### EPIDEMIOLOGICAL EVIDENCE ON ENVIRONMENTAL TOBACCO SMOKE AND LUNG CANCER

- 1. 95 epidemiological studies of lung cancer among lifelong nonsmokers have been published.
- 2. The overall evidence shows no statistically significant increased risk of lung cancer in relation to ETS exposure from parents in childhood, or in social situations, or to non-spousal ETS exposure at home.
- 3. The overall evidence shows that lung cancer risk among nonsmoking women is significantly associated with having a husband who smokes (with a similar association seen in nonsmoking men in relation to smoking by the wife, though based on less data). There is also evidence of a dose-response relationship,<sup>1</sup> with risk higher if the husband smokes more cigarettes per day or for a longer period of time. However, there are a number of reasons why this association and dose-response relationship cannot be interpreted as indicating a causal effect of ETS exposure including:
  - the association is weak and is not statistically significant in the great majority of studies: nearly 80% show no statistically significant association between smoking by the husband and the development of lung cancer;
  - some of the very largest studies show no association, including five of the six studies involving over 400 lung cancer cases. One<sup>2</sup> of these reported no statistically significant association between lung cancer and any index of ETS exposure, while another<sup>3</sup> even reported a statistically significantly reduced risk of lung cancer for non-smoking women married to smokers;
  - almost 20% of the studies have not adjusted for age in the analysis, a standard procedure in epidemiology to avoid bias. These studies report much stronger associations with spousal exposure than are reported by studies that did use age-adjustment.
  - spousal studies are particularly susceptible to various biasing factors. These include:
    - i) failure to consider diet, lifestyle, family medical history, education, socio-economic status and other factors believed to differ between smoking and non-smoking households; and
    - ii) the inappropriate inclusion of some misclassified current and former smokers among the lifelong non-smokers.
  - reliance on reported rather than objectively measured ETS exposure data, and failure to publish negative studies.

No-one has yet designed a study in such a way as to eliminate all these sources of bias. Analyses published in 2000-2002 demonstrated formally that the weak association and dose-response relationship between lung cancer and smoking by the husband would essentially disappear were proper adjustment made for age, diet, education and misclassification of smoking habits<sup>4-6</sup>, a conclusion confirmed based on more recent data<sup>7</sup>.

- 4. There is also some indication from the overall evidence that lung cancer risk among nonsmokers might be weakly associated with workplace ETS exposure. However, only five of 43 relative risk estimates are statistically significant and biases that apply to the spousal data are also likely to apply to the workplace data.
- 5. There is similarly weak evidence of an association with overall childhood ETS exposure. Here some of the largest studies give risk estimates below 1, but several of the moderate size studies report an increased risk.
- 6. Taken as a whole, the epidemiology does not support the claim that ETS causes lung cancer in non-smokers.

### THE DATA

The tables and figures that follow summarize the key evidence in relation to:

smoking by the husband (Figure 1, Table 1), smoking by the wife (Figure 2, Table 2), ETS exposure in the workplace (Figure 3, Table 3), and ETS exposure in childhood (Figure 4, Table 4).

The term "relative risk" is taken to include direct estimates of the relative risks from prospective studies, and indirect estimates (odds ratios) from case-control studies. Relative risk estimates and 95% confidence limits in Tables 1 to 4 are adjusted for covariates if adjusted data are available, and otherwise are unadjusted. Where, for some studies, the source publication provides more than one adjusted estimate, the data that are normally presented are those adjusted for most covariates. Where studies present appropriate data on numbers of cases and controls (or populations at risk) unadjusted relative risks and 95% confidence limits are calculated, or checked, as described by Morris and Gardner.<sup>8</sup>

Tables 1 and 2 show results for exposure to smoking by the spouse or the nearest equivalent available. Details are given in the footnotes to those tables.

Some studies reported adjusted relative risks and confidence intervals only by level of the exposure of interest. These adjusted risks and intervals were used to estimate corresponding "effective numbers" of cases and controls (or subjects at risk) at each level, which could then be combined to allow estimation of risks and intervals for overall exposure.<sup>9</sup>

The relative risks and 95% confidence limits are plotted graphically in the figures. In the figures, each study is represented by a square and a horizontal line. The square indicates both the value of the relative risk estimate (by its position) and the size of the study (by the area of the square, which is proportional to the inverse of the variance of the relative risk estimate, and is thus closely related to the number of lung cancers studied). The horizontal line indicates the confidence limits. By this means of presentation, large studies, which contribute more to the overall evidence, have more visual impact than small studies. The result of random-effects meta-analysis of the studies is represented at the bottom of the figure by use of a diamond, the centre of the diamond representing the relative risk and the width of the diamond representing the confidence interval.

The tables and figures are based on results from a total of 95 studies (see References to data sources, page 19). An appendix explains why results from certain other publications, which might have been thought to cite relevant data, are not included in the tables and figures.

Meta-analyses of these data are available.<sup>10-12</sup>

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### References to text

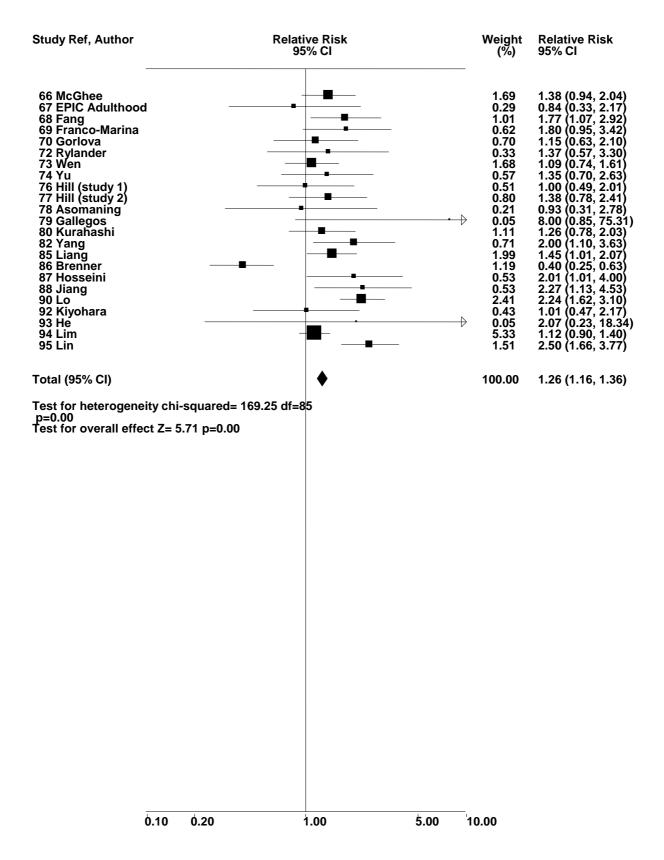
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#### Weight (%) Study Ref, Author **Relative Risk Relative Risk** 95% CI 95% CI $\begin{array}{c} 1.17 & (0.85, 1.61) \\ 0.75 & (0.43, 1.30) \\ 2.07 & (0.81, 5.25) \\ 2.08 & (1.20, 3.59) \\ 0.80 & (0.34, 1.90) \\ 1.45 & (1.02, 2.08) \\ 0.79 & (0.25, 2.45) \\ 1.23 & (0.81, 1.87) \\ 2.01 & (1.09, 3.72) \\ 1.20 & (0.50, 3.30) \\ 1.50 & (0.93, 2.76) \\ 1.00 & (0.37, 2.71) \\ 1.68 & (0.39, 6.90) \\ 1.30 & (0.87, 1.94) \\ 2.20 & (0.76, 6.56) \\ 1.64 & (0.87, 3.09) \\ 1.65 & (1.16, 2.35) \end{array}$ 1 Garfinkel 1 2.47 0.84 0.29 2 Chan 3 Correa **4** Trichopoulos 0.84 5 Buffler 0.34 6 Hirayama 7 Kabat 1 2.00 0.20 8 Garfinkel 2 9 Lam W 1.47 0.67 0.29 10 Wu 11 Akiba 12 Lee 0.26 13 Brownson 1 0.12 14 Gao 15 Humble 1 1.58 0.22 0.63 16 Koo 1.65 (1.16, 2.35) 1.20 (0.70, 2.10) 2.02 (0.48, 8.56) 2.16 (1.08, 4.29) 17 Lam T 2.02 18 Pershagen 0.84 19 Butler 0.12 2.02 (0.48, 8.56) 2.16 (1.08, 4.29) 2.25 (0.77, 8.85) 1.08 (0.64, 1.82) 1.63 (0.92, 2.87) 1.89 (0.22, 16.12) 1.07 (0.70, 1.64) 1.36 (0.53, 3.49) 0.75 (0.47, 1.20) 2.11 (1.09, 4.08) 20 Geng 0.54 21 Inoue 0.17 22 Shimizu 0.94 23 Choi 24 Hole 0.79 0.06 25 Schoenberg 26 Svensson 1.39 0.29 27 Janerich 1.16 28 Kalandidi 0.58 2.11 (1.09, 4.08 2.11 (1.09, 4.08 1.13 (0.78, 1.63) 0.70 (0.60, 0.90) 0.77 (0.30, 1.96) 1.00 (0.80, 1.20) 1.60 (0.80, 3.00) 1.09 (0.64, 1.85) 29 Sobue 1.87 30 Wu-Williams 6.17 31 Liu Z 0.29 32 Brownson 2 6.17 33 Stockwell 0.58 34 Du 0.90 1.72 (0.77, 1.29 (1.04, 3.87 1.60 35 Liu Q 0.39 36 Fontham 5.47 0.58 (0.30, 1.13 2.57 (0.84, 7.85 1.08 (0.60, 1.94 37 Layard 0.58 38 De Waard 0.20 39 Kabat 2 0.74 40 Schwartz 1.41 1.10 (0.72 1.68 41 Sun 42 Wang S (0.80. 1.81 0.52 1.16 2.53 1.69 1.26, 5.10 2.53 (1.26, 5.10) 1.11 (0.67, 1.84) 1.20 (0.80, 1.60) 2.52 (1.09, 5.85) 1.11 (0.88, 1.39) 0.75 (0.31, 1.78) 1.53 (1.06, 2.21) 1.00 (0.50, 1.90) 1.72 (0.93 3.18) 43 Wang T 44 Cardenas 0.98 2.11 0.36 45 Zheng 47 Boffetta 4.86 48 Shen 49 Zaridze 0.34 1.88 50 Boffetta 2 0.57 1.72 (0.93, 3.18) 1.20 (0.50, 2.90) 1.50 (0.30, 6.30) 1.10 (0.80, 1.50) 51 Jee 52 Rapiti 0.67 0.33 53 Speize 54 Zhong 55 Lee C-H 0.11 2.57 1.10 (0.80, 1.50) 1.87 (1.29, 2.71) 1.50 (0.77, 2.91) 1.03 (0.60, 1.70) 1.20 (0.62, 2.30) 1.15 (0.84, 1.58) 1.80 (0.67, 4.60) 1.00 (0.67, 1.49) 0.94 (0.66, 1.33) 0.48 (0.21, 1.09) 0.80 (0.50, 1.30) 1.84 56 Malats 0.57 57 Wang L 0.94 58 Johnson 0.59 59 Lagarde 2.54 60 Nishino 0.27 61 Ohno 1.59 63 Enstrom 2.07 64 Zatloukal 0.37 65 IARC: Kreuzer 1.11 **0.10** 0.20 1.00 5.00 10.00

