders are then chosen in Sections -1 to -3
(and those which actually differ from the adjusted results in Appendix Table F9 - 1 are marked 'x' in Section -1)
and results adjusted for the least confounders in Sections -4 to -6. (Those least adjusted results which
actually differ from the most adjusted are marked 'x' in column X in Section -4)

Section -7 shows excluded studies, together with the stage (as above) at which no qualifying results
were found. It then lists the potentially overlapping studies which have been included (1=principal,
2=subsidiary), and any results which would have been included in preference except that they had data
not complete enough for use in metaanalysis. It also lists their significance (yes/no), if known.

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Appendix Table F10 - 1

IASTAD - Meta-analysis of Workplace Exposure (preferring most recent)
Lifetime/Current Asthma
Adjusted

REF	NRR	CompF9	SEX	AST	SMOK	AGEL	AGEH	LOC	BEGYR	PUBYR	STTYP	ONS	ADJ	EXPOS	UNEXsrce	EXPOS-time	UNEXTI
JAAKK2	28	x	b	c	Never	21	63	Eu:Fin	1997	2003	CC	ons	8	Work	NotWork	current	non
JANSON	3		b	c	<1yr	20	48	multi	1990	2001	CS	prv	10	Work	NotWork	current	non
LARSS2	4		b	l	Never	15	64	Eu:Est	1995	2003	CS	prv	5	Work	NotWork	current	non
NHANES	2		b	c	Non	17	99	US:nat	1988	2002	CS	prv	0	Work	NotWork	current	non
ORYSZC	3		m	c	NevReg	25	54	Eu:Fra	*	2000	CC	prv	0	Work	NotWork	current	non
ORYSZC	4		f	c	NevReg	25	54	Eu:Fra	*	2000	CC	prv	0	Work	NotWork	current	non

Appendix Table F10 - 2

IASTAD - Meta-analysis of Workplace Exposure (preferring most recent)
Lifetime/Current Asthma
Adjusted

				Numbers						
				Numbers exposed		Non-exposed				
REF	NRR	SEX	ADJ	Case	Cont	Case	Cont	RR	95.00%CI	
JAAKK2	28	b	8	34	-	184	-	2.16 (	1.26-	3.72)
JANSON	3	b	10	-	-	-	-	1.90 (	1.25-	2.88)
LARSS2	4	b	5	-	-	-	-	1.13 (	0.80-	1.59)
NHANES	2	b	0	114	2069	326	8072	1.36 (	1.10-	1.70)
ORYSZC	3	m	0	3	7	13	24	0.79 (	0.17-	3.59)
ORYSZC	4	f	0	4	13	30	42	0.43 (	0.13-	1.45)
Subtotal ORYSZC								0.55 (	0.21-	1.41)
Partial Totals				155	2089	553	8138			

*prospective study

REF	NRR	SEX	ADJ	Ys	Ws	Qs	Ps
JAAKK2	28	b	8	0.77	13.11	2.51	0.0053
JANSON	3	b	10	0.64	22.06	2.12	0.0026
LARSS2	4	b	5	0.12	32.57	1.44	0.4855
NHANES	2	b	0	0.31	80.34	0.04	0.0054
ORYSZC	3	m	0	-0.23	1.68	0.54	0.7614
ORYSZC	4	f	0	-0.84	2.60	3.59	0.1742
Subtotal ORYSZC				-1.74	4.29	4.13	

	N	6
	NS	5
	Wt	152.36
Het	Chi	10.23
Het	df	5
Het	P	(*)
Fixed	RR	1.39
	RRl	1.19
	RRu	1.63
	P	+++
Random	RR	1.40
	RRl	1.06
	RRu	1.85
	P	+
Asymm	P	N.S.

Appendix Table F10 - 3

IASTAD - Meta-analysis of Workplace Exposure (preferring most recent)
Lifetime/Current Asthma
Adjusted

```
        N      6
        NS     5


        Wt  152.36
 Het Chi  10.23
 Het  df     5
 Het  P     (*)
Fixed RR   1.39
      RRl  1.19
      RRu  1.63
      P    +++
Random RR  1.40
      RRl  1.06
      RRu  1.85
      P      +
Asymm P    N.S.
```

	Sex			
	both	male	female	Total
N	4	1	1	6
NS	4	1	1	5
Wt	148.08	1.68	2.60	152.36
Het Chi	5.99	0.00	0.00	10.23
Het df	3	0	0	5
Het P	N.S.	N.S.	N.S.	(*)
Fixed RR	1.43	0.79	0.43	1.39
RRl	1.22	0.17	0.13	1.19
RRu	1.68	3.59	1.45	1.63
P	+++	N.S.	N.S.	+++
Random RR	1.49	0.79	0.43	1.40
RRl	1.16	0.17	0.13	1.06
RRu	1.92	3.59	1.45	1.85
P	++	N.S.	N.S.	+
Between Chi				4.24
Between df				2
Between P				N.S.

Asthma definition (lifetime/current)			
	lifetime	current	Total
N	1	5	6
NS	1	4	5
Wt	32.57	119.80	152.36
Het Chi	0.00	8.41	10.23
Het df	0	4	5
Het P	N.S.	(*)	(*)
Fixed RR	1.13	1.48	1.39
RRl	0.80	1.23	1.19
RRu	1.59	1.77	1.63
P	N.S.	+++	+++
Random RR	1.13	1.48	1.40
RRl	0.80	1.04	1.06
RRu	1.59	2.11	1.85
P	N.S.	+	+
Between Chi			1.83
Between df			1
Between P			N.S.

Appendix Table F10 - 3

IASTAD - Meta-analysis of Workplace Exposure (preferring most recent)
Lifetime/Current Asthma
Adjusted

| | | Continent | | | |
		NAmer	Europe	Oth/Mult	Total
	N	1	4	1	6
	NS	1	3	1	5
	Wt	80.34	49.96	22.06	152.36
Het	Chi	0.00	7.56	0.00	10.23
Het	df	0	3	0	5
Het	P	N.S.	(*)	N.S.	(*)
Fixed	RR	1.36	1.26	1.90	1.39
	RRl	1.10	0.95	1.25	1.19
	RRu	1.70	1.66	2.88	1.63
	P	++	N.S.	++	+++
Random	RR	1.36	1.16	1.90	1.40
	RRl	1.10	0.66	1.25	1.06
	RRu	1.70	2.07	2.88	1.85
	P	++	N.S.	++	+
Between	Chi				2.67
Between	df				2
Between	P				N.S.

| | | Start year of study | | | |
		<1990	1990-99	unknown	Total
	N	1	3	2	6
	NS	1	3	1	5
	Wt	80.34	67.74	4.29	152.36
Het	Chi	0.00	5.58	0.38	10.23
Het	df	0	2	1	5
Het	P	N.S.	(*)	N.S.	(*)
Fixed	RR	1.36	1.52	0.55	1.39
	RRl	1.10	1.20	0.21	1.19
	RRu	1.70	1.93	1.41	1.63
	P	++	+++	N.S.	+++
Random	RR	1.36	1.61	0.55	1.40
	RRl	1.10	1.07	0.21	1.06
	RRu	1.70	2.43	1.41	1.85
	P	++	+	N.S.	+
Between	Chi				4.28
Between	df				2
Between	P				N.S.

| | | Study type | | | |
		CC	Pr	CS	Total
	N	3		3	6
	NS	2		3	5
	Wt	17.40		134.97	152.36
Het	Chi	6.47		3.57	10.23
Het	df	2		2	5
Het	P	*		N.S.	(*)
Fixed	RR	1.54		1.38	1.39
	RRl	0.96		1.16	1.19
	RRu	2.46		1.63	1.63
	P	(+)		+++	+++
Random	RR	1.02		1.39	1.40
	RRl	0.34		1.09	1.06
	RRu	3.06		1.78	1.85
	P	N.S.		++	+
Between	Chi				0.19
Between	df				1
Between	P				N.S.

Appendix Table F10 - 3

IASTAD - Meta-analysis of Workplace Exposure (preferring most recent)
Lifetime/Current Asthma
Adjusted

Ex smokers

	excluded	included	Total
N	5	1	6
NS	4	1	5
Wt	72.02	80.34	152.36
Het Chi	10.15	0.00	10.23
Het df	4	0	5
Het P	*	N.S.	(*)
Fixed RR	1.43	1.36	1.39
RRl	1.13	1.10	1.19
RRu	1.80	1.70	1.63
P	++	++	+++
Random RR	1.36	1.36	1.40
RRl	0.88	1.10	1.06
RRu	2.10	1.70	1.85
P	N.S.	++	+
Between Chi			0.08
Between df			1
Between P			N.S.

Exposed group : when Exposed

	life	adult	child	current	unspec	Total
N				6		6
NS				5		5
Wt				152.36		152.36
Het Chi				10.23		10.23
Het df				5		5
Het P				(*)		(*)
Fixed RR				1.39		1.39
RRl				1.19		1.19
RRu				1.63		1.63
P				+++		+++
Random RR				1.40		1.40
RRl				1.06		1.06
RRu				1.85		1.85
P				+		+
Between Chi						
Between df						
Between P						N.S.

Appendix Table F10 - 4

IASTAD - Meta-analysis of Workplace Exposure (preferring most recent)
Lifetime/Current Asthma
Unadjusted

REF	NRR	X	SEX	AST	SMOK	AGEL	AGEH	LOC	BEGYR	PUBYR	STTYP	ONS	ADJ	EXPOS	UNEXsrce	EXPOS-time	UNEXTI
JAAKK2	4	x	b	c	Never	21	63	Eu:Fin	1997	2003	CC	ons	0	Work	NotWork	current	non
JANSON	3		b	c	<1yr	20	48	multi	1990	2001	CS	prv	10	Work	NotWork	current	non
LARSS2	4		b	l	Never	15	64	Eu:Est	1995	2003	CS	prv	5	Work	NotWork	current	non
NHANES	2		b	c	Non	17	99	US:nat	1988	2002	CS	prv	0	Work	NotWork	current	non
ORYSZC	3		m	c	NevReg	25	54	Eu:Fra	*	2000	CC	prv	0	Work	NotWork	current	non
ORYSZC	4		f	c	NevReg	25	54	Eu:Fra	*	2000	CC	prv	0	Work	NotWork	current	non

Appendix Table F10 - 5

IASTAD - Meta-analysis of Workplace Exposure (preferring most recent)
Lifetime/Current Asthma
Unadjusted

```
                              Numbers
                              Numbers exposed Non-exposed
REF     NRR     SEX ADJ       Case    Cont   Case   Cont    RR        95.00%CI
JAAKK2  4       b   0          34      41    184    415    1.87 ( 1.15-  3.04)
JANSON  3       b   10          -       -      -      -    1.90 ( 1.25-  2.88)
LARSS2  4       b   5           -       -      -      -    1.13 ( 0.80-  1.59)
NHANES  2       b   0         114    2069    326   8072    1.36 ( 1.10-  1.70)
ORYSZC  3       m   0           3       7     13     24    0.79 ( 0.17-  3.59)
ORYSZC  4       f   0           4      13     30     42    0.43 ( 0.13-  1.45)
Subtotal ORYSZC                                           0.55 ( 0.21-  1.41)
Partial Totals                155    2130    553   8553
*prospective study

REF     NRR     SEX ADJ                Ys      Ws     Qs       Ps

JAAKK2  4       b   0                 0.63   16.22   1.46    0.0117
JANSON  3       b   10                0.64   22.06   2.20    0.0026
LARSS2  4       b   5                 0.12   32.57   1.35    0.4855
NHANES  2       b   0                 0.31   80.34   0.02    0.0054
ORYSZC  3       m   0                -0.23    1.68   0.53    0.7614
ORYSZC  4       f   0                -0.84    2.60   3.55    0.1742
Subtotal ORYSZC                      -1.73    4.29   4.08
```

```
            N        6
            NS       5


           Wt   155.48
      Het Chi    9.11
      Het  df       5
      Het  P      N.S.
     Fixed  RR    1.39
            RRl   1.18
            RRu   1.62
            P     +++
    Random  RR    1.38
            RRl   1.07
            RRu   1.79
            P       +
     Asymm  P     N.S.
```

Appendix Table F10 - 6

IASTAD - Meta-analysis of Workplace Exposure (preferring most recent)
Lifetime/Current Asthma
Unadjusted

```
           N        6
          NS        5


          Wt    155.48
   Het Chi     9.11
   Het  df        5
   Het  P      N.S.
 Fixed  RR     1.39
        RRl     1.18
        RRu     1.62
         P      +++
Random  RR     1.38
        RRl     1.07
        RRu     1.79
         P       +
 Asymm  P      N.S.
```

	Sex			
	both	male	female	Total
N	4	1	1	6
NS	4	1	1	5
Wt	151.19	1.68	2.60	155.48
Het Chi	4.93	0.00	0.00	9.11
Het df	3	0	0	5
Het P	N.S.	N.S.	N.S.	N.S.
Fixed RR	1.42	0.79	0.43	1.39
RRl	1.21	0.17	0.13	1.18
RRu	1.67	3.59	1.45	1.62
P	+++	N.S.	N.S.	+++
Random RR	1.46	0.79	0.43	1.38
RRl	1.17	0.17	0.13	1.07
RRu	1.82	3.59	1.45	1.79
P	+++	N.S.	N.S.	+
Between Chi				4.18
Between df				2
Between P				N.S.

	Asthma definition (lifetime/current)		
	lifetime	current	Total
N	1	5	6
NS	1	4	5
Wt	32.57	122.91	155.48
Het Chi	0.00	7.41	9.11
Het df	0	4	5
Het P	N.S.	N.S.	N.S.
Fixed RR	1.13	1.46	1.39
RRl	0.80	1.23	1.18
RRu	1.59	1.74	1.62
P	N.S.	+++	+++
Random RR	1.13	1.46	1.38
RRl	0.80	1.06	1.07
RRu	1.59	2.01	1.79
P	N.S.	+	+
Between Chi			1.71
Between df			1
Between P			N.S.