### FIGURE 1: Lung cancer and husband's smoking

/Continued

### FIGURE 1 (continued)



Stud	У			Number of lung	Relative risk (95% confidence	Signi-		
Ref	Author	Year	Location	Туре	cancers	limits)	ficance	Notes
1	Garfinkel 1	1981	USA	Р	153	1.17 (0.85-1.61)		а
2	Chan	1982	Hong Kong	CC	84	0.75 (0.43-1.30)		u
3	Correa	1983	USA	CC	24	2.07 (0.81-5.25)		u
1	Trichopoulos	1983	Greece	CC	77	2.08 (1.20-3.59)	+	u
5	Buffler	1984	USA	CC	41	0.80 (0.34-1.90)		u
5	Hirayama	1984	Japan	Р	200	1.45 (1.02-2.08)	+	а
7	Kabat 1	1984	USA	CC	53	0.79 (0.25-2.45)		mr
5	Garfinkel 2	1985	USA	CC	134	1.23 (0.81-1.87)		mr
)	Lam W	1985	Hong Kong	CC	75	2.01 (1.09-3.72)	+	u
0	Wu	1985	USA	CC	31	1.20 (0.50-3.30)		а
1	Akiba Lee	1986 1986	Japan UK	CC CC	94 32	1.50 (0.93-2.76)		ar
						1.00 (0.37-2.71)		a
3	Brownson 1 Gao	1987 1987	USA China	CC CC	19 246	1.68 (0.39-6.90)		ar
.4	Humble	1987	USA	cc	246	1.30 (0.87-1.94) 2.20 (0.76-6.56)		ar ar
5 6a	Koo	1987	Hong Kong	cc	20 88	1.64 (0.87-3.09)		ar
.0a .7	Lam T	1987	Hong Kong	cc	202	1.65 (1.16-2.35)	+	u
8	Pershagen	1987	Sweden	cc	202	1.20 (0.70-2.10)	Ŧ	u ar
.0	Butler	1987	USA	P	8	2.02 (0.48-8.56)		ab
20	Geng	1988	China	CC	54	2.16 (1.08-4.29)	+	u
21	Inoue	1988	Japan	CC	28	2.10 (1.00-4.2)) 2.25 (0.77-8.85)		a
22	Shimizu	1988	Japan	CC	20 90	1.08 (0.64-1.82)		mr
23	Choi	1989	Korea	CC	75	1.63 (0.92-2.87)		u
4	Hole	1989	Scotland	P	6	1.89 (0.22-16.12)		uv
25	Schoenberg	1989	USA	CC	116	1.07 (0.70-1.64)		ar
6	Svensson	1989	Sweden	CC	38	1.36 (0.53-3.49)		a
27a	Janerich	1990	USA	CC	146	0.75 (0.47-1.20)		mrz
28	Kalandidi	1990	Greece	CC	91	2.11 (1.09-4.08)	+	ar
.9	Sobue	1990	Japan	CC	144	1.13 (0.78-1.63)		ar
0	Wu-Williams	1990	China	CC	417	0.70 (0.60-0.90)	-	ar
81	Liu Z	1991	China	CC	54	0.77 (0.30-1.96)		ar
32	Brownson 2	1992	USA	CC	432	1.00 (0.80-1.20)		ar
3	Stockwell	1992	USA	CC	210	1.60 (0.80-3.00)		ar
34	Du	1993	China	CC	75	1.09 (0.64-1.85)		dmr
5	Liu Q	1993	China	CC	38	1.72 (0.77-3.87)		r
36a	Fontham	1994	USA	CC	653	1.29 (1.04-1.60)	+	ar
37	Layard	1994	USA	CC	39	0.58 (0.30-1.13)		ar
38	deWaard	1995	Netherlands	CC	23	2.57 (0.84-7.85)		u
9	Kabat 2	1995	USA	CC	69	1.08 (0.60-1.94)		mr
10	Schwartz	1996	USA	CC	185	1.10 (0.72-1.68)		arz
1	Sun	1996	China	CC	230	1.16 (0.80-1.69)		ar
2	Wang S-Y	1996	China	CC	82	2.53 (1.26-5.10)	+	u
3	Wang T-J	1996	China	CC	135	1.11 (0.67-1.84)		m
4a	Cardenas	1997	USA	Р	246	1.20 (0.80-1.60)		ar
.5	Zheng	1997	China	CC	69	2.52 (1.09-5.85)	+	u
-7b	Boffetta 1	1998	West Europe	CC	509	1.11 (0.88-1.39)		ar
8	Shen	1998	China	CC	70	0.75 (0.31-1.78)		а
9	Zaridze	1998	Russia	CC	189	1.53 (1.06-2.21)	+	ar
0	Boffetta 2	1999	Europe	CC	66 70	1.00 (0.50-1.90)		ar
1	Jee Domiti	1999	Korea	P CC	79	1.72 (0.93-3.18)		ar
2	Rapiti	1999	India	CC	41	1.20 (0.50-2.90)		ar
3	Speizer	1999	USA China	P CC	35	1.50 (0.30-6.30)		a
4 5	Zhong	1999	China Taiwan	CC	504 268	1.10 (0.80-1.50)		ar
55	Lee C-H Malata	2000	Taiwan	CC	268	1.87 (1.29-2.71)	+	arv
56	Malats Wang I	2000	Europe/Brazil	CC	105	1.50 (0.77-2.91)		arz
57 58	Wang L Johnson	2000 2001	China Canada	CC CC	200 71	1.03 (0.60-1.70) 1.20 (0.62-2.30)		ar
58 59	Lagarde	2001	Sweden	cc	242	1.15 (0.84-1.58)		arv
59 50	Nishino	2001	Japan	P	242	1.15 (0.84-1.58) 1.80 (0.67-4.60)		artz
50 51	Ohno	2001	Japan Japan	P CC	24 191	1.00 (0.67-1.49)		ar acr
	CHIIO .	2002	Japan	u	171	1.00 (0.0/=1.42)		aci

# TABLE 1: Relative risk of lung cancer among lifelong nonsmoking women in relation to smoking by the husband

Study	у				Number of lung	Relative risk (95% confidence	Signi-	
Ref	Author	Year	Location	Туре	cancers	limits)	ficance	Notes
54	Zatloukal	2003	Czech Republic	CC	84	0.48 (0.21-1.09)		apr
55	IARC: Kreuzer	2004	Germany	CC	100	0.80 (0.50-1.30)		ar
66	McGhee	2005	Hong Kong	CC	179	1.38 (0.94-2.04)		ar
57b	EPIC Adulthood	2005	Western Europe	Р	43	0.84 (0.33-2.17)		arz
58	Fang	2006	China	CC	157	1.77 (1.07-2.92)	+	ar
59b	Franco-Marina	2006	Mexico	CC	72	1.80 (0.95-3.42)		u
0	Gorlova	2006	USA	CC	130	1.15 (0.63-2.10)		ar
2	Rylander	2006	Sweden	CC	31	1.37 (0.57-3.30)		az
'3	Wen	2006	China	Р	106	1.09 (0.74-1.61)		ar
'4a	Yu	2006	Hong Kong	CC	213	1.35 (0.70-2.63)		ar
6	Hill (study 1)	2007	New Zealand	Р	63	1.00 (0.49-2.01)		ar
7	Hill (study 2)	2007	New Zealand	Р	123	1.38 (0.78-2.41)		ar
8'8	Asomaning	2008	USA	CC	82	0.93 (0.31-2.78)		uz
9	Gallegos	2008	Mexico	CC	13	8.00 (0.85-75.31)		uz
30	Kurahashi	2008	Japan	Р	109	1.26 (0.78-2.03)		ar
32a	Yang	2008	UŜA	CC	74	2.00 (1.10-3.63)	+	arz
35	Liang	2009	China	CC	226	1.45 (1.01-2.07)	+	u
86	Brenner	2010	Canada	CC	110	0.40 (0.25-0.63)	-	uz
37	Hosseini	2010	Iran	CC	55	2.01 (1.01-4.00)	+	u
88	Jiang	2010	China	CC	98	2.27 (1.13-4.53)	+	arz
0a	Lo	2010	Taiwan	CC	339	2.24 (1.62-3.10)	+	arz
2	Kiyohara	2011	Japan	CC	49	1.01 (0.47-2.17)		az
)3	He	2012	China	Р	6	2.07 (0.23-18.34)		ar
94	Lim	2012	China	CC	433	1.12 (0.90-1.40)		u
95	Lin	2012	China	CC	226	2.50 (1.66-3.77)	+	u

## TABLE 1 (continued) Relative risk of lung cancer among lifelong nonsmoking women in relation to smoking by the husband

#### Notes for Table 1

Not considered in Table 1:

study 46 (Auvinen) – men only,

study 62 (Rachtan) - childhood ETS exposure only,

study 71 (Neuberger) - see below,

study 76 (Zeka) - workplace ETS exposure only,

study 81 (Pandey) - see below,

study 83 (Olivo-Marston) - childhood ETS exposure only,

study 84 (Tse) - men only,

study 89 (Lee YA) - see below, and

study 91 (EPIC Childhood) – childhood ETS exposure only.

Study 34 (Du) also reported that ETS was not statistically associated with lung cancer in an earlier similar study.

Study 67 (EPIC Adulthood) reported two type of analysis, each giving estimates of relative risk. The result quoted here is from the analysis of the whole cohort using Cox's proportional hazards model. A nested case-control analysis gave an odds ratio of 1.42 (0.63-3.20). Using this value rather than the result quoted above made no difference to meta-analyses of spousal smoking.

Study 71 (Neuberger), reporting a study of lung cancer in women in Iowa, stated that "Among never smokers no significant effect of ... passive smoking ... was detected." No further detail was given.

Study 81 (Pandey), reporting a study of never-smoking women in Nepal as an abstract only, gives an odds ratio of 2.2 (1.4-3.7) for greater than 40 smoker-years exposure to ETS in adult life compared with no exposure.

Study 89 (Lee YA), which is reported as an abstract only, gives an OR of 1.33 (1.18-1.50) for exposure to ETS (adjusted for age, sex, ethnicity and study site). This relates to an analysis of 17 studies by the International Lung Cancer Consortium. This Consortium pools results from many studies in many countries. While some of these studies are already included in our analyses it is not clear which were included in the result quoted. Also the report does not define the exposure measure. We have therefore not been able to include this result in our meta-analyses. The report also gives adjusted ORs for squamous cell carcinoma (1.38 (0.97-1.98)), adenocarcinoma (1.26 (1.08-1.46)), small cell lung cancer (2.92 (1.55-5.48)) and non-small cell lung cancer (1.30 (1.14-1.49)). For childhood exposure it states that "no apparent association was observed."

## TABLE 1 (continued 2) Relative risk of lung cancer among lifelong non-smoking women in relation to smoking by the husband

Index of exposure is based on smoking by the spouse or, if not available, the nearest equivalent as described below under 'Indices of ETS exposure used other than husband smoked'

- Study author is the name of the first author in the principal publication from which the data were extracted (see references).
- **Study year** is the year of that publication.
- Study type: CC case control; P prospective
- Number of lung cancers in lifelong non-smokers is study total for females. For specific exposures numbers may be lower. For some studies these numbers have been estimated.
- Where necessary, relative risks and 95% confidence limits were estimated from the data presented.
- Significance: + statistically significant increase at 95% confidence level significant decrease.
- Notes: see 'Notes column' below.

#### Notes column:

- a Adjusted for age.
- b Based on the "Spouse-Pairs Cohort" because the "AHSMOG Cohort" was not restricted to never smokers.
- c Based on data for hospital controls. Data for population controls was not used because non-response rate was very high.
- d Based on data for two control groups combined.
- m Lifelong non-smoking cases and controls matched for age but no age adjustment in analysis.
- p Based on data for two pathological groups of lung cancer combined.
- r Adjusted or matched for other factors (shown below).
- t Based on data by radon exposure.
- u Unadjusted for age or other factors.
- v Relative risks were presented adjusted for age but only by level of exposure.
- z Relative risks were presented for sexes combined. They were assumed to apply to each sex separately, with confidence intervals weighted according to numbers of subjects by sex.

#### Indices of ETS exposure used other than husband smoked

Study	Index	Study	Index
5	Household smoker smokes regularly	69	Exposed at home
13	Presence of persons smoking 4+ hours/day	70	Exposed at home at least weekly
24	Household smoker ever smoked	72	Exposed at home
26	Exposure at home and/or at work as an adult	74	Exposed at home and/or work
31	Smoker in household	76	Living in a smoking household
38	Urinary cotinine >9.2 ng/mg creatinine	77	Living in a smoking household
40	Exposed at home	78	Exposed at home
42	Exposed at home and/or work	79	Any exposure
45	Household exposure	82	Any exposure
48	Any exposure	85	Exposure in adulthood
53	Exposure in adulthood	86	Exposed at home
57	Exposed at home	88	Exposed at home and/or work
58	Exposed at home	90	Exposed at home, work and/or during leisure
59	Exposed at home		activities
64	Exposed at home and/or work >3 hrs/day	93	Exposed at home and/or work
66	Exposed at home	94	Exposed at home
67	Exposed at home	95	No details given, presumed to be any exposure
68	Exposed at home and/or work for 50+ person-years		

### TABLE 1 (continued 3) Relative risk of lung cancer among lifelong non-smoking women in relation to smoking by the husband

Factors other than age taken into account by adjustment or matching (applies to all studies considered in Tables 1-4, except where stated in the Notes)