Appendix Table F10 - 6

IASTAD - Meta-analysis of Workplace Exposure (preferring most recent)
Lifetime/Current Asthma
Unadjusted

		Continent			
		NAmer	Europe	Oth/Mult	Total
N		1	4	1	6
NS		1	3	1	5
Wt		80.34	53.07	22.06	155.48
Het	Chi	0.00	6.27	0.00	9.11
Het	df	0	3	0	5
Het	P	N.S.	(*)	N.S.	N.S.
Fixed	RR	1.36	1.24	1.90	1.39
	RRl	1.10	0.95	1.25	1.18
	RRu	1.70	1.63	2.88	1.62
	P	++	N.S.	++	+++
Random	RR	1.36	1.16	1.90	1.38
	RRl	1.10	0.71	1.25	1.07
	RRu	1.70	1.90	2.88	1.79
	P	++	N.S.	++	+
Between	Chi				2.84
Between	df				2
Between	P				N.S.

		Start year of study			
		<1990	1990-99	unknown	Total
N		1	3	2	6
NS		1	3	1	5
Wt		80.34	70.85	4.29	155.48
Het	Chi	0.00	4.63	0.38	9.11
Het	df	0	2	1	5
Het	P	N.S.	(*)	N.S.	N.S.
Fixed	RR	1.36	1.49	0.55	1.39
	RRl	1.10	1.18	0.21	1.18
	RRu	1.70	1.88	1.41	1.62
	P	++	+++	N.S.	+++
Random	RR	1.36	1.55	0.55	1.38
	RRl	1.10	1.08	0.21	1.07
	RRu	1.70	2.23	1.41	1.79
	P	++	+	N.S.	+
Between	Chi				4.10
Between	df				2
Between	P				N.S.

		Study type			
		CC	Pr	CS	Total
N		3		3	6
NS		2		3	5
Wt		20.51		134.97	155.48
Het	Chi	5.50		3.57	9.11
Het	df	2		2	5
Het	P	(*)		N.S.	N.S.
Fixed	RR	1.45		1.38	1.39
	RRl	0.94		1.16	1.18
	RRu	2.23		1.63	1.62
	P	(+)		+++	+++
Random	RR	0.99		1.39	1.38
	RRl	0.37		1.09	1.07
	RRu	2.67		1.78	1.79
	P	N.S.		++	+
Between	Chi				0.04
Between	df				1
Between	P				N.S.

Analysis run on 17-MAR-05

Appendix Table F10 - 6

IASTAD - Meta-analysis of Workplace Exposure (preferring most recent)
Lifetime/Current Asthma
Unadjusted

Ex smokers

		excluded	included	Total
	N	5	1	6
	NS	4	1	5
	Wt	75.13	80.34	155.48
Het	Chi	9.08	0.00	9.11
Het	df	4	0	5
Het	P	(*)	N.S.	N.S.
Fixed	RR	1.41	1.36	1.39
	RRl	1.12	1.10	1.18
	RRu	1.77	1.70	1.62
	P	++	++	+++
Random	RR	1.34	1.36	1.38
	RRl	0.90	1.10	1.07
	RRu	2.00	1.70	1.79
	P	N.S.	++	+
Between	Chi			0.04
Between	df			1
Between	P			N.S.

Appendix Table F10 - 7

IASTAD - Meta-analysis of Workplace Exposure (preferring most recent)
Lifetime/Current Asthma
Excluded studies (and stage at which they were excluded)


```
          1       2       3       4       5       6     7      8      9     10    11    12    13    14    15    16

1      BECKE2 JEDRYC LARSS1 MISHRA      NG PILOTT PLATTS RAHERI  THORN
2      ROBBIN
3      KRONQV SAPALD
```

Potentially overlapping studies

```
   REF| REFGP|PRINC|              OVERLAP|
 JANSON JANSON     p       JANSON/RAHERI
```


Adjusted - insufficient data for metaanalysis

```
   REF|NRR|SEX|AST|  SMOK|AGEL|AGEH|   LOC|BEGYR|PUBYR|STTYP|ONS|ADJ|EXPOS|UNEXsrce| EXPOS-time|UNEXTI|      RR|SIG|
 KRONQV  3   b   l  Never   15   65 Eu:Swe 1996  1999    CS prv   4  Work  NotWork    current    non       *    n
 SAPALD  6   b   l <20pks   18   60 Eu:Swi 1991  1994    CS prv   8  Work     None    current    non       *    n
```

_____

Appendix Table G1 -

<u>IASTAD - Meta-analysis of Total/Household/Workplace Exposure : Low Dose</u>
Lifetime/Current Asthma

This analysis is restricted to results for:
1) Total, household (overall) or workplace exposure
2) Results for low amount of exposure
3) Results complete enough for use in metaanalysis

Within each study, results are then selected (in the following order of preference, within each sex) for:
4) ASTHMA : lifetime, current
5) EXPOS   : total, household, workplace
6) MEAS   : number of cigarettes, hours per day (0 indicates <1)
7) For overlapping studies: principal rather than subsidiary studies
Finally for single sex results (m, f) in preference to results for both sexes combined (b).

Results adjusted for the most potential confounders are then chosen in Sections -1 to -3
and results adjusted for the least confounders in Sections -4 to -6. (Those least adjusted results which
actually differ from the most adjusted are marked 'x' in column X in Section -4)

Section -7 shows excluded studies, together with the stage (as above) at which no qualifying results
were found. It then lists the potentially overlapping studies which have been included (1=principal,
2=subsidiary), and any results which would have been included in preference except that they had data
not complete enough for use in metaanalysis. It also lists their significance (yes/no), if known.

Appendix Table G1 - 1

IASTAD - Meta-analysis of Total/Household/Workplace Exposure : Low Dose
Lifetime/Current Asthma
Adjusted

REF	NRR	SEX	AST		SMOK	AGEL	AGEH		LOC	BEGYR	PUBYR	TYP	ONS	ADJ	EXPOS	UNEXsrce	EXPOS-time	UNEXTI	MEAS	LO	HI	
JAAKK2	26	b	c	Never	21	63	Eu:Fin	1997	2003	CC	ons	7	Hh,Wk	None	current	non	cigs	1	9
JANSON	4	b	c	<1yr	20	48	multi	1990	2001	CS	prv	9	Hh,Wk	None	current	non	hours	1	3
LARSS2	1	b	l	Never	15	64	Eu:Est	1995	2003	CS	prv	5	Work	NotWork	current	non	hours	0	0
NG	4	f	c	<1yr	20	74	As:Sin	*	1993	CS	prv	6	Hh	NoHhMemb	lifetime	non	cigs	1	19

Appendix Table G1 - 2

IASTAD - Meta-analysis of Total/Household/Workplace Exposure : Low Dose
Lifetime/Current Asthma
Adjusted

				Numbers						
				Numbers exposed		Non-exposed				
REF	NRR	SEX	ADJ	Case	Cont	Case	Cont	RR	95.00%CI	
JAAKK2	26	b	7	17	-	196	-	2.13 (1.05-	4.30)
JANSON	4	b	9	-	-	-	-	0.99 (0.70-	1.40)
LARSS2	1	b	5	-	-	-	-	0.85 (0.54-	1.34)
NG	4	f	6	7	-	15	-	0.86 (0.34-	2.21)
Partial Totals				24	0	211	0			

*prospective study

REF	NRR	SEX	ADJ	Ys	Ws	Qs	Ps
JAAKK2	26	b	7	0.76	7.73	4.08	0.0355
JANSON	4	b	9	-0.01	31.98	0.05	0.9547
LARSS2	1	b	5	-0.16	18.60	0.68	0.4833
NG	4	f	6	-0.15	4.39	0.14	0.7521

N		4
NS		4
Wt		62.70
Het Chi		4.96
Het df		3
Het P		N.S.
Fixed RR		1.03
RRl		0.80
RRu		1.32
P		N.S.
Random RR		1.07
RRl		0.75
RRu		1.51
P		N.S.
Asymm P		N.S.

Appendix Table G1 - 3

IASTAD - Meta-analysis of Total/Household/Workplace Exposure : Low Dose
Lifetime/Current Asthma
Adjusted

```
          N       4
          NS      4


          Wt     62.70
  Het Chi  4.96
  Het df      3
  Het  P    N.S.
 Fixed RR   1.03
       RRl  0.80
       RRu  1.32
        P   N.S.
Random RR   1.07
       RRl  0.75
       RRu  1.51
        P   N.S.
 Asymm P    N.S.
```

		Sex		
	both	male	female	Total
N	3		1	4
NS	3		1	4
Wt	58.32		4.39	62.70
Het Chi	4.81		0.00	4.96
Het df	2		0	3
Het P	(*)		N.S.	N.S.
Fixed RR	1.04		0.86	1.03
RRl	0.81		0.34	0.80
RRu	1.35		2.19	1.32
P	N.S.		N.S.	N.S.
Random RR	1.12		0.86	1.07
RRl	0.73		0.34	0.75
RRu	1.72		2.19	1.51
P	N.S.		N.S.	N.S.
Between Chi				0.15
Between df				1
Between P				N.S.

	Asthma definition (lifetime/current)		
	lifetime	current	Total
N	1	3	4
NS	1	3	4
Wt	18.60	44.10	62.70
Het Chi	0.00	3.99	4.96
Het df	0	2	3
Het P	N.S.	N.S.	N.S.
Fixed RR	0.85	1.12	1.03
RRl	0.54	0.83	0.80
RRu	1.34	1.50	1.32
P	N.S.	N.S.	N.S.
Random RR	0.85	1.20	1.07
RRl	0.54	0.72	0.75
RRu	1.34	2.01	1.51
P	N.S.	N.S.	N.S.
Between Chi			0.97
Between df			1
Between P			N.S.

Appendix Table G1 - 3

IASTAD - Meta-analysis of Total/Household/Workplace Exposure : Low Dose
Lifetime/Current Asthma
Adjusted

Continent

		NAmer	Europe	Oth/Mult	Total
	N		2	2	4
	NS		2	2	4
	Wt		26.33	36.37	62.70
Het	Chi		4.61	0.08	4.96
Het	df		1	1	3
Het	P		*	N.S.	N.S.
Fixed	RR		1.11	0.97	1.03
	RRl		0.76	0.70	0.80
	RRu		1.63	1.35	1.32
	P		N.S.	N.S.	N.S.
Random	RR		1.29	0.97	1.07
	RRl		0.53	0.70	0.75
	RRu		3.17	1.35	1.51
	P		N.S.	N.S.	N.S.
Between	Chi				0.28
Between	df				1
Between	P				N.S.

Start year of study

		<1990	1990-99	unknown	Total
	N		3	1	4
	NS		3	1	4
	Wt		58.32	4.39	62.70
Het	Chi		4.81	0.00	4.96
Het	df		2	0	3
Het	P		(*)	N.S.	N.S.
Fixed	RR		1.04	0.86	1.03
	RRl		0.81	0.34	0.80
	RRu		1.35	2.19	1.32
	P		N.S.	N.S.	N.S.
Random	RR		1.12	0.86	1.07
	RRl		0.73	0.34	0.75
	RRu		1.72	2.19	1.51
	P		N.S.	N.S.	N.S.
Between	Chi				0.15
Between	df				1
Between	P				N.S.

Study type

		CC	Pr	CS	Total
	N	1		3	4
	NS	1		3	4
	Wt	7.73		54.97	62.70
Het	Chi	0.00		0.30	4.96
Het	df	0		2	3
Het	P	N.S.		N.S.	N.S.
Fixed	RR	2.13		0.93	1.03
	RRl	1.05		0.71	0.80
	RRu	4.31		1.21	1.32
	P	+		N.S.	N.S.
Random	RR	2.13		0.93	1.07
	RRl	1.05		0.71	0.75
	RRu	4.31		1.21	1.51
	P	+		N.S.	N.S.
Between	Chi				4.66
Between	df				1
Between	P				*

Appendix Table G1 - 4

IASTAD - Meta-analysis of Total/Household/Workplace Exposure : Low Dose
Lifetime/Current Asthma
Unadjusted

REF	NRR	X	SEX	AST	SMOK	AGEL	AGEH	LOC	BEGYR	PUBYR	TYP	ONS	ADJ	EXPOS	UNEXsrce	EXPOS-time	UNEXTI	MEAS	LO	HI
JAAKK2	2	x	b	c	Never	21	63	Eu:Fin	1997	2003	CC	ons	0	Hh,Wk	None	current	non	cigs	1	9
JANSON	4		b	c	<1yr	20	48	multi	1990	2001	CS	prv	9	Hh,Wk	None	current	non	hours	1	3
LARSS2	1		b	l	Never	15	64	Eu:Est	1995	2003	CS	prv	5	Work	NotWork	current	non	hours	0	0
NG	1	x	f	c	<1yr	20	74	As:Sin	*	1993	CS	prv	0	Hh	NoHhMemb	lifetime	non	cigs	1	19

_____

Analysis run on 21-MAR-05

Appendix Table G1 - 5

IASTAD - Meta-analysis of Total/Household/Workplace Exposure : Low Dose
Lifetime/Current Asthma
Unadjusted

```
                             Numbers
                             Numbers exposed Non-exposed
REF      NRR      SEX ADJ    Case    Cont    Case    Cont    RR        95.00%CI
JAAKK2 2         b   0       17      22      196     436     1.72 (  0.89-   3.31)
JANSON 4         b   9       -       -       -       -       0.99 (  0.70-   1.40)
LARSS2 1         b   5       -       -       -       -       0.85 (  0.54-   1.34)
NG     1         f   0       7       337     15      604     0.84 (  0.34-   2.07)
Partial Totals               24      359     211     1040
*prospective study

REF      NRR      SEX ADJ            Ys      Ws      Qs      Ps

JAAKK2 2         b   0               0.54    8.95    2.53    0.1050
JANSON 4         b   9               -0.01   31.98   0.01    0.9547
LARSS2 1         b   5               -0.16   18.60   0.56    0.4833
NG     1         f   0               -0.18   4.67    0.17    0.6995
```

```
                N       4
                NS      4


                Wt      64.21
        Het  Chi        3.26
        Het  df         3
        Het  P          N.S.
       Fixed RR         1.01
             RRl        0.79
             RRu        1.29
             P          N.S.
      Random RR         1.01
             RRl        0.78
             RRu        1.32
             P          N.S.
       Asymm P          N.S.
```

Appendix Table G1 - 6

IASTAD - Meta-analysis of Total/Household/Workplace Exposure : Low Dose
Lifetime/Current Asthma
Unadjusted

N	4
NS	4
Wt	64.21
Het Chi	3.26
Het df	3
Het P	N.S.
Fixed RR	1.01
RRl	0.79
RRu	1.29
P	N.S.
Random RR	1.01
RRl	0.78
RRu	1.32
P	N.S.
Asymm P	N.S.