Study	Factors	Study	Factors
7	Race, hospital.	62	Beer, vodka, milk, butter, margarine, cheese, meat, fruit
8	Hospital.		vegetables, carrots, spinach, siblings with cancer,
11	City, vital status, participation in		tuberculosis, place of residence, any of six defined
	medical examinations.		occupational exposures.
13	Income, occupation.	63	Race, education, exercise, body mass index (BMI),
14	Education.		urbanisation, fruit or fruit juice inake, health status.
15	Ethnicity.	64	Residence, education.
16	Live births, years since exposure	65	Region.
	ceased, schooling.	66	Education.
18	Vital status.	67	Country, school years, energy intake, fruit and vegetable
22	Hospital.		consumption, physical activity.
25	Race, education, occupation, vegetables, vital	68	Consumption of internal organs of animals, occupational
	status.		exposure to dust, bad ventilation at work, consumption
26	Residence, direct/surrogate interview.		of vegetables, taking vitamins, income level, age of first
28	Years of schooling, interviewer, total energy		procreation.
	intake, fruit consumption.	69	Access to health care.
29	Education.	70	Race, education, socio-economic status.
30	Education, study area.	73	Education, occupation, income, physical activity, BMI,
31	Age of starting to cook, years of cooking.		intake of meat, vegetables, fruit.
32	History of lung disease.	74	Education, employment, history of lung diseases, family
33	Race, education.		history of lung cancer, radon, kerosene use, firewood
34	Residence.		use, incense burning, mosquito coil use, years of cooking,
35	Education, occupation, living area.		orange/yellow vegetables, dark green vegetables, meats,
36	Race, area, education, fruits, vegetables and		citrus fruits, salted fish, pickled vegetables,
	supplemental vitamin index, family history of		multivitamins, coffee, tea.
	lung cancer, employment in high risk occupations.	76	Ethnicity.
37	Race.	77	Ethnicity, marital status, SES, household car access,
39	Race, hospital, date of interview, years of		tenure, small-area deprivation index.
	education.	80	Study area, alcohol, family history of lung cancer,
40	Race.		menopausal status.
41	Education.	82	Any exposure (Tables 1 & 2): COPD, $\alpha_1$ ATD carrier
44	Race, education, blue collar employment,		status.
	vegetable consumption, fat consumption,		Childhood exposure (Table 4): sex, ETS in adulthood,
	occupational exposure to asbestos, history of		education, family history of lung cancer.
	chronic lung disease.	83	Sex, ETS in adulthood, education, family history of
47	Study centre.		lung cancer.
49	Education.	84	Place of birth, alcohol, radon, history of lung disease,
50	Centre.		family history of cancer, meat, exposure to lung
51	Socio-economic status, residence, husband's		carcinogens, adoption of dust control.
	vegetable consumption, husband's occupation.	88	BMI, moved to a renovated home, family history of
52	Residence, religion.		cancer: first degree relatives and second/third degree
54	Income, vitamin C, respondent status, smokiness		relatives, eating fruit and/or vegetables, exercise,
	of kitchen, family history of lung cancer,		mental/psychological factors: lack of emotional
	potentially high risk occupation.		regulation, heavy work pressure, poor sleep quality.
55	Residential area, education, occupation,	90	ATM 59783T>C genotype.
	tuberculosis, cooking fumes, fume extractor.	91	Study centre, education, alcohol, body mass index,
56	Centre.		physical activity, vegetable intake, fruit intake,
57	Ownership of colour TV, number of cattle,		non-alcohol energy intake, adulthood passive
	prefecture, childhood ETS exposure.		smoking.
58	Province, education, total fruit and vegetables.	93	Education, marital status, occupation, alcohol,
59	Radon, SES, occupation, residence, urban/rural.		BMI, diastolic BP, triglycerides, cholesterol
60	Alcohol, green and yellow vegetables, fruit, meat,	95	Education, eggs, fruit, tea, cooking oil fumes, age at
60	Alcohol, green and yellow vegetables, fruit, meat, study area, history of respiratory disease. Research institution (region).	95	Education, eggs, fruit, tea, cooking oil fumes, age at menarche, physical activity.

Study Ref, Author				tive Risk 5% Cl		Weight (%)	Relative Risk 95% Cl
3 Correa 5 Buffler 6 Hirayama 7 Kabat 1 11 Akiba 12 Lee 15 Humble 1 23 Choi 24 Hole 27 Janerich 37 Layard 39 Kabat 2 40 Schwartz 44 Cardenas 45 Zheng 46 Auvinen 47 Boffetta 56 Malats 57 Wang L 59 Lagarde 63 Enstrom 65 IARC: Kreuzer 66 McGhee 67 EPIC Adulthoc 69 Franco-Marina 70 Gorlova 72 Rylander 76 Hill (study 1) 77 Hill (study 1) 77 Hill (study 2) 78 Asomaning 79 Gallegos 82 Yang 84 Tse 86 Brenner 87 Hosseini 88 Jiang 90 Lo 92 Kiyohara 93 He	bd					$\begin{array}{cccccccccccccccccccccccccccccccccccc$	$\begin{array}{c} 1.97 & (0.38, 10.32) \\ 0.51 & (0.14, 1.79) \\ 2.25 & (1.05, 4.76) \\ 1.00 & (0.20, 5.07) \\ 1.80 & (0.39, 6.96) \\ 1.30 & (0.38, 4.39) \\ 4.08 & (0.70, 23.91) \\ 2.73 & (0.49, 15.21) \\ 3.52 & (0.32, 38.65) \\ 0.75 & (0.31, 1.78) \\ 1.47 & (0.55, 3.94) \\ 1.60 & (0.67, 3.82) \\ 1.10 & (0.60, 2.03) \\ 1.10 & (0.60, 2.03) \\ 1.10 & (0.60, 1.80) \\ 0.67 & (0.22, 2.04) \\ 0.69 & (0.28, 1.74) \\ 1.47 & (0.81, 2.66) \\ 1.50 & (0.41, 5.43) \\ 0.56 & (0.20, 1.40) \\ 1.15 & (0.81, 1.63) \\ 0.63 & (0.33, 1.22) \\ 0.40 & (0.10, 3.00) \\ 1.34 & (0.82, 2.17) \\ 0.84 & (0.18, 3.86) \\ 1.80 & (0.80, 4.03) \\ 1.41 & (0.60, 3.30) \\ 1.37 & (0.53, 3.53) \\ 1.08 & (0.56, 2.09) \\ 1.45 & (0.75, 2.81) \\ 0.93 & (0.23, 3.70) \\ 8.00 & (1.11, 3.59) \\ 0.90 & (0.57, 1.41) \\ 0.40 & (0.20, 0.80) \\ 0.70 \sim & (0.04, 13.34) \\ 2.27 & (0.62, 8.27) \\ 2.24 & (1.31, 3.83) \\ 1.01 & (0.59, 1.71) \\ 1.86 & (0.45, 7.73) \\ \end{array}$
Total (95% Cl) Test for heterogen p=0.12 Test for overall eff	-	-	l8.22 df=3	8		100.00	1.20 (1.03, 1.39)
~ With 0.5 adjustn							
	<b>0.10</b>	<b>0.20</b>		1.00	5.00	10.00	

## FIGURE 2: Lung cancer and wife's smoking

Study					Number of lung	Relative risk (95% confidence	Signi-	
Ref	Author	Year	Location	Туре	cancers	limits)	ficance	Notes
3	Correa	1983	USA	CC	8	1.97 (0.38-10.32)		u
5	Buffler	1984	USA	CC	11	0.51 (0.14-1.79)		u
6	Hirayama	1984	Japan	Р	64	2.25 (1.05-4.76)	+	а
7	Kabat 1	1984	USA	CC	25	1.00 (0.20-5.07)		mr
1	Akiba	1986	Japan	CC	19	1.80 (0.39-6.96)		ar
2	Lee	1986	UK	CC	15	1.30 (0.38-4.39)		а
5	Humble	1987	USA	CC	8	4.08 (0.70-23.91)		ar
3	Choi	1989	Korea	CC	13	2.73 (0.49-15.21)		u
4	Hole	1989	Scotland	Р	3	3.52 (0.32-38.65)		u
7a	Janerich	1990	USA	CC	45	0.75 (0.31-1.78)		mrz
7	Layard	1994	USA	CC	21	1.47 (0.55-3.94)		ar
9	Kabat 2	1995	USA	CC	41	1.60 (0.67-3.82)		mr
0	Schwartz	1996	USA	CC	72	1.10 (0.60-2.03)		arz
4a	Cardenas	1997	USA	Р	116	1.10 (0.60-1.80)		ar
5	Zheng	1997	China	CC	25	0.67 (0.22-2.04)		u
6	Auvinen	1998	Finland	CC	44	0.69 (0.28-1.74)		as
7b	Boffetta 1	1998	West Europe	CC	141	1.47 (0.81-2.66)		ar
6	Malats	2000	Europe/Brazil	CC	17	1.50 (0.41-5.43)		arz
7	Wang L	2000	China	CC	33	0.56 (0.20-1.40)		ar
9	Lagarde	2001	Sweden	CC	191	1.15 (0.81-1.63)		artz
3	Enstrom	2003	USA	Р	79	0.63 (0.33-1.22)		ar
5	IARC: Kreuzer	2004	Germany	CC	23	0.40 (0.10-3.00)		u
6	McGhee	2005	Hong Kong	CC	145	1.34 (0.82-2.17)		ar
7b	EPIC Adulthood	2005	Western Europe		16	0.84 (0.18-3.86)		arz
9b	Franco-Marina	2006	Mexico	CC	22	1.80 (0.80-4.03)		arz
0	Gorlova	2006	USA	CC	63	1.41 (0.60-3.30)		ar
2	Rylander	2006	Sweden	CC	18	1.37 (0.53-3.53)		az
6	Hill (study 1)	2000	New Zealand	P	84	1.08 (0.56-2.09)		av
7	Hill (study 2)	2007	New Zealand	P	111	1.45 (0.75-2.81)		aw
8	Asomaning	2007	USA	CC	56	0.93 (0.23-3.70)		uz
9	Gallegos	2008	Mexico	CC	19	8.00 (1.13-56.52)	+	uz
2a	Yang	2008	USA	CC	84	2.00 (1.11-3.59)	+	arz
2a 4	Tse	2000	Hong Kong	CC	132	0.90 (0.57-1.41)	I	ar
4 6	Brenner	2009	Canada	CC	46	0.40 (0.20-0.80)	_	uz
7	Hosseini	2010	Iran	CC	40 26	0.40 (0.20-0.80)	-	pu
88 88	Jiang	2010	China	CC	20 47	2.27 (0.62-8.27)		arz
0a	Lo	2010	Taiwan	CC	123	2.24 (1.31-3.83)	+	arz
10a 12	Kiyahora	2010	Japan	CC	123	1.01 (0.59-1.71)	т	
12 13	He	2011	China	P	104			az
5	пе	2012	China	r	10	1.86 (0.45-7.73)		ar