Sex

	both	male	female	Total
N	3		1	4
NS	3		1	4
Wt	59.54		4.67	64.21
Het Chi	3.08		0.00	3.26
Het df	2		0	3
Het P	N.S.		N.S.	N.S.
Fixed RR	1.03		0.84	1.01
RRl	0.80		0.34	0.79
RRu	1.32		2.07	1.29
P	N.S.		N.S.	N.S.
Random RR	1.05		0.84	1.01
RRl	0.75		0.34	0.78
RRu	1.46		2.07	1.32
P	N.S.		N.S.	N.S.
Between Chi				0.18
Between df				1
Between P				N.S.

Asthma definition (lifetime/current)

	lifetime	current	Total
N	1	3	4
NS	1	3	4
Wt	18.60	45.61	64.21
Het Chi	0.00	2.48	3.26
Het df	0	2	3
Het P	N.S.	N.S.	N.S.
Fixed RR	0.85	1.08	1.01
RRl	0.54	0.81	0.79
RRu	1.34	1.45	1.29
P	N.S.	N.S.	N.S.
Random RR	0.85	1.11	1.01
RRl	0.54	0.78	0.78
RRu	1.34	1.58	1.32
P	N.S.	N.S.	N.S.
Between Chi			0.78
Between df			1
Between P			N.S.

Appendix Table G1 - 6

IASTAD - Meta-analysis of Total/Household/Workplace Exposure : Low Dose
Lifetime/Current Asthma
Unadjusted

		Continent			
	NAmer	Europe	Oth/Mult	Total
N		2	2	4
NS		2	2	4
Wt		27.56	36.65	64.21
Het Chi		3.00	0.12	3.26
Het df		1	1	3
Het P		(*)	N.S.	N.S.
Fixed RR		1.07	0.97	1.01
RRl		0.74	0.70	0.79
RRu		1.55	1.34	1.29
P		N.S.	N.S.	N.S.
Random RR		1.16	0.97	1.01
RRl		0.58	0.70	0.78
RRu		2.30	1.34	1.32
P		N.S.	N.S.	N.S.
Between Chi				0.15
Between df				1
Between P				N.S.

	Start year of study			
	<1990	1990-99	unknown	Total
N		3	1	4
NS		3	1	4
Wt		59.54	4.67	64.21
Het Chi		3.08	0.00	3.26
Het df		2	0	3
Het P		N.S.	N.S.	N.S.
Fixed RR		1.03	0.84	1.01
RRl		0.80	0.34	0.79
RRu		1.32	2.07	1.29
P		N.S.	N.S.	N.S.
Random RR		1.05	0.84	1.01
RRl		0.75	0.34	0.78
RRu		1.46	2.07	1.32
P		N.S.	N.S.	N.S.
Between Chi				0.18
Between df				1
Between P				N.S.

	Study type			
	CC	Pr	CS	Total
N	1		3	4
NS	1		3	4
Wt	8.95		55.25	64.21
Het Chi	0.00		0.33	3.26
Het df	0		2	3
Het P	N.S.		N.S.	N.S.
Fixed RR	1.72		0.93	1.01
RRl	0.89		0.71	0.79
RRu	3.31		1.21	1.29
P	N.S.		N.S.	N.S.
Random RR	1.72		0.93	1.01
RRl	0.89		0.71	0.78
RRu	3.31		1.21	1.32
P	N.S.		N.S.	N.S.
Between Chi				2.94
Between df				1
Between P				(*)

Analysis run on 21-MAR-05

Appendix Table G1 - 7

IASTAD - Meta-analysis of Total/Household/Workplace Exposure : Low Dose
Lifetime/Current Asthma
Excluded studies (and stage at which they were excluded)


```
       1       2       3       4       5       6       7       8       9      10      11      12      13      14      15      16

2    BECKE2 JEDRYC KRONQV LARSS1 MISHRA NHANES ORYSZC PILOTT PLATTS RAHERI ROBBIN SAPALD  THORN
                                          Potentially overlapping studies
   REF| REFGP|PRINC|            OVERLAP|
JANSON JANSON     p      JANSON/RAHERI
```

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Appendix Table G2 -

IASTAD - Meta-analysis of Total/Household/Workplace Exposure : High Dose
Lifetime/Current Asthma

This analysis is restricted to results for:
1) Total, household (overall) or workplace exposure
2) Results for high amount of exposure
3) Results complete enough for use in metaanalysis

Within each study, results are then selected (in the following order of preference, within each sex) for:
4) ASTHMA : lifetime, current
5) EXPOS   : total, household, workplace
6) MEAS   : number of cigarettes, hours per day (999 indicates no upper limit)
7) For overlapping studies: principal rather than subsidiary studies
Finally for single sex results (m, f) in preference to results for both sexes combined (b).

Results adjusted for the most potential confounders are then chosen in Sections -1 to -3
and results adjusted for the least confounders in Sections -4 to -6. (Those least adjusted results which
actually differ from the most adjusted are marked 'x' in column X in Section -4)

Section -7 shows excluded studies, together with the stage (as above) at which no qualifying results
were found. It then lists the potentially overlapping studies which have been included (1=principal,
2=subsidiary), and any results which would have been included in preference except that they had data
not complete enough for use in metaanalysis. It also lists their significance (yes/no), if known.

Appendix Table G2 - 1

IASTAD - Meta-analysis of Total/Household/Workplace Exposure : High Dose
Lifetime/Current Asthma
Adjusted

REF	NRR	SEX	AST	SMOK	AGEL	AGEH	LOC	BEGYR	PUBYR	TYP	ONS	ADJ	EXPOS	UNEXsrce	EXPOS-time	UNEXTI	MEAS	LO	HI
JAAKK2	27	b	c	Never	21	63	Eu:Fin	1997	2003	CC	ons	7	Hh,Wk	None	current	non	cigs	10	999
JANSON	6	b	c	<1yr	20	48	multi	1990	2001	CS	prv	9	Hh,Wk	None	current	non	hours	8	999
LARSS2	3	b	l	Never	15	64	Eu:Est	1995	2003	CS	prv	5	Work	NotWork	current	non	hours	6	999
NG	5	f	c	<1yr	20	74	As:Sin	*	1993	CS	prv	6	Hh	NoHhMemb	lifetime	non	cigs	20	999

Appendix Table G2 - 2

IASTAD - Meta-analysis of Total/Household/Workplace Exposure : High Dose
Lifetime/Current Asthma
Adjusted

```
                                 Numbers
                                 Numbers exposed Non-exposed
REF     NRR      SEX ADJ         Case    Cont    Case    Cont      RR         95.00%CI
JAAKK2 27        b   7           14      -       196     -         2.14 ( 0.95-  4.82)
JANSON 6         b   9           -       -       -       -         1.39 ( 0.86-  2.25)
LARSS2 3         b   5           -       -       -       -         1.79 ( 1.02-  3.16)
NG     5         f   6           11      -       15      -         1.60 ( 0.69-  3.70)
Partial Totals                   25      0       211     0
*prospective study

REF     NRR      SEX ADJ                 Ys      Ws      Qs        Ps

JAAKK2 27        b   7                    0.76    5.83    0.43      0.0663
JANSON 6         b   9                    0.33    16.61   0.42      0.1795
LARSS2 3         b   5                    0.58    12.02   0.11      0.0436
NG     5         f   6                    0.47    5.45    0.00      0.2726
```

```
                    N       4
                    NS      4


                    Wt      39.90
              Het Chi       0.96
              Het  df       3
              Het  P        N.S.
            Fixed  RR       1.63
                   RRl      1.19
                   RRu      2.22
                   P        ++
            Random RR       1.63
                   RRl      1.19
                   RRu      2.22
                   P        ++
            Asymm  P        N.S.
```

Appendix Table G2 - 3

IASTAD - Meta-analysis of Total/Household/Workplace Exposure : High Dose
Lifetime/Current Asthma
Adjusted

N	4	
NS	4	

Wt	39.90
Het Chi	0.96
Het df	3
Het P	N.S.
Fixed RR	1.63
RRl	1.19
RRu	2.22
P	++
Random RR	1.63
RRl	1.19
RRu	2.22
P	++
Asymm P	N.S.

Sex

	both	male	female	Total
N	3		1	4
NS	3		1	4
Wt	34.46		5.45	39.90
Het Chi	0.96		0.00	0.96
Het df	2		0	3
Het P	N.S.		N.S.	N.S.
Fixed RR	1.63		1.60	1.63
RRl	1.17		0.69	1.19
RRu	2.28		3.71	2.22
P	++		N.S.	++
Random RR	1.63		1.60	1.63
RRl	1.17		0.69	1.19
RRu	2.28		3.71	2.22
P	++		N.S.	++
Between Chi				0.00
Between df				1
Between P				N.S.

Asthma definition (lifetime/current)

	lifetime	current	Total
N	1	3	4
NS	1	3	4
Wt	12.02	27.89	39.90
Het Chi	0.00	0.81	0.96
Het df	0	2	3
Het P	N.S.	N.S.	N.S.
Fixed RR	1.79	1.56	1.63
RRl	1.02	1.08	1.19
RRu	3.15	2.27	2.22
P	+	+	++
Random RR	1.79	1.56	1.63
RRl	1.02	1.08	1.19
RRu	3.15	2.27	2.22
P	+	+	++
Between Chi			0.15
Between df			1
Between P			N.S.

Appendix Table G2 - 3

IASTAD - Meta-analysis of Total/Household/Workplace Exposure : High Dose
Lifetime/Current Asthma
Adjusted

	Continent			
	NAmer	Europe	Oth/Mult	Total
N		2	2	4
NS		2	2	4
Wt		17.84	22.06	39.90
Het Chi		0.13	0.08	0.96
Het df		1	1	3
Het P		N.S.	N.S.	N.S.
Fixed RR		1.90	1.44	1.63
RRl		1.19	0.95	1.19
RRu		3.02	2.18	2.22
P		++	(+)	++
Random RR		1.90	1.44	1.63
RRl		1.19	0.95	1.19
RRu		3.02	2.18	2.22
P		++	(+)	++
Between Chi				0.75
Between df				1
Between P				N.S.

	Start year of study			
	<1990	1990-99	unknown	Total
N		3	1	4
NS		3	1	4
Wt		34.46	5.45	39.90
Het Chi		0.96	0.00	0.96
Het df		2	0	3
Het P		N.S.	N.S.	N.S.
Fixed RR		1.63	1.60	1.63
RRl		1.17	0.69	1.19
RRu		2.28	3.71	2.22
P		++	N.S.	++
Random RR		1.63	1.60	1.63
RRl		1.17	0.69	1.19
RRu		2.28	3.71	2.22
P		++	N.S.	++
Between Chi				0.00
Between df				1
Between P				N.S.

	Study type			
	CC	Pr	CS	Total
N	1		3	4
NS	1		3	4
Wt	5.83		34.08	39.90
Het Chi	0.00		0.45	0.96
Het df	0		2	3
Het P	N.S.		N.S.	N.S.
Fixed RR	2.14		1.55	1.63
RRl	0.95		1.11	1.19
RRu	4.82		2.17	2.22
P	(+)		+	++
Random RR	2.14		1.55	1.63
RRl	0.95		1.11	1.19
RRu	4.82		2.17	2.22
P	(+)		+	++
Between Chi				0.51
Between df				1
Between P				N.S.

Appendix Table G2 - 4

IASTAD - Meta-analysis of Total/Household/Workplace Exposure : High Dose
Lifetime/Current Asthma
Unadjusted

REF	NRR	X	SEX	AST	SMOK	AGEL	AGEH	LOC	BEGYR	PUBYR	TYP	ONS	ADJ	EXPOS	UNEXsrce	EXPOS-time	UNEXTI	MEAS	LO	HI
JAAKK2	3	x	b	c	Never	21	63	Eu:Fin	1997	2003	CC	ons	0	Hh,Wk	None	current	non	cigs	10	999
JANSON	6		b	c	<1yr	20	48	multi	1990	2001	CS	prv	9	Hh,Wk	None	current	non	hours	8	999
LARSS2	3		b	l	Never	15	64	Eu:Est	1995	2003	CS	prv	5	Work	NotWork	current	non	hours	6	999
NG	2	x	f	c	<1yr	20	74	As:Sin	*	1993	CS	prv	0	Hh	NoHhMemb	lifetime	non	cigs	20	999

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Analysis run on 21-MAR-05

Appendix Table G2 - 5

IASTAD - Meta-analysis of Total/Household/Workplace Exposure : High Dose
Lifetime/Current Asthma
Unadjusted

```
                                  Numbers
                                  Numbers exposed Non-exposed
REF      NRR      SEX ADJ         Case    Cont    Case    Cont     RR        95.00%CI
JAAKK2 3          b   0           14      17      196     436      1.83 (  0.89-   3.79)
JANSON 6          b   9           -       -       -       -        1.39 (  0.86-   2.25)
LARSS2 3          b   5           -       -       -       -        1.79 (  1.02-   3.16)
NG     2          f   0           11      308     15      604      1.44 (  0.65-   3.17)
Partial Totals                    25      325     211     1040
*prospective study

REF      NRR      SEX ADJ                 Ys      Ws      Qs       Ps

JAAKK2 3          b   0                   0.61    7.26    0.17     0.1027
JANSON 6          b   9                   0.33    16.61   0.26     0.1795
LARSS2 3          b   5                   0.58    12.02   0.20     0.0436
NG     2          f   0                   0.36    6.15    0.05     0.3674
```

```
              N       4
              NS      4


              Wt    42.05
         Het Chi    0.67
         Het  df       3
         Het  P     N.S.
       Fixed  RR    1.58
              RRl   1.16
              RRu   2.13
               P      ++
      Random  RR    1.58
              RRl   1.16
              RRu   2.13
               P      ++
       Asymm  P     N.S.
```

Appendix Table G2 - 6

IASTAD - Meta-analysis of Total/Household/Workplace Exposure : High Dose
Lifetime/Current Asthma
Unadjusted

N	4
NS	4

Wt	42.05
Het Chi	0.67
Het df	3
Het P	N.S.
Fixed RR	1.58
RRl	1.16
RRu	2.13
P	++
Random RR	1.58
RRl	1.16
RRu	2.13
P	++
Asymm P	N.S.

	Sex			
	both	male	female	Total
N	3		1	4
NS	3		1	4
Wt	35.89		6.15	42.05
Het Chi	0.61		0.00	0.67
Het df	2		0	3
Het P	N.S.		N.S.	N.S.
Fixed RR	1.60		1.44	1.58
RRl	1.15		0.65	1.16
RRu	2.22		3.17	2.13
P	++		N.S.	++
Random RR	1.60		1.44	1.58
RRl	1.15		0.65	1.16
RRu	2.22		3.17	2.13
P	++		N.S.	++
Between Chi				0.06
Between df				1
Between P				N.S.

	Asthma definition (lifetime/current)		
	lifetime	current	Total
N	1	3	4
NS	1	3	4
Wt	12.02	30.03	42.05
Het Chi	0.00	0.40	0.67
Het df	0	2	3
Het P	N.S.	N.S.	N.S.
Fixed RR	1.79	1.50	1.58
RRl	1.02	1.05	1.16
RRu	3.15	2.14	2.13
P	+	+	++
Random RR	1.79	1.50	1.58
RRl	1.02	1.05	1.16
RRu	3.15	2.14	2.13
P	+	+	++
Between Chi			0.28
Between df			1
Between P			N.S.

Appendix Table G2 - 6

IASTAD - Meta-analysis of Total/Household/Workplace Exposure : High Dose
Lifetime/Current Asthma
Unadjusted

| | Continent | | | |
	NAmer	Europe	Oth/Mult	Total
N		2	2	4
NS		2	2	4
Wt		19.28	22.77	42.05
Het Chi		0.00	0.01	0.67
Het df		1	1	3
Het P		N.S.	N.S.	N.S.
Fixed RR		1.81	1.40	1.58
RRl		1.16	0.93	1.16
RRu		2.82	2.12	2.13
P		++	N.S.	++
Random RR		1.81	1.40	1.58
RRl		1.16	0.93	1.16
RRu		2.82	2.12	2.13
P		++	N.S.	++
Between Chi				0.67
Between df				1
Between P				N.S.

| | Start year of study | | | |
	<1990	1990-99	unknown	Total
N		3	1	4
NS		3	1	4
Wt		35.89	6.15	42.05
Het Chi		0.61	0.00	0.67
Het df		2	0	3
Het P		N.S.	N.S.	N.S.
Fixed RR		1.60	1.44	1.58
RRl		1.15	0.65	1.16
RRu		2.22	3.17	2.13
P		++	N.S.	++
Random RR		1.60	1.44	1.58
RRl		1.15	0.65	1.16
RRu		2.22	3.17	2.13
P		++	N.S.	++
Between Chi				0.06
Between df				1
Between P				N.S.

| | Study type | | | |
	CC	Pr	CS	Total
N	1		3	4
NS	1		3	4
Wt	7.26		34.78	42.05
Het Chi	0.00		0.47	0.67
Het df	0		2	3
Het P	N.S.		N.S.	N.S.
Fixed RR	1.83		1.53	1.58
RRl	0.89		1.09	1.16
RRu	3.79		2.13	2.13
P	N.S.		+	++
Random RR	1.83		1.53	1.58
RRl	0.89		1.09	1.16
RRu	3.79		2.13	2.13
P	N.S.		+	++
Between Chi				0.20
Between df				1
Between P				N.S.

Appendix Table G2 - 7

IASTAD - Meta-analysis of Total/Household/Workplace Exposure : High Dose
Lifetime/Current Asthma
Excluded studies (and stage at which they were excluded)

```
       1      2      3      4      5      6      7      8      9     10     11     12     13     14     15     16

2    BECKE2 JEDRYC KRONQV LARSS1 MISHRA NHANES ORYSZC PILOTT PLATTS RAHERI ROBBIN SAPALD  THORN
                            Potentially overlapping studies
    REF| REFGP|PRINC|           OVERLAP|
 JANSON JANSON     p      JANSON/RAHERI
```

_____

Appendix Table G3 -

IASTAD - Meta-analysis of Household Exposure : Low Dose
Lifetime/Current Asthma

This analysis is restricted to results for:
1) Household (overall) exposure
2) Results for low amount of exposure
3) Results complete enough for use in metaanalysis

Within each study, results are then selected (in the following order of preference, within each sex) for:
4) ASTHMA : lifetime, current
5) MEAS   : number of cigarettes, hours per day
6) For overlapping studies: principal rather than subsidiary studies
Finally for single sex results (m, f) in preference to results for both sexes combined (b).

Results adjusted for the most potential confounders are then chosen in Sections -1 to -3
(and those which actually differ from the adjusted results in Appendix Table G1 - 1 are marked 'x' in Section -1)
and results adjusted for the least confounders in Sections -4 to -6. (Those least adjusted results which
actually differ from the most adjusted are marked 'x' in column X in Section -4)

Appendix Table G3 - 1

IASTAD - Meta-analysis of Household Exposure : Low Dose
Lifetime/Current Asthma
Adjusted

REF	NRR	CompG1	SEX	AST	SMOK	AGEL	AGEH	LOC	BEGYR	PUBYR	TYP	ONS	ADJ	EXPOS	UNEXsrce	EXPOS-time	UNEXTI	MEAS	LO	HI
JAAKK2	32	x	b	c	Never	21	63	Eu:Fin	1997	2003	CC	ons	8	Hh	NoHhMemb	current	non	cigs	1	9
NG	4		f	c	<1yr	20	74	As:Sin	*	1993	CS	prv	6	Hh	NoHhMemb	lifetime	non	cigs	1	19

_____

Appendix Table G3 - 2

IASTAD - Meta-analysis of Household Exposure : Low Dose
Lifetime/Current Asthma
Adjusted

```
                              Numbers
                              Numbers exposed Non-exposed
REF     NRR      SEX ADJ      Case    Cont    Case    Cont    RR        95.00%CI
JAAKK2 32        b   8        4       -       224     -       3.93 ( 0.80-  19.40)
NG     4         f   6        7       -       15      -       0.86 ( 0.34-   2.21)
Partial Totals                11      0       239     0
*prospective study

REF     NRR      SEX ADJ              Ys      Ws      Qs      Ps

JAAKK2 32        b   8                1.37    1.51    1.93    0.0924
NG     4         f   6                -0.15   4.39    0.67    0.7521



                    N       2
                    NS      2


                    Wt      5.90
              Het Chi       2.60
              Het  df       1
              Het  P        N.S.
            Fixed  RR       1.27
                   RRl      0.57
                   RRu      2.85
                   P        N.S.
            Random RR       1.59
                   RRl      0.37
                   RRu      6.88
                   P        N.S.
            Asymm  P
```

Appendix Table G3 - 4

IASTAD - Meta-analysis of Household Exposure : Low Dose
Lifetime/Current Asthma
Unadjusted

REF	NRR	X	SEX	AST	SMOK	AGEL	AGEH	LOC	BEGYR	PUBYR	TYP	ONS	ADJ	EXPOS	UNEXsrce	EXPOS-time	UNEXTI	MEAS	LO	HI
JAAKK2	8	x	b	c	Never	21	63	Eu:Fin	1997	2003	CC	ons	0	Hh	NoHhMemb	current	non	cigs	1	9
NG	1	x	f	c	<1yr	20	74	As:Sin	*	1993	CS	prv	0	Hh	NoHhMemb	lifetime	non	cigs	1	19

Appendix Table G3 - 5

IASTAD - Meta-analysis of Household Exposure : Low Dose
Lifetime/Current Asthma
Unadjusted

```
                               Numbers
                               Numbers exposed Non-exposed
REF      NRR      SEX ADJ      Case    Cont    Case    Cont     RR         95.00%CI
JAAKK2 8          b   0          4       3     224     475     2.83 (  0.63-  12.74)
NG     1          f   0          7     337      15     604     0.84 (  0.34-   2.07)
Totals                          11     340     239    1079
*prospective study

REF      NRR      SEX ADJ               Ys      Ws      Qs      Ps

JAAKK2 8          b   0                1.04    1.70    1.35    0.1760
NG     1          f   0               -0.18    4.67    0.49    0.6995
```

```
              N       2
              NS      2


              Wt      6.36
      Het Chi        1.85
      Het  df           1
      Het  P         N.S.
    Fixed  RR        1.16
           RRl       0.53
           RRu       2.52
             P       N.S.
   Random  RR        1.32
           RRl       0.42
           RRu       4.18
             P       N.S.
    Asymm  P
```

Appendix Table G4 -

IASTAD - Meta-analysis of Household Exposure : High Dose
Lifetime/Current Asthma

This analysis is restricted to results for:
1) Household (overall) exposure
2) Results for high amount of exposure
3) Results complete enough for use in metaanalysis

Within each study, results are then selected (in the following order of preference, within each sex) for:
4) ASTHMA : lifetime, current
5) MEAS   : number of cigarettes, hours per day (999 indicates no upper limit)
6) For overlapping studies: principal rather than subsidiary studies
Finally for single sex results (m, f) in preference to results for both sexes combined (b).

Results adjusted for the most potential confounders are then chosen in Sections -1 to -3
(and those which actually differ from the adjusted results in Appendix Table G2 - 1 are marked 'x' in Section -1)
and results adjusted for the least confounders in Sections -4 to -6. (Those least adjusted results which
actually differ from the most adjusted are marked 'x' in column X in Section -4)

Appendix Table G4 - 1

IASTAD - Meta-analysis of Household Exposure : High Dose
Lifetime/Current Asthma
Adjusted

REF	NRR	CompG2	SEX	AST	SMOK	AGEL	AGEH	LOC	BEGYR	PUBYR	TYP	ONS	ADJ	EXPOS	UNEXsrce	EXPOS-time	UNEXTI	MEAS	LO	HI
JAAKK2	33		x	b	c	Never	21	63	Eu:Fin	1997	2003	CC	ons	8	Hh	NoHhMemb	current	non	cigs	10	999
NG	5			f	c	<1yr	20	74	As:Sin	*	1993	CS	prv	6	Hh	NoHhMemb	lifetime	non	cigs	20	999

_____

Appendix Table G4 - 2

IASTAD - Meta-analysis of Household Exposure : High Dose
Lifetime/Current Asthma
Adjusted

```
                                     Numbers
                                     Numbers exposed Non-exposed
REF      NRR      SEX ADJ            Case    Cont    Case    Cont     RR          95.00%CI
JAAKK2 33         b   8               2       -      224      -      0.75 ( 0.13-   4.29)
NG       5        f   6              11       -       15      -      1.60 ( 0.69-   3.70)
Partial Totals                       13       0      239      0
*prospective study

REF      NRR      SEX ADJ                    Ys      Ws      Qs      Ps

JAAKK2 33         b   8              -0.29    1.26    0.48    0.7471
NG       5        f   6               0.47    5.45    0.11    0.2726
```

```
                    N      2
                    NS     2


                    Wt     6.71
              Het Chi      0.59
              Het  df      1
              Het  P       N.S.
              Fixed RR     1.39
                    RRl    0.65
                    RRu    2.96
                    P      N.S.
              Random RR    1.39
                    RRl    0.65
                    RRu    2.96
                    P      N.S.
              Asymm  P
```

Appendix Table G4 - 4

IASTAD - Meta-analysis of Household Exposure : High Dose
Lifetime/Current Asthma
Unadjusted

REF	NRR	X	SEX	AST		SMOK	AGEL	AGEH		LOC	BEGYR	PUBYR	TYP	ONS	ADJ	EXPOS	UNEXsrce	EXPOS-time	UNEXTI	MEAS	LO	HI	
JAAKK2	9	x	b	c	Never	21	63	Eu:Fin	1997	2003	CC	ons	0	Hh	NoHhMemb	current	non	cigs	10	999		
NG	2	x	f	c	<1yr	20	74	As:Sin	*	1993	CS	prv	0	Hh	NoHhMemb	lifetime	non	cigs	20	999		

_____

Appendix Table G4 - 5

IASTAD - Meta-analysis of Household Exposure : High Dose
Lifetime/Current Asthma
Unadjusted

```
                                  Numbers
                                  Numbers exposed Non-exposed
REF     NRR     SEX ADJ           Case    Cont    Case    Cont    RR          95.00%CI
JAAKK2  9       b   0             2       5       224     475     0.85 (  0.16-   4.41)
NG      2       f   0             11      308     15      604     1.44 (  0.65-   3.17)
Totals                           13      313     239     1079
*prospective study

REF     NRR     SEX ADJ                   Ys      Ws      Qs      Ps

JAAKK2  9       b   0                      -0.16   1.42    0.26    0.8447
NG      2       f   0                      0.36    6.15    0.06    0.3674
```

```
                N       2
                NS      2


                Wt      7.57
        Het Chi 0.32
        Het  df    1
        Het  P   N.S.
      Fixed  RR  1.30
             RRl  0.64
             RRu  2.66
               P  N.S.
     Random  RR  1.30
             RRl  0.64
             RRu  2.66
               P  N.S.
      Asymm  P
```

Appendix Table G5 -

IASTAD - Meta-analysis of Workplace Exposure : Low Dose
Lifetime/Current Asthma

This analysis is restricted to results for:
1) Workplace exposure
2) Results for low amount of exposure
3) Results complete enough for use in metaanalysis

Within each study, results are then selected (in the following order of preference, within each sex) for:
4) ASTHMA : lifetime, current
5) MEAS   : number of cigarettes, hours per day (0 indicates <1)
6) For overlapping studies: principal rather than subsidiary studies
Finally for single sex results (m, f) in preference to results for both sexes combined (b).