## TABLE 2: Relative risk of lung cancer among lifelong nonsmoking men in relation to smoking by the wife

#### Notes for Table 2

Study 34 (Du) also reported that ETS was not statistically associated with lung cancer in an earlier similar study

Study 67 (EPIC Adulthood) reported two type of analysis, each giving estimates of relative risk. The result quoted here is from the analysis of the whole cohort using Cox's proportional hazards model. A nested case-control analysis gave an odds ratio of 1.42 (0.63-3.20). Using this value rather than the result quoted above made no difference to meta-analyses of spousal smoking.

Index of exposure based on smoking by the spouse or, if not available, the nearest equivalent, as described below.

- Study author is the name of first author in the principal publication from which the data were extracted (see references).
- **Study year** is the year of that publication.
- Study type: CC case control P prospective
- Number of lung cancers in lifelong nonsmokers are study totals for males. For specific exposures numbers may be less. For some studies these numbers have been estimated.
- Where necessary, relative risks and 95% confidence limits were estimated from the data presented.

## TABLE 2 (continued)Relative risk of lung cancer among lifelong nonsmoking men in<br/>relation to smoking by the wife

- Significance: + statistically significant increase at 95% confidence level significant decrease.
- Notes: see 'Notes column' below.

#### Notes column:

- a Adjusted for age.
- m Lifelong nonsmoking cases and controls matched for age but no age adjustment in analysis.
- p Estimated from numbers of subjects, with 0 exposed cases.
- r Adjusted or matched for other risk factors (see Table 1).
- s Adjusted for sex; data were only given for sexes combined but as 93% of cases were male the result has been assumed to apply to males.
- t Based on data by radon exposure.
- u Unadjusted for age or other factors.
- v Adjusted as for Hill (study 2) in Table 1.
- w Adjusted for age and ethnicity only.
- z Relative risks were presented for sexes combined. They were assumed to apply to each sex separately, with confidence intervals weighted according to numbers of subjects by sex.

#### Indices of ETS exposure used other than wife smoked

#### Study Index

- 5 Household member smokes regularly
- 24 Household member ever smoked
- 40 Exposed at home
- 45 Household exposure
- 46 Passive smoking
- 57 Exposed at home
- 59 Exposed at home
- 66 Exposed at home
- 67 Exposed at home
- 69 Exposed at home
- 70 Exposed at home at least weekly
- 72 Exposed at home
- 76 Living in a smoking household
- 77 Living in a smoking household
- 78 Exposed at home
- 79 Any exposure
- 82 Any exposure
- 84 Lived with a smoker for at least a year and was exposed regularly
- 86 Exposed at home
- 88 Exposed at home and/or work
- 90 Exposed at home, work and/or during leisure activities
- 93 Exposed at home and/or work

### FIGURE 3: Lung cancer and workplace ETS exposure

Study Ref, Sex, Author		Relative Risk 95% Cl		Weight (%)	Relative Risk 95% Cl
7 m Kabat 1 7 f Kabat 1 8 f Garfinkel 2 10 f Wu 12 m Lee 12 f Lee 16 f Koo 22 f Shimizu 27 c Janerich 28 f Kalandidi 30 f Wu-Williams 32 f Brownson 2 36 f Fontham 39 m Kabat 2 39 f Kabat 2 40 c Schwartz 41 f Sun 43 f Wang T 44 m Cardenas 44 f Cardenas 44 f Cardenas 47 m Boffetta 49 f Zaridze 50 c Boffetta 2 52 c Rapiti 54 f Zhong 55 f Lee C-H 57 c Wang L 58 f Johnson 61 f Ohno 65 m IARC: Kreuzer 65 f IARC: Kreuzer 65 f IARC: Kreuzer 65 f IARC: Kreuzer 67 c EPIC Adulthood 70 m Gorlova 72 c Rylander 73 f Wen 78 c Asomaning 80 f Kurahashi 84 m Tse 86 c Brenner 87 m Hosseini 87 f Hosseini			· · · · · · · · · · · · · · · · · · ·	$\begin{array}{c} 0.39\\ 0.91\\ 2.01\\ 0.60\\ 0.27\\ 0.31\\ 0.65\\ 1.89\\ 3.38\\ 0.66\\ 6.82\\ 6.55\\ 8.13\\ 1.04\\ 1.40\\ 3.44\\ 3.56\\ 1.23\\ 1.69\\ 2.87\\ 2.11\\ 9.51\\ 2.41\\ 1.22\\ 0.31\\ 6.56\\ 1.65\\ 0.89\\ 1.90\\ 3.33\\ 0.61\\ 2.09\\ 1.31\\ 0.73\\ 1.39\\ 0.68\\ 2.18\\ 3.53\\ 2.79\\ 2.81\\ 3.86\\ 0.30\\ 0.05\\ 100.00\\ \end{array}$	3.27 (1.01, 10.62) 0.68 (0.32, 1.47) 0.93 (0.55, 1.55) 1.30 (0.50, 3.30) 1.61 (0.39, 6.60) 0.63 (0.17, 2.33) 1.19 (0.48, 2.95) 1.18 (0.70, 2.01) 0.91 (0.61, 1.35) 1.70 (0.69, 4.18) 1.06 (0.80, 1.40) 0.98 (0.74, 1.31) 1.56 (1.21, 2.02) 1.02 (0.50, 2.09) 1.15 (0.62, 2.13) 1.50 (1.00, 2.20) 1.38 (0.94, 2.04) 0.89 (0.46, 1.73) 1.09 (0.62, 1.91) 1.00 (0.65, 1.54) 1.13 (0.68, 1.86) 1.19 (0.94, 1.51) 0.88 (0.55, 1.41) 1.50 (0.80, 3.00) 1.10 (0.30, 4.10) 1.70 (1.30, 2.30) 0.91 (0.52, 1.62) 1.56 (0.70, 3.30) 1.36 (0.80, 2.31) 1.38 (0.92, 2.05) 0.50 (0.20, 1.30) 1.40 (0.80, 2.20) 1.28 (0.67, 3.70) 1.95 (1.05, 3.62) 2.26 (0.93, 5.48) 1.79 (1.09, 2.93) 1.21 (0.82, 1.78) 1.32 (0.85, 2.04) 1.15 (0.74, 1.77) 1.26 (0.87, 1.82) 1.58 (0.42, 5.95) 6.58~ (0.26, 164.08)
Test for heterogeneity chi p=0.50 Test for overall effect Z= 5		38 df=42		100.00	1.24 (1.13, 1.33)
~ With 0.5 adjustment for	zero				
0.10	0.20	1.00	5.00 1	0.00	