Results adjusted for the most potential confounders are then chosen in Sections -1 to -3
(and those which actually differ from the adjusted results in Appendix Table G1 - 1 are marked 'x' in Section -1)
and results adjusted for the least confounders in Sections -4 to -6. (Those least adjusted results which
actually differ from the most adjusted are marked 'x' in column X in Section -4)

_____

Appendix Table G5 - 1

IASTAD - Meta-analysis of Workplace Exposure : Low Dose
Lifetime/Current Asthma
Adjusted

REF	NRR	CompG1	SEX	AST	SMOK	AGEL	AGEH	LOC	BEGYR	PUBYR	TYP	ONS	ADJ	EXPOS	UNEXsrce	EXPOS-time	UNEXTI	MEAS	LO	HI
JAAKK2	29	x	b	c	Never	21	63	Eu:Fin	1997	2003	CC	ons	8	Work	NotWork	current	non	cigs	1	9
LARSS2	1		b	l	Never	15	64	Eu:Est	1995	2003	CS	prv	5	Work	NotWork	current	non	hours	0	0

Appendix Table G5 - 2

IASTAD - Meta-analysis of Workplace Exposure : Low Dose
Lifetime/Current Asthma
Adjusted


```
                                Numbers
                                Numbers exposed Non-exposed
REF     NRR      SEX ADJ        Case    Cont    Case    Cont      RR        95.00%CI
JAAKK2  29       b   8          15      -       184     -         2.06 (  0.97-   4.36)
LARSS2  1        b   5          -       -       -       -         0.85 (  0.54-   1.34)
Partial Totals                  15      0       184     0
*prospective study

REF     NRR      SEX ADJ                Ys      Ws      Qs        Ps

JAAKK2  29       b   8                  0.72    6.80    2.86      0.0594
LARSS2  1        b   5                 -0.16   18.60    1.05      0.4833
```

```
                  N       2
                  NS      2


                  Wt    25.40
            Het Chi      3.90
            Het  df         1
            Het  P          *
          Fixed  RR      1.08
                 RRl     0.73
                 RRu     1.59
                 P      N.S.
          Random  RR     1.26
                 RRl     0.53
                 RRu     2.97
                 P      N.S.
          Asymm  P
```

Appendix Table G5 - 4

IASTAD - Meta-analysis of Workplace Exposure : Low Dose
Lifetime/Current Asthma
Unadjusted

REF	NRR	X	SEX	AST	SMOK	AGEL	AGEH	LOC	BEGYR	PUBYR	TYP	ONS	ADJ	EXPOS	UNEXsrce	EXPOS-time	UNEXTI	MEAS	LO	HI
JAAKK2	5	x	b	c	Never	21	63	Eu:Fin	1997	2003	CC	ons	0	Work	NotWork	current	non	cigs	1	9
LARSS2	1		b	l	Never	15	64	Eu:Est	1995	2003	CS	prv	5	Work	NotWork	current	non	hours	0	0

Appendix Table G5 - 5

IASTAD - Meta-analysis of Workplace Exposure : Low Dose
Lifetime/Current Asthma
Unadjusted

```
                              Numbers
                              Numbers exposed Non-exposed
REF      NRR      SEX ADJ     Case    Cont    Case    Cont    RR        95.00%CI
JAAKK2 5          b   0        15      19      184     415    1.78 (  0.89-   3.58)
LARSS2 1          b   5         -       -       -       -     0.85 (  0.54-   1.34)
Partial Totals                 15      19      184     415
*prospective study

REF      NRR      SEX ADJ            Ys      Ws      Qs      Ps

JAAKK2 5          b   0             0.58    7.87    2.12    0.1056
LARSS2 1          b   5            -0.16   18.60    0.90    0.4833
```

```
                N        2
               NS        2


               Wt    26.47
          Het Chi     3.02
          Het  df        1
          Het  P      (*)
        Fixed  RR     1.06
               RRl    0.72
               RRu    1.55
                P     N.S.
       Random  RR     1.17
               RRl    0.57
               RRu    2.40
                P     N.S.
        Asymm  P
```

Appendix Table G6 -

IASTAD - Meta-analysis of Workplace Exposure : High Dose
Lifetime/Current Asthma

This analysis is restricted to results for:
1) Workplace exposure
2) Results for high amount of exposure
3) Results complete enough for use in metaanalysis

Within each study, results are then selected (in the following order of preference, within each sex) for:
4) ASTHMA : lifetime, current
5) MEAS   : number of cigarettes, hours per day (999 indicates no upper limit)
6) For overlapping studies: principal rather than subsidiary studies
Finally for single sex results (m, f) in preference to results for both sexes combined (b).

Results adjusted for the most potential confounders are then chosen in Sections -1 to -3
(and those which actually differ from the adjusted results in Appendix Table G2 - 1 are marked 'x' in Section -1)
and results adjusted for the least confounders in Sections -4 to -6. (Those least adjusted results which
actually differ from the most adjusted are marked 'x' in column X in Section -4)

_____

Appendix Table G6 - 1

IASTAD - Meta-analysis of Workplace Exposure : High Dose
Lifetime/Current Asthma
Adjusted

REF	NRR	CompG2	SEX	AST	SMOK	AGEL	AGEH	LOC	BEGYR	PUBYR	TYP	ONS	ADJ	EXPOS	UNEXsrce	EXPOS-time	UNEXTI	MEAS	LO	HI
JAAKK2	30	x	b	c	Never	21	63	Eu:Fin	1997	2003	CC	ons	8	Work	NotWork	current	non	cigs	10	999
LARSS2	3		b	l	Never	15	64	Eu:Est	1995	2003	CS	prv	5	Work	NotWork	current	non	hours	6	999

_____

Appendix Table G6 - 2

IASTAD - Meta-analysis of Workplace Exposure : High Dose
Lifetime/Current Asthma
Adjusted

```
                                Numbers
                                Numbers exposed Non-exposed
REF      NRR      SEX ADJ        Case    Cont    Case    Cont    RR         95.00%CI
JAAKK2 30         b   8          12      -       184     -       2.90 (  1.14-   7.34)
LARSS2 3          b   5          -       -       -       -       1.79 (  1.02-   3.16)
Partial Totals                   12      0       184     0
*prospective study

REF      NRR      SEX ADJ               Ys      Ws      Qs      Ps

JAAKK2 30         b   8                 1.06    4.43    0.55    0.0250
LARSS2 3          b   5                 0.58    12.02   0.20    0.0436
```

```
                N      2
                NS     2


                Wt     16.45
            Het Chi    0.75
            Het  df    1
            Het  P     N.S.
         Fixed  RR     2.04
                RRl    1.26
                RRu    3.31
                P      ++
        Random  RR     2.04
                RRl    1.26
                RRu    3.31
                P      ++
         Asymm  P
```

Appendix Table G6 - 4

IASTAD - Meta-analysis of Workplace Exposure : High Dose
Lifetime/Current Asthma
Unadjusted


```
  REF|NRR|X|SEX|AST|  SMOK|AGEL|AGEH|   LOC|BEGYR|PUBYR|TYP|ONS|ADJ|EXPOS|UNEXsrce|EXPOS-time|UNEXTI| MEAS| LO| HI|

JAAKK2  6 x  b   c  Never   21   63 Eu:Fin 1997  2003  CC ons   0  Work NotWork    current    non cigs 10 999
LARSS2  3    b   l  Never   15   64 Eu:Est 1995  2003  CS prv   5  Work NotWork    current    non hours  6 999
```

_____

Appendix Table G6 - 5

IASTAD - Meta-analysis of Workplace Exposure : High Dose
Lifetime/Current Asthma
Unadjusted

```
                                  Numbers
                                  Numbers exposed Non-exposed
REF      NRR       SEX ADJ        Case    Cont    Case    Cont    RR         95.00%CI
JAAKK2 6          b   0           12      12      184     415     2.26 ( 0.99-   5.11)
LARSS2 3          b   5           -       -       -       -       1.79 ( 1.02-   3.16)
Partial Totals                    12      12      184     415
*prospective study

REF      NRR       SEX ADJ                Ys      Ws      Qs      Ps

JAAKK2 6          b   0                   0.81    5.73    0.14    0.0515
LARSS2 3          b   5                   0.58    12.02   0.07    0.0436
```

```
              N       2
              NS      2


              Wt    17.75
        Het Chi     0.21
        Het  df       1
        Het  P      N.S.
      Fixed  RR     1.93
             RRl    1.21
             RRu    3.07
              P      ++
     Random  RR     1.93
             RRl    1.21
             RRu    3.07
              P      ++
      Asymm  P
```

Appendix Table G7 -

<u>IASTAD - Meta-analysis of Total/Household/Workplace Exposure : Low Dose</u>
Lifetime/Current Asthma

This analysis is restricted to results for:
1) Total, household (overall) or workplace exposure
2) Results for low amount of exposure
3) Results complete enough for use in metaanalysis

Within each study, results are then selected (in the following order of preference, within each sex) for:
4) ASTHMA : lifetime, current
5) EXPOS   : total, household, workplace
6) MEAS   : pack-years, number of cigarettes, hours per day (0 indicates <1)
7) For overlapping studies: principal rather than subsidiary studies
Finally for single sex results (m, f) in preference to results for both sexes combined (b).

Results adjusted for the most potential confounders are then chosen in Sections -1 to -3
(and those which actually differ from the adjusted results in Appendix Table G1 - 1 are marked 'x' in Section -1)
and results adjusted for the least confounders in Sections -4 to -6. (Those least adjusted results which
actually differ from the most adjusted are marked 'x' in column X in Section -4)

Section -7 shows excluded studies, together with the stage (as above) at which no qualifying results
were found. It then lists the potentially overlapping studies which have been included (1=principal,
2=subsidiary), and any results which would have been included in preference except that they had data
not complete enough for use in metaanalysis. It also lists their significance (yes/no), if known.

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Appendix Table G7 - 1

IASTAD - Meta-analysis of Total/Household/Workplace Exposure : Low Dose
Lifetime/Current Asthma
Adjusted

REF	NRR	CompG1	SEX	AST	SMOK	AGEL	AGEH	LOC	BEGYR	PUBYR	TYP	ONS	ADJ	EXPOS	UNEXsrce	EXPOS-time	UNEXTI	MEAS	LO	HI
JAAKK2	35	x	b	c	Never	21	63	Eu:Fin	1997	2003	CC	ons	7	Hh,Wk	None	lifetime	non	pkyrs	1	49
JANSON	4		b	c	<1yr	20	48	multi	1990	2001	CS	prv	9	Hh,Wk	None	current	non	hours	1	3
LARSS2	1		b	l	Never	15	64	Eu:Est	1995	2003	CS	prv	5	Work	NotWork	current	non	hours	0	0
NG	4		f	c	<1yr	20	74	As:Sin	*	1993	CS	prv	6	Hh	NoHhMemb	lifetime	non	cigs	1	19

Appendix Table G7 - 2

IASTAD - Meta-analysis of Total/Household/Workplace Exposure : Low Dose
Lifetime/Current Asthma
Adjusted

```
                              Numbers
                              Numbers exposed Non-exposed
REF      NRR     SEX ADJ      Case    Cont    Case    Cont    RR        95.00%CI
JAAKK2 35        b   7        26      -       104     -       0.80 (  0.48-   1.36)
JANSON 4         b   9        -       -       -       -       0.99 (  0.70-   1.40)
LARSS2 1         b   5        -       -       -       -       0.85 (  0.54-   1.34)
NG     4         f   6        7       -       15      -       0.86 (  0.34-   2.21)
Partial Totals                33      0       119     0
*prospective study

REF      NRR     SEX ADJ              Ys      Ws      Qs      Ps

JAAKK2 35        b   7                -0.22   14.17   0.20    0.4010
JANSON 4         b   9                -0.01   31.98   0.28    0.9547
LARSS2 1         b   5                -0.16   18.60   0.06    0.4833
NG     4         f   6                -0.15   4.39    0.01    0.7521



                    N       4
                    NS      4


                    Wt    69.14
             Het Chi      0.56
             Het  df         3
             Het  P       N.S.
           Fixed  RR      0.90
                    RRl     0.71
                    RRu     1.14
                    P       N.S.
           Random  RR      0.90
                    RRl     0.71
                    RRu     1.14
                    P       N.S.
           Asymm  P        N.S.
```

Appendix Table G7 - 3

IASTAD - Meta-analysis of Total/Household/Workplace Exposure : Low Dose
Lifetime/Current Asthma
Adjusted

N	4
NS	4
Wt	69.14
Het Chi	0.56
Het df	3
Het P	N.S.
Fixed RR	0.90
RRl	0.71
RRu	1.14
P	N.S.
Random RR	0.90
RRl	0.71
RRu	1.14
P	N.S.
Asymm P	N.S.

Sex

	both	male	female	Total
N	3		1	4
NS	3		1	4
Wt	64.75		4.39	69.14
Het Chi	0.55		0.00	0.56
Het df	2		0	3
Het P	N.S.		N.S.	N.S.
Fixed RR	0.90		0.86	0.90
RRl	0.71		0.34	0.71
RRu	1.15		2.19	1.14
P	N.S.		N.S.	N.S.
Random RR	0.90		0.86	0.90
RRl	0.71		0.34	0.71
RRu	1.15		2.19	1.14
P	N.S.		N.S.	N.S.
Between Chi				0.01
Between df				1
Between P				N.S.

Asthma definition (lifetime/current)

	lifetime	current	Total
N	1	3	4
NS	1	3	4
Wt	18.60	50.53	69.14
Het Chi	0.00	0.47	0.56
Het df	0	2	3
Het P	N.S.	N.S.	N.S.
Fixed RR	0.85	0.92	0.90
RRl	0.54	0.70	0.71
RRu	1.34	1.21	1.14
P	N.S.	N.S.	N.S.
Random RR	0.85	0.92	0.90
RRl	0.54	0.70	0.71
RRu	1.34	1.21	1.14
P	N.S.	N.S.	N.S.
Between Chi			0.09
Between df			1
Between P			N.S.