Study Ref	Author	Location	Sex	Relative risk (95% confidence limits)	Significance	Notes
7	Kabat 1	USA	Males Females	3.27 (1.01-10.62) 0.68 (0.32-1.47)	+	mr mr
3	Garfinkel 2	USA	Females	0.93 (0.55-1.55)		mr
0	Wu	USA	Females	1.30 (0.50-3.30)		а
2	Lee	UK	Males Females	1.61 (0.39-6.60) 0.63 (0.17-2.33)		u u
6b	Koo	Hong Kong	Females	1.19 (0.48-2.95)		u
2	Shimizu	Japan	Females	1.18 (0.70-2.01)		mr
7a	Janerich	USA	Combined	0.91 (0.61-1.35)		mrx
8	Kalandidi	Greece	Females	1.70 (0.69-4.18)		uy
)	Wu-Williams	China	Females	1.06 (0.80-1.40)		arw
2	Brownson 2	USA	Females	0.98 (0.74-1.31)		arz
5b	Fontham	USA	Females	1.56 (1.21-2.02)	+	ar
9	Kabat 2	USA	Males Females	1.02 (0.50-2.09) 1.15 (0.62-2.13)		mr mr
)	Schwartz	USA	Combined	1.50 (1.00-2.20)	?	ar
	Sun	China	Females	1.38 (0.94-2.04)		ar
;	Wang T-J	China	Females	0.89 (0.46-1.73)		m
łb	Cardenas	USA	Males Females	1.09 (0.62-1.91) 1.00 (0.65-1.54)		ar ar
7b	Boffetta 1	West Europe	Males Females	1.13 (0.68-1.86) 1.19 (0.94-1.51)		ar
)	Zaridze	Russia	Females	0.88 (0.55-1.41)		ar
)	Boffetta 2	Europe	Combined	1.50 (0.80-3.00)		ar
2	Rapiti	India	Combined	1.10 (0.30-4.10)		ar
4	Zhong	China	Females	1.70 (1.30-2.30)	+	ar
5	Lee C-H	Taiwan	Females	0.91 (0.52-1.62)		ar
7	Wang L	China	Combined	1.56 (0.70-3.30)		arh
8	Johnson	Canada	Females	1.36 (0.80-2.31)		arv
l	Ohno	Japan	Females	1.38 (0.92-2.05)		ar
5	IARC: Kreuzer	Germany	Males Females	0.50 (0.20-1.30) 1.40 (0.80-2.20)		u ar
7b	EPIC Adulthood	Western Europe	Combined	1.28 (0.67-2.40)		ar
)	Gorlova	USA	Males Females	1.58 (0.67-3.70) 1.95 (1.05-3.62)	+	ar ar
2	Rylander	Sweden	Combined	2.26 (0.93-5.48)		а
3	Wen	China	Females	1.79 (1.09-2.93)	+	ar
3	Asomaning	USA	Combined	1.21 (0.82-1.78)		u
)	Kurahashi	Japan	Females	1.32 (0.85-2.04)		ar
4	Tse	Hong Kong	Males	1.15 (0.74-1.77)		ar
6	Brenner	Canada	Combined	1.26 (0.87-1.82)		u
7	Hosseini	Iran	Males Females	1.58 (0.42-5.95) 6.58 (0.26-164.08)		u pu

# TABLE 3: Relative risk of lung cancer among lifelong nonsmokers in relation to ETS exposure in the workplace

## TABLE 3 (continued)Relative risk of lung cancer among lifelong nonsmokers in<br/>relation to ETS exposure in the workplace

#### Notes for Table 3

The Stockwell study (33) also reported finding no association but gave no detailed results.

An additional study by Zeka (75) gave results by level of exposure but in insufficient detail for an overall risk estimate to be calculated. The results presented (adjusted for occupational exposures and secondhand smoking at home) are:

Exposure level	RR (95% CI)
≤22 years exposure	0.95 (0.61-1.5)
>22 years exposure	1.30 (0.88-2.0)

- Study author is the name of the first author in the principal publication from which the data were extracted (see references).
- Where necessary, relative risks and 95% confidence limits were estimated from data presented.
- Significance: + statistically significant increase at 95% confidence level -significant decrease ? borderline.
- Notes: see 'Notes column' below.

#### Notes column:

- a Adjusted for age.
- c Based on hospital controls.
- h Adjusted for household ETS exposure.
- m Lifelong non smoking cases and controls matched for age but no age adjustment in analysis.
- p Estimated from numbers of subjects, with 0 exposed controls.
- r Adjusted or matched for other risk factors (see Table 1).
- u Unadjusted for age or other factors.

- Relative risks were presented adjusted for age but only by level of exposure.
- w Estimate comes from California EPA report.
- x Risk per 150 person-years of exposure.
- y Some vs. minimal exposure.
- Results reported in 1994 by WJ Butler in comments submitted to OSHA on their proposed indoor air quality rules, reference 31 merely reporting finding no association and giving no detailed results.

### FIGURE 4: Lung cancer and childhood ETS exposure

Study Ref, Sex, Author		Relative Risk 95% Cl		Weight (%)	Relative Risk 95% Cl
8 f Garfinkel 2 10 f Wu 14 f Gao 16 f Koo 18 f Pershagen 26 f Svensson 27 c Janerich 29 f Sobue 32 f Brownson 2 33 f Stockwell 36 f Fontham 39 m Kabat 2 39 f Kabat 2 41 f Sun 43 f Wang T 47 m Boffetta 47 f Boffetta 49 f Zaridze 50 c Boffetta 2 52 m Rapiti 54 f Zhong 55 f Lee C-H 57 m Wang L 58 f Johnson 61 f Ohno 62 f Rachtan 64 f Zatloukal 65 m IARC: Kreuzer 73 f Wen 80 f Kurahashi 82 c Yang 83 c Olivo-Marston 85 f Liang 86 c Brenner 91 c EPIC Childhood Total (95% CI) Test for heterogeneity c p=0.00 Test for overall effect Z=			· · · · · · · · · · · · · · · · · · ·	2.66 0.47 2.71 0.55 0.70 0.16 2.79 1.53 5.80 1.00 11.87 0.96 1.57 3.59 2.24 2.99 9.49 4.07 1.11 0.47 1.53 8.17 3.27 0.64 3.43 1.89 1.16 0.57 2.44 0.57 2.01 2.34 1.58 3.64 0.89 4.31 3.64 2.05	$\begin{array}{c} 0.91 & (0.58, 1.42) \\ 0.60 & (0.20, 1.70) \\ 1.10 & (0.70, 1.70) \\ 0.56 & (0.21, 1.50) \\ 1.00 & (0.40, 2.30) \\ 3.30 & (0.50, 18.80) \\ 1.33 & (0.86, 2.06) \\ 1.28 & (0.71, 2.31) \\ 0.80 & (0.60, 1.10) \\ 1.66 & (0.80, 3.44) \\ 0.89 & (0.72, 1.10) \\ 0.90 & (0.43, 1.89) \\ 1.63 & (0.91, 2.92) \\ 2.29 & (1.56, 3.37) \\ 0.91 & (0.56, 1.48) \\ 0.79 & (0.52, 1.21) \\ 0.77 & (0.61, 0.98) \\ 0.92 & (0.64, 1.32) \\ 0.60 & (0.30, 1.20) \\ 1.09 & (0.38, 3.18) \\ 12.00 & (4.30, 32.00) \\ 0.93 & (0.72, 1.20) \\ 2.10 & (1.40, 3.14) \\ 1.46 & (0.60, 3.70) \\ 1.51 & (1.00, 2.20) \\ 1.38 & (0.81, 2.34) \\ 1.00 & (0.51, 1.98) \\ 3.31 & (1.26, 8.69) \\ 1.61 & (1.01, 2.57) \\ 0.97 & (0.40, 2.30) \\ 0.93 & (0.52, 1.66) \\ 1.47 & (1.00, 2.15) \\ 2.25 & (1.04, 4.90) \\ 1.21 & (0.85, 1.72) \\ 0.80 & (0.54, 1.17) \\ 1.34 & (0.80, 2.22) \\ 1.16 & (1.02, 1.32) \\ \end{array}$
0.10	0.20	1.00	5.00 1	10.00	

#### Study Relative risk Ref Author Location Sex (95% confidence limits) Significance Notes 8 USA Garfinkel 2 Females 0.91 (0.58-1.42) mr 10 Wu USA Females 0.60 (0.20-1.70) а 14 Gao China Females 1.10 (0.70-1.70) ar Females 0.56 (0.21-1.50) 16a Koo Hong Kong ar 18 Pershagen Sweden Females 1.00 (0.40-2.30) ar 26 Svensson Sweden Females 3.30 (0.50-18.80) a 27a USA Combined 1.33 (0.86-2.06) Janerich mr 29 Sobue Japan Females 1.28 (0.71-2.31) ar 32 Brownson 2 USA Females 0.80 (0.60-1.10) ar 33 USA Stockwell Females 1.66 (0.80-3.44) ar 36a Fontham USA Females 0.89 (0.72-1.10) ar 39 Kabat 2 USA Males 0.90 (0.43-1.89) mr 1.63 (0.91-2.92) Females mr 41 Sun China Females 2.29 (1.56-3.37) ar + 43 Wang T-J 0.91 (0.56-1.48) China Females m 47b Boffetta 1 West Europe Males 0.79 (0.52-1.21) ar Females 0.77 (0.61-0.98) ar 49 Zaridze Females 0.92 (0.64-1.32) Russia ar 50 Boffetta 2 Europe Combined 0.60 (0.30-1.20) ar 53 Rapiti India Males 1.09 (0.38-3.18) ar Females 12.0 (4.30-32.0) +ar 54 Zhong China Females 0.93 (0.72-1.20) ar 55 Lee C-H Taiwan Females 2.10 (1.40-3.14) ar +57 1.46 (0.60-3.70) Wang L China Males arh Females 1.51 (1.00-2.20) arh 58 Johnson Canada Females 1.38 (0.81-2.34) arv 61 Ohno Japan Females 1.00 (0.51-1.98) acr Poland 62 Rachtan Females 3.31 (1.26-8.69) ar +1.61 (1.01-2.57) 64 Zatloukal Czech Republic Females + apr 65 IARC: Kreuzer Germany Males 0.97 (0.40-2.30) ar 0.90 (0.50-1.40) Females ar 73 Wen China Females 0.88 (0.55-1.43) ar 80 Kurahashi Japan Females 0.93 (0.52-1.66) ar 82b USA Combined ? Yang 1.47 (1.00-2.15) ar 83 Olivo-Marston USA Combined 2.25 (1.04-4.90) + ar 85 China Females 1.21 (0.85-1.72) Liang u 86 Combined 0.80 (0.54-1.17) Brenner Canada u 91 EPIC Childhood Western Europe Combined 1.34 (0.80-2.22) ar