Appendix Table G7 - 3

IASTAD - Meta-analysis of Total/Household/Workplace Exposure : Low Dose
Lifetime/Current Asthma
Adjusted

		Continent			
		NAmer	Europe	Oth/Mult	Total
N			2	2	4
NS			2	2	4
Wt			32.77	36.37	69.14
Het	Chi		0.03	0.08	0.56
Het	df		1	1	3
Het	P		N.S.	N.S.	N.S.
Fixed	RR		0.83	0.97	0.90
	RRl		0.59	0.70	0.71
	RRu		1.17	1.35	1.14
	P		N.S.	N.S.	N.S.
Random	RR		0.83	0.97	0.90
	RRl		0.59	0.70	0.71
	RRu		1.17	1.35	1.14
	P		N.S.	N.S.	N.S.
Between	Chi				0.45
Between	df				1
Between	P				N.S.

		Start year of study			
		<1990	1990-99	unknown	Total
N			3	1	4
NS			3	1	4
Wt			64.75	4.39	69.14
Het	Chi		0.55	0.00	0.56
Het	df		2	0	3
Het	P		N.S.	N.S.	N.S.
Fixed	RR		0.90	0.86	0.90
	RRl		0.71	0.34	0.71
	RRu		1.15	2.19	1.14
	P		N.S.	N.S.	N.S.
Random	RR		0.90	0.86	0.90
	RRl		0.71	0.34	0.71
	RRu		1.15	2.19	1.14
	P		N.S.	N.S.	N.S.
Between	Chi				0.01
Between	df				1
Between	P				N.S.

		Study type			
		CC	Pr	CS	Total
N		1		3	4
NS		1		3	4
Wt		14.17		54.97	69.14
Het	Chi	0.00		0.30	0.56
Het	df	0		2	3
Het	P	N.S.		N.S.	N.S.
Fixed	RR	0.80		0.93	0.90
	RRl	0.48		0.71	0.71
	RRu	1.35		1.21	1.14
	P	N.S.		N.S.	N.S.
Random	RR	0.80		0.93	0.90
	RRl	0.48		0.71	0.71
	RRu	1.35		1.21	1.14
	P	N.S.		N.S.	N.S.
Between	Chi				0.25
Between	df				1
Between	P				N.S.

Appendix Table G7 - 4

IASTAD - Meta-analysis of Total/Household/Workplace Exposure : Low Dose
Lifetime/Current Asthma
Unadjusted

REF	NRR	X	SEX	AST	SMOK	AGEL	AGEH	LOC	BEGYR	PUBYR	TYP	ONS	ADJ	EXPOS	UNEXsrce	EXPOS-time	UNEXTI	MEAS	LO	HI
JAAKK2	11	x	b	c	Never	21	63	Eu:Fin	1997	2003	CC	ons	0	Hh,Wk	None	lifetime	non	pkyrs	1	49
JANSON	4		b	c	<1yr	20	48	multi	1990	2001	CS	prv	9	Hh,Wk	None	current	non	hours	1	3
LARSS2	1		b	l	Never	15	64	Eu:Est	1995	2003	CS	prv	5	Work	NotWork	current	non	hours	0	0
NG	1	x	f	c	<1yr	20	74	As:Sin	*	1993	CS	prv	0	Hh	NoHhMemb	lifetime	non	cigs	1	19

Appendix Table G7 - 5

IASTAD - Meta-analysis of Total/Household/Workplace Exposure : Low Dose
Lifetime/Current Asthma
Unadjusted

```
                                  Numbers
                                  Numbers exposed Non-exposed
REF       NRR      SEX ADJ        Case   Cont    Case    Cont      RR        95.00%CI
JAAKK2 11          b   0          26     91      104     231     0.63 (  0.39-   1.04)
JANSON 4           b   9          -      -       -       -       0.99 (  0.70-   1.40)
LARSS2 1           b   5          -      -       -       -       0.85 (  0.54-   1.34)
NG     1           f   0          7      337     15      604     0.84 (  0.34-   2.07)
Partial Totals                    33     428     119     835
*prospective study

REF       NRR      SEX ADJ                 Ys      Ws      Qs      Ps

JAAKK2 11          b   0                  -0.45   15.77   1.37    0.0709
JANSON 4           b   9                  -0.01   31.98   0.72    0.9547
LARSS2 1           b   5                  -0.16   18.60   0.00    0.4833
NG     1           f   0                  -0.18   4.67    0.00    0.6995
```

```
                 N      4
                 NS     4


                 Wt    71.03
         Het  Chi      2.09
         Het  df       3
         Het  P        N.S.
       Fixed  RR       0.85
              RRl      0.68
              RRu      1.08
              P        N.S.
      Random  RR       0.85
              RRl      0.68
              RRu      1.08
              P        N.S.
       Asymm  P        N.S.
```

Appendix Table G7 - 6

IASTAD - Meta-analysis of Total/Household/Workplace Exposure : Low Dose
Lifetime/Current Asthma
Unadjusted

N	4	
NS	4	

Wt	71.03	
Het Chi	2.09	
Het df	3	
Het P	N.S.	
Fixed RR	0.85	
RRl	0.68	
RRu	1.08	
P	N.S.	
Random RR	0.85	
RRl	0.68	
RRu	1.08	
P	N.S.	
Asymm P	N.S.	

	Sex		
	both	male	female	Total

	both	male	female	Total
N	3		1	4
NS	3		1	4

	both	male	female	Total
Wt	66.36		4.67	71.03
Het Chi	2.09		0.00	2.09
Het df	2		0	3
Het P	N.S.		N.S.	N.S.
Fixed RR	0.85		0.84	0.85
RRl	0.67		0.34	0.68
RRu	1.09		2.07	1.08
P	N.S.		N.S.	N.S.
Random RR	0.85		0.84	0.85
RRl	0.67		0.34	0.68
RRu	1.09		2.07	1.08
P	N.S.		N.S.	N.S.
Between Chi				0.00
Between df				1
Between P				N.S.

	Asthma definition (lifetime/current)		
	lifetime	current	Total

	lifetime	current	Total
N	1	3	4
NS	1	3	4

	lifetime	current	Total
Wt	18.60	52.43	71.03
Het Chi	0.00	2.09	2.09
Het df	0	2	3
Het P	N.S.	N.S.	N.S.
Fixed RR	0.85	0.85	0.85
RRl	0.54	0.65	0.68
RRu	1.34	1.12	1.08
P	N.S.	N.S.	N.S.
Random RR	0.85	0.85	0.85
RRl	0.54	0.64	0.68
RRu	1.34	1.13	1.08
P	N.S.	N.S.	N.S.
Between Chi			0.00
Between df			1
Between P			N.S.

Appendix Table G7 - 6

IASTAD - Meta-analysis of Total/Household/Workplace Exposure : Low Dose
Lifetime/Current Asthma
Unadjusted

		Continent			
		NAmer	Europe	Oth/Mult	Total
	N		2	2	4
	NS		2	2	4
	Wt		34.38	36.65	71.03
Het	Chi		0.73	0.12	2.09
Het	df		1	1	3
Het	P		N.S.	N.S.	N.S.
Fixed	RR		0.74	0.97	0.85
	RRl		0.53	0.70	0.68
	RRu		1.04	1.34	1.08
	P		(-)	N.S.	N.S.
Random	RR		0.74	0.97	0.85
	RRl		0.53	0.70	0.68
	RRu		1.04	1.34	1.08
	P		(-)	N.S.	N.S.
Between	Chi				1.25
Between	df				1
Between	P				N.S.

		Start year of study			
		<1990	1990-99	unknown	Total
	N		3	1	4
	NS		3	1	4
	Wt		66.36	4.67	71.03
Het	Chi		2.09	0.00	2.09
Het	df		2	0	3
Het	P		N.S.	N.S.	N.S.
Fixed	RR		0.85	0.84	0.85
	RRl		0.67	0.34	0.68
	RRu		1.09	2.07	1.08
	P		N.S.	N.S.	N.S.
Random	RR		0.85	0.84	0.85
	RRl		0.67	0.34	0.68
	RRu		1.09	2.07	1.08
	P		N.S.	N.S.	N.S.
Between	Chi				0.00
Between	df				1
Between	P				N.S.

		Study type			
		CC	Pr	CS	Total
	N	1		3	4
	NS	1		3	4
	Wt	15.77		55.25	71.03
Het	Chi	0.00		0.33	2.09
Het	df	0		2	3
Het	P	N.S.		N.S.	N.S.
Fixed	RR	0.63		0.93	0.85
	RRl	0.39		0.71	0.68
	RRu	1.04		1.21	1.08
	P	(-)		N.S.	N.S.
Random	RR	0.63		0.93	0.85
	RRl	0.39		0.71	0.68
	RRu	1.04		1.21	1.08
	P	(-)		N.S.	N.S.
Between	Chi				1.76
Between	df				1
Between	P				N.S.

Appendix Table G7 - 7

IASTAD - Meta-analysis of Total/Household/Workplace Exposure : Low Dose
Lifetime/Current Asthma
Excluded studies (and stage at which they were excluded)

```
        1       2       3       4       5       6       7       8       9      10      11      12      13      14      15      16

2     BECKE2 JEDRYC KRONQV LARSS1 MISHRA NHANES ORYSZC PILOTT PLATTS RAHERI ROBBIN SAPALD  THORN
                                           Potentially overlapping studies
     REF| REFGP|PRINC|            OVERLAP|
  JANSON JANSON     p     JANSON/RAHERI
```

_____

Appendix Table G8 -

IASTAD - Meta-analysis of Total/Household/Workplace Exposure : High Dose
Lifetime/Current Asthma

This analysis is restricted to results for:
1) Total, household (overall) or workplace exposure
2) Results for high amount of exposure
3) Results complete enough for use in metaanalysis

Within each study, results are then selected (in the following order of preference, within each sex) for:
4) ASTHMA : lifetime, current
5) EXPOS   : total, household, workplace
6) MEAS   : pack-years, number of cigarettes, hours per day (999 indicates no upper limit)
7) For overlapping studies: principal rather than subsidiary studies
Finally for single sex results (m, f) in preference to results for both sexes combined (b).

Results adjusted for the most potential confounders are then chosen in Sections -1 to -3
(and those which actually differ from the adjusted results in Appendix Table G2 - 1 are marked 'x' in Section -1)
and results adjusted for the least confounders in Sections -4 to -6. (Those least adjusted results which
actually differ from the most adjusted are marked 'x' in column X in Section -4)

Section -7 shows excluded studies, together with the stage (as above) at which no qualifying results
were found. It then lists the potentially overlapping studies which have been included (1=principal,
2=subsidiary), and any results which would have been included in preference except that they had data
not complete enough for use in metaanalysis. It also lists their significance (yes/no), if known.

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Appendix Table G8 - 1

IASTAD - Meta-analysis of Total/Household/Workplace Exposure : High Dose
Lifetime/Current Asthma
Adjusted

REF	NRR	CompG2	SEX	AST	SMOK	AGEL	AGEH	LOC	BEGYR	PUBYR	TYP	ONS	ADJ	EXPOS	UNEXsrce	EXPOS-time	UNEXTI	MEAS	LO	HI
JAAKK2	38	x	b	c	Never	21	63	Eu:Fin	1997	2003	CC	ons	7	Hh,Wk	None	lifetime	non	pkyrs	150	999
JANSON	6		b	c	<1yr	20	48	multi	1990	2001	CS	prv	9	Hh,Wk	None	current	non	hours	8	999
LARSS2	3		b	l	Never	15	64	Eu:Est	1995	2003	CS	prv	5	Work	NotWork	current	non	hours	6	999
NG	5		f	c	<1yr	20	74	As:Sin	*	1993	CS	prv	6	Hh	NoHhMemb	lifetime	non	cigs	20	999

Appendix Table G8 - 2

IASTAD - Meta-analysis of Total/Household/Workplace Exposure : High Dose
Lifetime/Current Asthma
Adjusted

```
                                Numbers
                                Numbers exposed Non-exposed
REF      NRR      SEX ADJ       Case    Cont    Case    Cont      RR        95.00%CI
JAAKK2 38         b   7         68      -       104     -        1.84 (  1.21-   2.80)
JANSON 6          b   9         -       -       -       -        1.39 (  0.86-   2.25)
LARSS2 3          b   5         -       -       -       -        1.79 (  1.02-   3.16)
NG     5          f   6         11      -       15      -        1.60 (  0.69-   3.70)
Partial Totals                  79      0       119     0
*prospective study

REF      NRR      SEX ADJ                Ys      Ws      Qs       Ps

JAAKK2 38         b   7                  0.61    21.83   0.23     0.0044
JANSON 6          b   9                  0.33    16.61   0.52     0.1795
LARSS2 3          b   5                  0.58    12.02   0.07     0.0436
NG     5          f   6                  0.47    5.45    0.01     0.2726
```

```
                N     4
                NS    4


             Wt    55.91
        Het Chi   0.83
        Het df       3
        Het P     N.S.
      Fixed RR    1.66
            RRl   1.28
            RRu   2.16
            P     +++
     Random RR    1.66
            RRl   1.28
            RRu   2.16
            P     +++
      Asymm P     N.S.
```

Appendix Table G8 - 3

IASTAD - Meta-analysis of Total/Household/Workplace Exposure : High Dose
Lifetime/Current Asthma
Adjusted

	N	4
	NS	4

	Wt	55.91
Het	Chi	0.83
Het	df	3
Het	P	N.S.
Fixed	RR	1.66
	RRl	1.28
	RRu	2.16
	P	+++
Random	RR	1.66
	RRl	1.28
	RRu	2.16
	P	+++
Asymm	P	N.S.

		Sex		
		both	male female	Total
	N	3	1	4
	NS	3	1	4
	Wt	50.46	5.45	55.91
Het	Chi	0.82	0.00	0.83
Het	df	2	0	3
Het	P	N.S.	N.S.	N.S.
Fixed	RR	1.67	1.60	1.66
	RRl	1.26	0.69	1.28
	RRu	2.20	3.71	2.16
	P	+++	N.S.	+++
Random	RR	1.67	1.60	1.66
	RRl	1.26	0.69	1.28
	RRu	2.20	3.71	2.16
	P	+++	N.S.	+++
Between	Chi			0.01
Between	df			1
Between	P			N.S.

		Asthma definition (lifetime/current)		
		lifetime	current	Total
	N	1	3	4
	NS	1	3	4
	Wt	12.02	43.89	55.91
Het	Chi	0.00	0.74	0.83
Het	df	0	2	3
Het	P	N.S.	N.S.	N.S.
Fixed	RR	1.79	1.63	1.66
	RRl	1.02	1.21	1.28
	RRu	3.15	2.19	2.16
	P	+	++	+++
Random	RR	1.79	1.63	1.66
	RRl	1.02	1.21	1.28
	RRu	3.15	2.19	2.16
	P	+	++	+++
Between	Chi			0.09
Between	df			1
Between	P			N.S.

Appendix Table G8 - 3

<u>IASTAD - Meta-analysis of Total/Household/Workplace Exposure : High Dose</u>
Lifetime/Current Asthma
Adjusted

		<u>Continent</u>		
	NAmer	Europe	Oth/Mult	Total
N		2	2	4
NS		2	2	4
Wt		33.85	22.06	55.91
Het Chi		0.01	0.08	0.83
Het df		1	1	3
Het P		N.S.	N.S.	N.S.
Fixed RR		1.82	1.44	1.66
RRl		1.30	0.95	1.28
RRu		2.55	2.18	2.16
P		+++	(+)	+++
Random RR		1.82	1.44	1.66
RRl		1.30	0.95	1.28
RRu		2.55	2.18	2.16
P		+++	(+)	+++
Between Chi				0.74
Between df				1
Between P				N.S.

		<u>Start year of study</u>		
	<1990	1990-99	unknown	Total
N		3	1	4
NS		3	1	4
Wt		50.46	5.45	55.91
Het Chi		0.82	0.00	0.83
Het df		2	0	3
Het P		N.S.	N.S.	N.S.
Fixed RR		1.67	1.60	1.66
RRl		1.26	0.69	1.28
RRu		2.20	3.71	2.16
P		+++	N.S.	+++
Random RR		1.67	1.60	1.66
RRl		1.26	0.69	1.28
RRu		2.20	3.71	2.16
P		+++	N.S.	+++
Between Chi				0.01
Between df				1
Between P				N.S.

		<u>Study type</u>		
	CC	Pr	CS	Total
N	1		3	4
NS	1		3	4
Wt	21.83		34.08	55.91
Het Chi	0.00		0.45	0.83
Het df	0		2	3
Het P	N.S.		N.S.	N.S.
Fixed RR	1.84		1.55	1.66
RRl	1.21		1.11	1.28
RRu	2.80		2.17	2.16
P	++		+	+++
Random RR	1.84		1.55	1.66
RRl	1.21		1.11	1.28
RRu	2.80		2.17	2.16
P	++		+	+++
Between Chi				0.38
Between df				1
Between P				N.S.

Appendix Table G8 - 4

IASTAD - Meta-analysis of Total/Household/Workplace Exposure : High Dose
Lifetime/Current Asthma
Unadjusted

REF	NRR	X	SEX	AST	SMOK	AGEL	AGEH	LOC	BEGYR	PUBYR	TYP	ONS	ADJ	EXPOS	UNEXsrce	EXPOS-time	UNEXTI	MEAS	LO	HI
JAAKK2	14	x	b	c	Never	21	63	Eu:Fin	1997	2003	CC	ons	0	Hh,Wk	None	lifetime	non	pkyrs	150	999
JANSON	6		b	c	<1yr	20	48	multi	1990	2001	CS	prv	9	Hh,Wk	None	current	non	hours	8	999
LARSS2	3		b	l	Never	15	64	Eu:Est	1995	2003	CS	prv	5	Work	NotWork	current	non	hours	6	999
NG	2	x	f	c	<1yr	20	74	As:Sin	*	1993	CS	prv	0	Hh	NoHhMemb	lifetime	non	cigs	20	999

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Analysis run on 21-MAR-05

Appendix Table G8 - 5

IASTAD - Meta-analysis of Total/Household/Workplace Exposure : High Dose
Lifetime/Current Asthma
Unadjusted

```
                                 Numbers
                                 Numbers exposed Non-exposed
REF      NRR      SEX ADJ        Case    Cont    Case    Cont    RR        95.00%CI
JAAKK2 14        b   0           68      96      104     231     1.57 (  1.07-   2.32)
JANSON 6         b   9           -       -       -       -       1.39 (  0.86-   2.25)
LARSS2 3         b   5           -       -       -       -       1.79 (  1.02-   3.16)
NG     2         f   0           11      308     15      604     1.44 (  0.65-   3.17)
Partial Totals                   79      404     119     835
*prospective study

REF      NRR      SEX ADJ                Ys      Ws      Qs      Ps

JAAKK2 14        b   0                   0.45    25.60   0.01    0.0219
JANSON 6         b   9                   0.33    16.61   0.19    0.1795
LARSS2 3         b   5                   0.58    12.02   0.26    0.0436
NG     2         f   0                   0.36    6.15    0.03    0.3674
```

```
                N      4
                NS     4


               Wt  60.38
          Het Chi   0.49
          Het  df     3
          Het   P   N.S.
        Fixed  RR   1.55
               RRl  1.20
               RRu  1.99
                P   +++
        Random RR   1.55
               RRl  1.20
               RRu  1.99
                P   +++
        Asymm  P   N.S.
```

Appendix Table G8 - 6

IASTAD - Meta-analysis of Total/Household/Workplace Exposure : High Dose
Lifetime/Current Asthma
Unadjusted

N	4	
NS	4	

Wt	60.38
Het Chi	0.49
Het df	3
Het P	N.S.
Fixed RR	1.55
RRl	1.20
RRu	1.99
P	+++
Random RR	1.55
RRl	1.20
RRu	1.99
P	+++
Asymm P	N.S.

Sex

	both	male	female	Total
N	3		1	4
NS	3		1	4
Wt	54.23		6.15	60.38
Het Chi	0.45		0.00	0.49
Het df	2		0	3
Het P	N.S.		N.S.	N.S.
Fixed RR	1.56		1.44	1.55
RRl	1.19		0.65	1.20
RRu	2.03		3.17	1.99
P	++		N.S.	+++
Random RR	1.56		1.44	1.55
RRl	1.19		0.65	1.20
RRu	2.03		3.17	1.99
P	++		N.S.	+++
Between Chi				0.04
Between df				1
Between P				N.S.

Asthma definition (lifetime/current)

	lifetime	current	Total
N	1	3	4
NS	1	3	4
Wt	12.02	48.36	60.38
Het Chi	0.00	0.16	0.49
Het df	0	2	3
Het P	N.S.	N.S.	N.S.
Fixed RR	1.79	1.49	1.55
RRl	1.02	1.12	1.20
RRu	3.15	1.98	1.99
P	+	++	+++
Random RR	1.79	1.49	1.55
RRl	1.02	1.12	1.20
RRu	3.15	1.98	1.99
P	+	++	+++
Between Chi			0.32
Between df			1
Between P			N.S.

Appendix Table G8 - 6

IASTAD - Meta-analysis of Total/Household/Workplace Exposure : High Dose
Lifetime/Current Asthma
Unadjusted

Continent

	NAmer	Europe	Oth/Mult	Total
N		2	2	4
NS		2	2	4
Wt		37.61	22.77	60.38
Het Chi		0.14	0.01	0.49
Het df		1	1	3
Het P		N.S.	N.S.	N.S.
Fixed RR		1.64	1.40	1.55
RRl		1.19	0.93	1.20
RRu		2.26	2.12	1.99
P		++	N.S.	+++
Random RR		1.64	1.40	1.55
RRl		1.19	0.93	1.20
RRu		2.26	2.12	1.99
P		++	N.S.	+++
Between Chi				0.34
Between df				1
Between P				N.S.

Start year of study

	<1990	1990-99	unknown	Total
N		3	1	4
NS		3	1	4
Wt		54.23	6.15	60.38
Het Chi		0.45	0.00	0.49
Het df		2	0	3
Het P		N.S.	N.S.	N.S.
Fixed RR		1.56	1.44	1.55
RRl		1.19	0.65	1.20
RRu		2.03	3.17	1.99
P		++	N.S.	+++
Random RR		1.56	1.44	1.55
RRl		1.19	0.65	1.20
RRu		2.03	3.17	1.99
P		++	N.S.	+++
Between Chi				0.04
Between df				1
Between P				N.S.

Study type

	CC	Pr	CS	Total
N	1		3	4
NS	1		3	4
Wt	25.60		34.78	60.38
Het Chi	0.00		0.47	0.49
Het df	0		2	3
Het P	N.S.		N.S.	N.S.
Fixed RR	1.57		1.53	1.55
RRl	1.07		1.09	1.20
RRu	2.32		2.13	1.99
P	+		+	+++
Random RR	1.57		1.53	1.55
RRl	1.07		1.09	1.20
RRu	2.32		2.13	1.99
P	+		+	+++
Between Chi				0.01
Between df				1
Between P				N.S.

Appendix Table G8 - 7

IASTAD - Meta-analysis of Total/Household/Workplace Exposure : High Dose
Lifetime/Current Asthma
Excluded studies (and stage at which they were excluded)

    1   2   3   4   5   6   7   8   9   10   11   12   13   14   15   16

2   BECKE2 JEDRYC KRONQV LARSS1 MISHRA NHANES ORYSZC PILOTT PLATTS RAHERI ROBBIN SAPALD THORN
                              Potentially overlapping studies
   REF| REFGP|PRINC| OVERLAP|
JANSON JANSON   p   JANSON/RAHERI

Appendix Table G9 -

IASTAD - Meta-analysis of Household Exposure : Low Dose
Lifetime/Current Asthma

This analysis is restricted to results for:
1) Household (overall) exposure
2) Results for low amount of exposure
3) Results complete enough for use in metaanalysis

Within each study, results are then selected (in the following order of preference, within each sex) for:
4) ASTHMA : lifetime, current
5) MEAS   : pack-years, number of cigarettes, hours per day
6) For overlapping studies: principal rather than subsidiary studies
Finally for single sex results (m, f) in preference to results for both sexes combined (b).

Results adjusted for the most potential confounders are then chosen in Sections -1 to -3
(and those which actually differ from the adjusted results in Appendix Table G3 - 1 are marked 'x' in Section -1)
and results adjusted for the least confounders in Sections -4 to -6. (Those least adjusted results which
actually differ from the most adjusted are marked 'x' in column X in Section -4)

Appendix Table G9 - 1

IASTAD - Meta-analysis of Household Exposure : Low Dose
Lifetime/Current Asthma
Adjusted

```
   REF|NRR|CompG3|SEX|AST|  SMOK|AGEL|AGEH|   LOC|BEGYR|PUBYR|TYP|ONS|ADJ|EXPOS|UNEXsrce|EXPOS-time|UNEXTI| MEAS| LO| HI

JAAKK2  45       x   b   c  Never   21   63 Eu:Fin 1997  2003  CC ons  8   Hh NoHhMemb   lifetime    non pkyrs  1  49
   NG    4           f   c  <1yr    20   74 As:Sin    *  1993  CS prv  6   Hh NoHhMemb   lifetime    non cigs   1  19
```

_____

Appendix Table G9 - 2

IASTAD - Meta-analysis of Household Exposure : Low Dose
Lifetime/Current Asthma
Adjusted


```
                              Numbers
                              Numbers exposed Non-exposed
REF      NRR     SEX ADJ      Case    Cont    Case    Cont      RR        95.00%CI
JAAKK2   45      b   8          24     -       140     -      0.95 ( 0.55-  1.64)
NG       4       f   6           7     -        15     -      0.86 ( 0.34-  2.21)
Partial Totals                  31     0       155     0
*prospective study

REF      NRR     SEX ADJ                Ys      Ws      Qs        Ps

JAAKK2   45      b   8                 -0.05   12.87   0.01     0.8540
NG       4       f   6                 -0.15    4.39   0.02     0.7521
```


```
                    N       2
                    NS      2


                    Wt     17.26
               Het Chi      0.03
               Het  df       1
               Het  P       N.S.
             Fixed  RR      0.93
                    RRl     0.58
                    RRu     1.48
                    P       N.S.
            Random  RR      0.93
                    RRl     0.58
                    RRu     1.48
                    P       N.S.
             Asymm  P
```

Appendix Table G9 - 4

IASTAD - Meta-analysis of Household Exposure : Low Dose
Lifetime/Current Asthma
Unadjusted

REF	NRR	X	SEX	AST	SMOK	AGEL	AGEH	LOC	BEGYR	PUBYR	TYP	ONS	ADJ	EXPOS	UNEXsrce	EXPOS-time	UNEXTI	MEAS	LO	HI
JAAKK2	21	x	b	c	Never	21	63	Eu:Fin	1997	2003	CC	ons	0	Hh	NoHhMemb	lifetime	non	pkyrs	1	49
NG	1	x	f	c	<1yr	20	74	As:Sin	*	1993	CS	prv	0	Hh	NoHhMemb	lifetime	non	cigs	1	19

Appendix Table G9 - 5

IASTAD - Meta-analysis of Household Exposure : Low Dose
Lifetime/Current Asthma
Unadjusted


```
                                   Numbers
                                   Numbers exposed Non-exposed
REF      NRR      SEX ADJ          Case    Cont    Case    Cont      RR          95.00%CI
JAAKK2   21       b   0            24      66      140     293       0.76 (  0.46-   1.27)
NG       1        f   0             7     337      15      604       0.84 (  0.34-   2.07)
Totals                            31     403      155     897
*prospective study

REF      NRR      SEX ADJ                  Ys      Ws      Qs      Ps

JAAKK2   21       b   0                   -0.27   14.84    0.01    0.2928
NG       1        f   0                   -0.18    4.67    0.02    0.6995
```


```
                 N        2
                 NS       2


                 Wt      19.51
         Het Chi         0.03
         Het  df          1
         Het  P          N.S.
         Fixed RR        0.78
               RRl       0.50
               RRu       1.21
               P         N.S.
         Random RR       0.78
               RRl       0.50
               RRu       1.21
               P         N.S.
         Asymm  P
```

Appendix Table G10 -

IASTAD - Meta-analysis of Household Exposure : High Dose
Lifetime/Current Asthma

This analysis is restricted to results for:
1) Household (overall) exposure
2) Results for high amount of exposure
3) Results complete enough for use in metaanalysis

Within each study, results are then selected (in the following order of preference, within each sex) for:
4) ASTHMA : lifetime, current
5) MEAS   : pack-years, number of cigarettes, hours per day (999 indicates no upper limit)
6) For overlapping studies: principal rather than subsidiary studies
Finally for single sex results (m, f) in preference to results for both sexes combined (b).