## TABLE 4: Relative risk of lung cancer among lifelong nonsmokers in relation to ETS exposure in childhood

## TABLE 4 (continued)Relative risk of lung cancer among lifelong nonsmokers in<br/>relation to ETS exposure in childhood

#### Notes for Table 4

Three other studies, Correa (3), Akiba (11) and Lee YA (89), reported finding no association but gave no detailed results.

- Where the study only provided relative risk estimates for individual sources of ETS exposure, that for maternal smoking was used.
- Where the study provided relative risk estimates for different **time points**, that for the earliest was used.
- Study author is the name of the first author in the principal publication from which the data were extracted (see references).
- Where necessary, relative risks and 95% confidence limits were estimated from data presented.
- Significance: + statistically significant increase at 95% confidence level significant decrease ? borderline.
- Notes: see 'Notes column' below.

#### Notes column

- a Adjusted for age.
- c Based on hospital controls.
- h Adjusted for household ETS exposure.
- m Lifelong nonsmoking cases and controls matched for age but no age adjustment in analysis.
- p Based on data for two pathological groups of lung cancer combined.
- r Adjusted or matched for other risk factors (see Table 1).
- u Unadjusted for age or other factors.
- v Relative risks were presented adjusted for age but only by level of exposure.

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#### APPENDIX

#### STUDIES/ANALYSES NOT INCLUDED IN TABLES AND FIGURES

In preparing the tables and figures in this document certain papers which might be thought to cite relevant data have not been referred to. The studies (their year of publication, country of origin and reference) and the reasons for not referring to them are given in this appendix.

Hirayama (1981, Japan, ref A1) - results superseded by 1984 paper (ref 6).

Trichopoulos (1981, Greece, ref A2) - results superseded by 1983 paper (ref 4).

Chan (1982, Hong Kong, ref A3) – results given in other 1982 paper (ref 2).

Hirayama (1983, Japan, ref A4) – results superseded by 1984 paper (ref 6).

Knoth (1983, Germany, refs A5, A6) - no control population.

Koo (1983, Hong Kong, ref A7) - results superseded by 1987 paper (ref 16a).

Gillis (1984, Scotland, ref A8) - results superseded by Hole paper (ref 24).

Hirayama (1984, Japan, ref A9) - results given in other 1984 paper (ref 6).

Miller (1984, USA, ref A10) - only five cases of lung cancer included and results for these not separately presented.

Ziegler (1984, USA, ref A11) - data only presented (by Dalager, ref A17) in combination with those of Buffler (ref 5) and Correa (ref 3). One can infer (see Lee, 1992) there was some negative association in males with ETS exposure but no relative risk estimates can be obtained.

Hirayama (1985, Japan, ref A12) - results already given in 1984 paper (ref 6).

Koo (1985, Hong Kong, ref A13) - results already given in 1984 (ref 16b) and 1987 paper (ref 16a).

Sandler (1985, USA, refs A14-16) - only two cases of lung cancer included.

Dalager (1986, USA, ref A17) - the paper only presents combined results from three studies already considered: Buffler (ref 5), Correa (ref 3) and Ziegler (ref A11).

Lloyd (1986, Scotland, ref A18) - no results presented for never smokers.

Hirayama (1987, Japan, ref A19) - results already given in 1984 paper (ref 6).

Reynolds (1987, USA, ref A20) - results presented only for cancers of smoking-related sites, and not lung cancer.

Axelson (1988, Sweden, ref A21) - study designed to investigate effects of radon and not ETS and, as such, the controls, many with smoking-related diseases, were inappropriate; furthermore, not stated whether ETS findings related to never smokers, non-smokers, or whole population.

Hirayama (1988, Japan, ref A22) - results already given in 1984 paper (ref 6).

Katada (1988, Japan, ref A23) - numbers of never smoking cases and controls unexposed to ETS too small for any sort of reliable risk estimates to be calculated.

Lam (1988, Hong Kong, ref A24) – review presenting results for three studies already considered, Chan (ref 2), Koo (ref 16) and Lam T (ref 17).

Pershagen (1988, Sweden, ref A25) - results already given in 1987 paper (ref 18).

Svensson (1988, Sweden, ref A26) - results superseded by 1989 paper (ref 26).

Hirayama (1989, Japan, ref A27) – although results are given adjusted for various dietary components, confidence intervals could not readily be calculated, so data in the 1984 paper (ref 6) were used.

Li (1989, China, ref A28) - no results presented for never smokers.

Sandler (1989, US, ref A29) - results presented only for cancers of smoking-related sites and not for lung cancer.

Wang (1989, China, ref A30) – index of ETS exposure not given, not stated whether results referred to never smokers, and relative risk not given.

Chen (1990, Taiwan, ref A31) - results seem not to be presented for never smokers, and no details given of index of ETS exposure used.

Hirayama (1990, Japan, refs A32, A33) - results already given in 1984 paper (ref 6).

Kabat (1990, USA, ref A34) - results superseded by 1995 paper (ref 39).

Liu (1990, China, ref A35) – results superseded by 1991 paper (ref 31).

Miller (1990, US, ref A36) - results concern respiratory, not lung cancer and only include three cases in spousal smoking analyses.

Sobue (1990, Japan, ref A37) - results given in other 1990 paper (ref 29).

Stellman (1990, USA, ref A38) – results already given in 1985 Garfinkel paper (ref 8).

Ye (1990, China, ref A39) - no results presented for never smokers.

Fontham (1991, USA, ref A40) - results superseded by 1994 paper (ref 36a).

He (1991, China, ref A41) - results given in 1991 Liu paper (ref 31).

Holowaty (1991, Canada, ref A42) - no results presented for never smokers.

Jöckel (1991, Germany, ref A43) - results mainly included as part of Boffetta 1 study (ref 47).

Stockwell (1991, USA, ref A44) – results superseded by 1992 paper (ref 33).

Ger (1992, China, ref A45) - no results presented for never smokers.

Hirayama (1992, Japan, ref A46) – results already given in 1984 paper (ref 6).

Jöckel (1992, Germany, ref A47) - results mainly included as part of Boffetta 1 study (ref 47).

Fontham (1993, USA, refs A48, A49) - results superseded by 1994 paper (ref 36a).

Ger (1993, China, ref A50) - no results presented for never smokers.

Järvholm (1993, Sweden, ref A51) - only six lung cancers in never smoking women and cited odds ratio for ETS inconsistent with data presented.

Lan (1993, China, ref A52) - index of ETS exposure not given, not stated whether results referred to never smokers and odds ratios and confidence limits cited inconsistent with each other and with tabular data given.

Siegel (1993, USA, ref A53) - review paper of lung cancer risk in food-service workers, data generally relating to smokers and non-smokers combined.

Wang (1993, China, ref A54) - believed to be based on a subset of subjects from Wu-Williams study (ref 30).

Alavanja (1994, USA, ref A55) - results already given in 1992 Brownson paper (ref 32).

Geng (1994, China, ref A56) - results already given in 1988 paper (ref 20).

Kabat (1994, USA, ref A57) - results superseded by 1995 paper (ref 39).

Miller (1994, USA, ref A58) - control group (formed from decedents from all causes of death except lung cancer) contains many with diseases associated with smoking.

Shen (1994, China, ref A59) – no results presented for never smokers, and superseded by 1998 paper (ref 48).

Wang (1994, China, ref A60) - believed to be based on subset of subjects from Wu-Williams study (ref 30).

Zaridze (1994, Russia, ref A61) - results superseded by the 1998 paper (ref 49).

Alavanja (1995, USA, ref A62) - results already given in 1992 Brownson paper (ref 32).