Results adjusted for the most potential confounders are then chosen in Sections -1 to -3
(and those which actually differ from the adjusted results in Appendix Table G4 - 1 are marked 'x' in Section -1)
and results adjusted for the least confounders in Sections -4 to -6. (Those least adjusted results which
actually differ from the most adjusted are marked 'x' in column X in Section -4)

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Appendix Table G10 - 1

IASTAD - Meta-analysis of Household Exposure : High Dose
Lifetime/Current Asthma
Adjusted

REF	NRR	CompG4	SEX	AST	SMOK	AGEL	AGEH	LOC	BEGYR	PUBYR	TYP	ONS	ADJ	EXPOS	UNEXsrce	EXPOS-time	UNEXTI	MEAS	LO	HI
JAAKK2	48	x	b	c	Never	21	63	Eu:Fin	1997	2003	CC	ons	8	Hh	NoHhMemb	lifetime	non	pkyrs	150	999
NG	5		f	c	<1yr	20	74	As:Sin	*	1993	CS	prv	6	Hh	NoHhMemb	lifetime	non	cigs	20	999

Appendix Table G10 - 2

IASTAD - Meta-analysis of Household Exposure : High Dose
Lifetime/Current Asthma
Adjusted

```
                                  Numbers
                                  Numbers exposed Non-exposed
REF     NRR     SEX ADJ           Case    Cont    Case    Cont    RR        95.00%CI
JAAKK2  48      b   8             50      -       140     -       1.37 ( 0.87-  2.16)
NG      5       f   6             11      -       15      -       1.60 ( 0.69-  3.70)
Partial Totals                    61      0       155     0
*prospective study

REF     NRR     SEX ADJ                   Ys      Ws      Qs      Ps

JAAKK2  48      b   8                      0.31    18.58   0.02    0.1748
NG      5       f   6                      0.47    5.45    0.08    0.2726
```

```
                N       2
                NS      2


                Wt      24.03
        Het Chi         0.10
        Het  df         1
        Het  P          N.S.
        Fixed RR        1.42
                RRl     0.95
                RRu     2.12
                P       (+)
        Random RR       1.42
                RRl     0.95
                RRu     2.12
                P       (+)
        Asymm P
```

Appendix Table G10 - 4

IASTAD - Meta-analysis of Household Exposure : High Dose
Lifetime/Current Asthma
Unadjusted

 REF|NRR|X|SEX|AST| SMOK|AGEL|AGEH| LOC|BEGYR|PUBYR|TYP|ONS|ADJ|EXPOS|UNEXsrce|EXPOS-time|UNEXTI| MEAS| LO| HI|

JAAKK2 24 x   b   c Never   21   63 Eu:Fin 1997 2003 CC ons   0   Hh NoHhMemb   lifetime   non pkyrs 150 999
    NG   2 x   f   c <1yr   20   74 As:Sin   * 1993 CS prv   0   Hh NoHhMemb   lifetime   non cigs 20 999

_____
                                                                                         Analysis run on 21-MAR-05

Appendix Table G10 - 5

IASTAD - Meta-analysis of Household Exposure : High Dose
Lifetime/Current Asthma
Unadjusted

```
                              Numbers
                              Numbers exposed Non-exposed
REF     NRR     SEX ADJ       Case    Cont    Case    Cont    RR          95.00%CI
JAAKK2  24      b   0          50      69     140     293     1.52 (  1.00-   2.30)
NG      2       f   0          11     308      15     604     1.44 (  0.65-   3.17)
Totals                         61     377     155     897
*prospective study

REF     NRR     SEX ADJ               Ys      Ws      Qs      Ps

JAAKK2  24      b   0                 0.42   22.20    0.00    0.0498
NG      2       f   0                 0.36    6.15    0.01    0.3674
```

```
                N       2
                NS      2


                Wt     28.35
        Het Chi        0.01
        Het  df           1
        Het  P        N.S.
        Fixed RR       1.50
              RRl      1.04
              RRu      2.17
                P         +
        Random RR      1.50
              RRl      1.04
              RRu      2.17
                P         +
        Asymm  P
```

Appendix Table G11 -

IASTAD - Meta-analysis of Workplace Exposure : Low Dose
Lifetime/Current Asthma

This analysis is restricted to results for:
1) Workplace exposure
2) Results for low amount of exposure
3) Results complete enough for use in metaanalysis

Within each study, results are then selected (in the following order of preference, within each sex) for:
4) ASTHMA : lifetime, current
5) MEAS   : pack-years, number of cigarettes, hours per day (0 indicates <1)
6) For overlapping studies: principal rather than subsidiary studies
Finally for single sex results (m, f) in preference to results for both sexes combined (b).

Results adjusted for the most potential confounders are then chosen in Sections -1 to -3
(and those which actually differ from the adjusted results in Appendix Table G5 - 1 are marked 'x' in Section -1)
and results adjusted for the least confounders in Sections -4 to -6. (Those least adjusted results which
actually differ from the most adjusted are marked 'x' in column X in Section -4)

_____

Appendix Table G11 - 1

IASTAD - Meta-analysis of Workplace Exposure : Low Dose
Lifetime/Current Asthma
Adjusted

REF	NRR	CompG5	SEX	AST	SMOK	AGEL	AGEH	LOC	BEGYR	PUBYR	TYP	ONS	ADJ	EXPOS	UNEXsrce	EXPOS-time	UNEXTI	MEAS	LO	HI
JAAKK2	40	x	b	c	Never	21	63	Eu:Fin	1997	2003	CC	ons	8	Work	NotWork	lifetime	non	pkyrs	1	49
LARSS2	1		b	l	Never	15	64	Eu:Est	1995	2003	CS	prv	5	Work	NotWork	current	non	hours	0	0

_____

Appendix Table G11 - 2

IASTAD - Meta-analysis of Workplace Exposure : Low Dose
Lifetime/Current Asthma
Adjusted

```
                                 Numbers
                                 Numbers exposed Non-exposed
REF      NRR      SEX ADJ        Case     Cont    Case     Cont     RR        95.00%CI
JAAKK2 40         b   8           32       -       163      -       1.17 ( 0.71-  1.93)
LARSS2 1          b   5           -        -       -        -       0.85 ( 0.54-  1.34)
Partial Totals                    32       0       163      0
*prospective study

REF      NRR      SEX ADJ                  Ys       Ws       Qs       Ps

JAAKK2 40         b   8                    0.16     15.37    0.47     0.5383
LARSS2 1          b   5                   -0.16     18.60    0.39     0.4833
```

```
              N        2
              NS       2


              Wt      33.97
       Het Chi        0.86
       Het  df         1
       Het  P         N.S.
       Fixed RR       0.98
             RRl      0.70
             RRu      1.37
              P       N.S.
       Random RR      0.98
             RRl      0.70
             RRu      1.37
              P       N.S.
       Asymm  P
```

Appendix Table G11 - 4

IASTAD - Meta-analysis of Workplace Exposure : Low Dose
Lifetime/Current Asthma
Unadjusted

REF	NRR	X	SEX	AST	SMOK	AGEL	AGEH	LOC	BEGYR	PUBYR	TYP	ONS	ADJ	EXPOS	UNEXsrce	EXPOS-time	UNEXTI	MEAS	LO	HI
JAAKK2	16	x	b	c	Never	21	63	Eu:Fin	1997	2003	CC	ons	0	Work	NotWork	lifetime	non	pkyrs	1	49
LARSS2	1		b	l	Never	15	64	Eu:Est	1995	2003	CS	prv	5	Work	NotWork	current	non	hours	0	0

Appendix Table G11 - 5

IASTAD - Meta-analysis of Workplace Exposure : Low Dose
Lifetime/Current Asthma
Unadjusted

```
                              Numbers
                              Numbers exposed Non-exposed
REF     NRR      SEX ADJ      Case    Cont   Case   Cont     RR        95.00%CI
JAAKK2 16        b   0         32      70    163    355    1.00 ( 0.63-  1.57)
LARSS2 1         b   5          -       -      -      -    0.85 ( 0.54-  1.34)
Partial Totals                 32      70    163    355
*prospective study

REF     NRR      SEX ADJ              Ys      Ws      Qs      Ps

JAAKK2 16        b   0             -0.00   18.35    0.12    0.9850
LARSS2 1         b   5             -0.16   18.60    0.11    0.4833



                    N       2
                    NS      2


                    Wt     36.96
              Het Chi      0.23
              Het  df       1
              Het  P       N.S.
            Fixed  RR      0.92
                   RRl     0.67
                   RRu     1.27
                    P      N.S.
            Random RR      0.92
                   RRl     0.67
                   RRu     1.27
                    P      N.S.
            Asymm  P
```

Appendix Table G12 -

IASTAD - Meta-analysis of Workplace Exposure : High Dose
Lifetime/Current Asthma

This analysis is restricted to results for:
1) Workplace exposure
2) Results for high amount of exposure
3) Results complete enough for use in metaanalysis

Within each study, results are then selected (in the following order of preference, within each sex) for:
4) ASTHMA : lifetime, current
5) MEAS   : pack-years, number of cigarettes, hours per day (999 indicates no upper limit)
6) For overlapping studies: principal rather than subsidiary studies
Finally for single sex results (m, f) in preference to results for both sexes combined (b).

Results adjusted for the most potential confounders are then chosen in Sections -1 to -3
(and those which actually differ from the adjusted results in Appendix Table G6 - 1 are marked 'x' in Section -1)
and results adjusted for the least confounders in Sections -4 to -6. (Those least adjusted results which
actually differ from the most adjusted are marked 'x' in column X in Section -4)

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Appendix Table G12 - 1

IASTAD - Meta-analysis of Workplace Exposure : High Dose
Lifetime/Current Asthma
Adjusted

REF	NRR	CompG6	SEX	AST	SMOK	AGEL	AGEH	LOC	BEGYR	PUBYR	TYP	ONS	ADJ	EXPOS	UNEXsrce	EXPOS-time	UNEXTI	MEAS	LO	HI
JAAKK2	43	x	b	c	Never	21	63	Eu:Fin	1997	2003	CC	ons	8	Work	NotWork	lifetime	non	pkyrs	150	999
LARSS2	3		b	l	Never	15	64	Eu:Est	1995	2003	CS	prv	5	Work	NotWork	current	non	hours	6	999

_____

Appendix Table G12 - 2

IASTAD - Meta-analysis of Workplace Exposure : High Dose
Lifetime/Current Asthma
Adjusted

				Numbers Numbers exposed		Non-exposed				
REF	NRR	SEX	ADJ	Case	Cont	Case	Cont	RR		95.00%CI
JAAKK2	43	b	8	22	–	163	–	2.21 (	1.15-	4.27)
LARSS2	3	b	5	–	–	–	–	1.79 (	1.02-	3.16)
Partial Totals				22	0	163	0			

*prospective study

REF	NRR	SEX	ADJ	Ys	Ws	Qs	Ps
JAAKK2	43	b	8	0.79	8.93	0.13	0.0178
LARSS2	3	b	5	0.58	12.02	0.10	0.0436

```
                N       2
                NS      2


                Wt     20.95
           Het Chi      0.23
           Het  df        1
           Het  P       N.S.
         Fixed  RR      1.96
                RRl     1.28
                RRu     3.01
                 P       ++
        Random  RR      1.96
                RRl     1.28
                RRu     3.01
                 P       ++
         Asymm  P
```

Appendix Table G12 - 4

IASTAD - Meta-analysis of Workplace Exposure : High Dose
Lifetime/Current Asthma
Unadjusted

```
    REF|NRR|X|SEX|AST|  SMOK|AGEL|AGEH|   LOC|BEGYR|PUBYR|TYP|ONS|ADJ|EXPOS|UNEXsrce|EXPOS-time|UNEXTI| MEAS| LO| HI|

JAAKK2  19 x   b   c  Never   21   63 Eu:Fin  1997  2003  CC ons   0  Work  NotWork   lifetime    non pkyrs 150 999
LARSS2   3     b   l  Never   15   64 Eu:Est  1995  2003  CS prv   5  Work  NotWork    current    non hours   6 999
```

```
                             Appendix Table G12 - 5

                 IASTAD - Meta-analysis of Workplace Exposure : High Dose
                               Lifetime/Current Asthma
                                     Unadjusted



                             Numbers
                             Numbers exposed Non-exposed
REF      NRR      SEX ADJ    Case   Cont   Case   Cont     RR        95.00%CI
JAAKK2 19        b   0        22     27    163    355     1.77 (  0.98-   3.21)
LARSS2 3         b   5         -      -      -      -     1.79 (  1.02-   3.16)
Partial Totals               22     27    163    355
*prospective study

REF      NRR      SEX ADJ            Ys     Ws     Qs      Ps

JAAKK2 19        b   0              0.57  10.94   0.00    0.0579
LARSS2 3         b   5              0.58  12.02   0.00    0.0436




                       N        2
                      NS        2


                      Wt    22.95
               Het Chi    0.00
               Het  df       1
               Het  P     N.S.
             Fixed  RR    1.78
                    RRl   1.18
                    RRu   2.68
                     P      ++
            Random  RR    1.78
                    RRl   1.18
                    RRu   2.68
                     P      ++
             Asymm  P
```