Du (1995, China, ref A63) - results already given in 1993 Du paper (ref 34).

Ellard (1995, UK, ref A64) – gives results for total nicotine metabolites. Results for cotinine already given in deWaard study (ref 38).

Auvinen (1996, Finland, ref A65) - corrected results given in 1998 (ref 46).

Dai (1996, China, ref A66) - exposure to ETS recorded (source unstated) but not significant in regression analysis and relative risk not given.

Du (1996, China, ref A67) - results already given in 1993 Du paper (ref 34).

Lei (1996, China, ref A68) - results already given in 1993 Du paper (ref 34).

Luo (1996, China, ref A69) - no results presented for never smokers.

Shen (1996, China, ref A70) - results superseded by 1998 paper (ref 48).

Shen (1996, China, ref A71) – no results presented for never smokers, and superseded by 1998 paper (ref 48).

Shen (1996, China, ref A72) - no results presented for never smokers.

Wang (1996, China, ref A73) - believed to be based on subset of subjects from Wu-Williams study (ref 30).

Yu S-Z (1996, China, ref A74) - gives pooled odds ratio for ETS from three case-control studies in China. Two of the studies are refs A29 and A40 (already rejected) and the third actually presents no ETS data at all.

Yu Z (1996, China, ref A75) - no results presented for never smokers.

Cardenas (1997, USA, ref A76) – gives corrected age-standardized results for Cardenas study (ref 44), but results used are adjusted for age and other factors.

Dai (1997, China, ref A77) - no results presented for never smokers.

Jöckel (1997, Germany, ref A78) - results mainly included as part of Boffetta 1 study (ref 47).

Ko (1997, Taiwan, ref A79) - results superseded by Lee C-H report (ref 55).

Nyberg (1997, Sweden, ref A80) - results mainly included as part of Boffetta 1 study (ref 47).

Yang (1997, USA, ref A81) - no results presented for never smokers.

Boffetta (1998, West Europe, refs A82) - results given in 1998 papers cited (ref 47).

Jöckel (1998, Germany, ref A83) - results mainly included as part of Boffetta 1 study (ref 47).

Nyberg (1998, Sweden, ref A84) - results mainly included as part of Boffetta 1 study (ref 47).

Wichmann (1998, Germany, ref A85) - results mainly included as part of Boffetta 1 study (ref 47).

Zaridze (1998, Russia, ref A86) – results superseded by other 1998 paper (ref 49).

Zemlianaja (1998, Russia, ref A87) - results superseded by 1998 Zaridze paper (ref 49).

Bennett (1999, USA, ref A88) - main results already given in 1992 Brownson paper (ref 32).

Boffetta (1999, West Europe, ref A89) - main results already given by Boffetta 1 (ref 47).

Brennan (2000, West Europe, ref A90) - main results already given by Boffetta 1 (ref 47).

Johnson (2000, USA, refs A91, A92) - results superseded by 2001 paper (ref 58).

Kleinerman (2000, China, ref A93) - results superseded by Wang L paper (ref 57).

Ko (2000, Taiwan, ref A94) - results superseded by Lee C-H paper (ref 55).

Kreuzer (2000, Germany, ref A95) - results included as parts of Boffetta 1 study (ref 47) and IARC: Kreuzer study (ref 65).

Li (2000, China, ref A96) - no results presented for never smokers.

Zhou (2000, China, ref A97) - no results presented for never smokers.

Goldoni (2001, Italy, ref A98) - no results presented for never smokers.

Kreuzer (2001, Germany, ref A99) - results mainly included as part of Boffetta 1 study (ref 47).

Kubík (2001, Czech Republic, ref A100) - results superseded by 2003 Zatloukal paper (ref 64).

Lee (2001, Taiwan, ref A101) - no results presented for never smokers. Results for never smokers given in 2000 paper (ref 55).

Liu (2001, China, ref A102) – proved unobtainable.

Hu (2002, Canada, ref A103) - similar analyses to those given by Johnson (ref 58), but based on fewer controls.

Kreuzer (2002, Germany, ref A104) - results mainly included as part of Boffetta 1 study (ref 47).

Kubík (2002, Czech Republic, ref A105) - results superseded by 2003 Zatloukal paper (ref 64).

Merrill (2002, Morocco, ref A106) - abstract reporting same study as 2002 paper by Sasco (ref A109).

Miller (2002, USA, ref A107) - abstract with no relative risks cited.

Rachtan (2002, Poland, ref A108) - no results presented for never smokers. Results for never smokers given in another Rachtan paper (ref 62).

Sasco (2002, Morocco, ref A109) - no results presented for never smokers.

Seow (2002, Singapore, ref A110) – results superseded by Lim (ref 94).

Chan-Yeung (2003, Hong Kong, ref A111) – control group includes many with diseases associated with smoking.

Chen (2003, China, ref A112) – no results presented for never smokers.

Gallegos-Arreola (2003, Mexico, ref A113) – only four lung cancer cases and definition of never smoker includes current smokers of <3 cigarettes per day.

Kiyohara (2003, Japan, ref A114) - subset of subjects from Ohno study (ref 61).

Miller (2003, USA, ref A115) - ETS exposure is based on home, work and leisure activities so unexposed group may have substantial ETS exposure, e.g. home and work only.

Brennan (2004, USA and West Europe, ref A116) – combined analysis of Fontham and Boffetta 1 studies (refs 36 and 47).

Cohet (2004, Europe and Brazil, ref A117) – largely same subjects as previously reported in Malats study (ref 56). Cohet includes a few more subjects, but gives less detailed ETS analysis.

Hernández-Garduño (2004, Mexico, ref A118) - control group predominantly lung disease patients.

Behera (2005, India, ref A119) – control group with non-malignant respiratory disease and results for nonsmokers only given as "not significant."

Bock (2005, USA, ref A120) – believed to be based mainly on a subset of subjects from Schwartz (ref 40).

Holcátová (2005, Central East Europe, ref A121) – control group includes smoking-related diseases, results only for sexes combined and prevalence of smoking in controls implausibly low for partners (5%).

Ng (2005, Singapore, ref A122) – subset of Seow study (ref A110).

Wenzlaff (2005, USA, refs A123, A124) – believed to be based mainly on a subset of subjects from Schwartz (ref 40).

Yang (2005, USA, ref A125) – no results presented for never smokers.

Boffetta (2006, Norway, ref A126) – no results presented for never smokers (analyses presented as being of never smokers include former smokers who quit >5 years before enrollment).

Cassidy (2006, England, ref A127) – no results presented for never smokers.

Hemminki (2006, Sweden, ref A128) - no results presented for never smokers.

Spitz (2007, USA, ref A129) – results previously reported by Gorlova (ref 70) using a more detailed ETS exposure index (though based on slightly fewer subjects).

Veglia (2007, Western Europe, ref A130) – results not already reported prevously for EPIC Adulthood (ref 67) are not for never smokers and relate to working in bars or restaurants, not overall workplace ETS exposure.

Vineis (2007, Western Europe, ref A131) - no results presented for never smokers.

Aldington (2008, New Zealand, ref A132) - no results presented for never smokers.

Gorlova (2008, USA, ref A133) – results previously reported by Gorlova (ref 70) using a more detailed ETS exposure index and with separate results for males and females (though based on fewer subjects).

Lan (2008, China, ref A134) - no results presented for never smokers.

Vardavas (2008, Greece, ref A135) - no original results, only estimates of expected numbers of cancers.

Weiss (2008, Shanghai, ref A136) – result not previously reported by Wen (ref 73) is unadjusted and is for very little extra follow-up. The estimate reported is inconsistent with the stated numbers of subjects.

Pronk (2009, Shanghai, ref A137) – the result available, for any lifetime exposure, is unadjusted, is restricted to working women and relates to the study previously reported by Wen (ref 73) in which a similar, adjusted result is available, based on only slightly fewer subjects.

Chiu (2010, Hong Kong, ref A138) – results previously reported by Wang (ref 74b) which used fuller adjustment for possible confounders.

Tang (2010, Singapore, ref A139) - no results presented for never smokers.

Fowke (2011, Shanghai, ref A140) - results previously reported by Wen (ref 73).

Gorlova (2011, USA, ref A141) – results previously reported by Gorlova (ref 70) using a more detailed ETS exposure index and with separate results for males and females (though based on fewer subjects).

Raaschou-Nielsen (2011, Denmark, ref A142) - no results presented for never smokers.

Spitz (2011a, USA, ref A143) – results previously reported by Gorlova (ref 70) using a more detailed ETS exposure index and with separate results for males and females (though based on fewer subjects).

Tse (2011, Hong Kong, ref A144) – no results presented for never smokers.

Tse (2011, Hong Kong, ref A145) – results previously reported by Tse (ref 84).

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