

EPIDEMIOLOGICAL EVIDENCE ON ENVIRONMENTAL TOBACCO SMOKE AND LUNG CANCER

1. Over 70 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 far less data). There is also evidence of a dose-response relationship,¹ 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; over 80% show no statistically significant association between smoking by the husband and the development of lung cancer;
 - the combined results vary over time, with the association being significantly weaker in the studies published from 1990 than in those published in the 1980s;
 - some of the very largest studies show no association, including four of the five studies involving over 400 lung cancer cases. One² of these reported no statistically significant association between lung cancer and any index of ETS exposure, while another³ 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 habits⁴⁻⁶, a conclusion confirmed based on more recent data⁷.

4. There is also some indication from the overall evidence that lung cancer risk among non-smokers might be weakly associated with workplace ETS exposure. However, only six of 37 relative risk estimates are statistically significant and biases that apply to the spousal data are also likely to apply to the workplace data.
5. 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, using the CIA program described by Morris and Gardner.⁸

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.⁹

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 75 studies. 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.

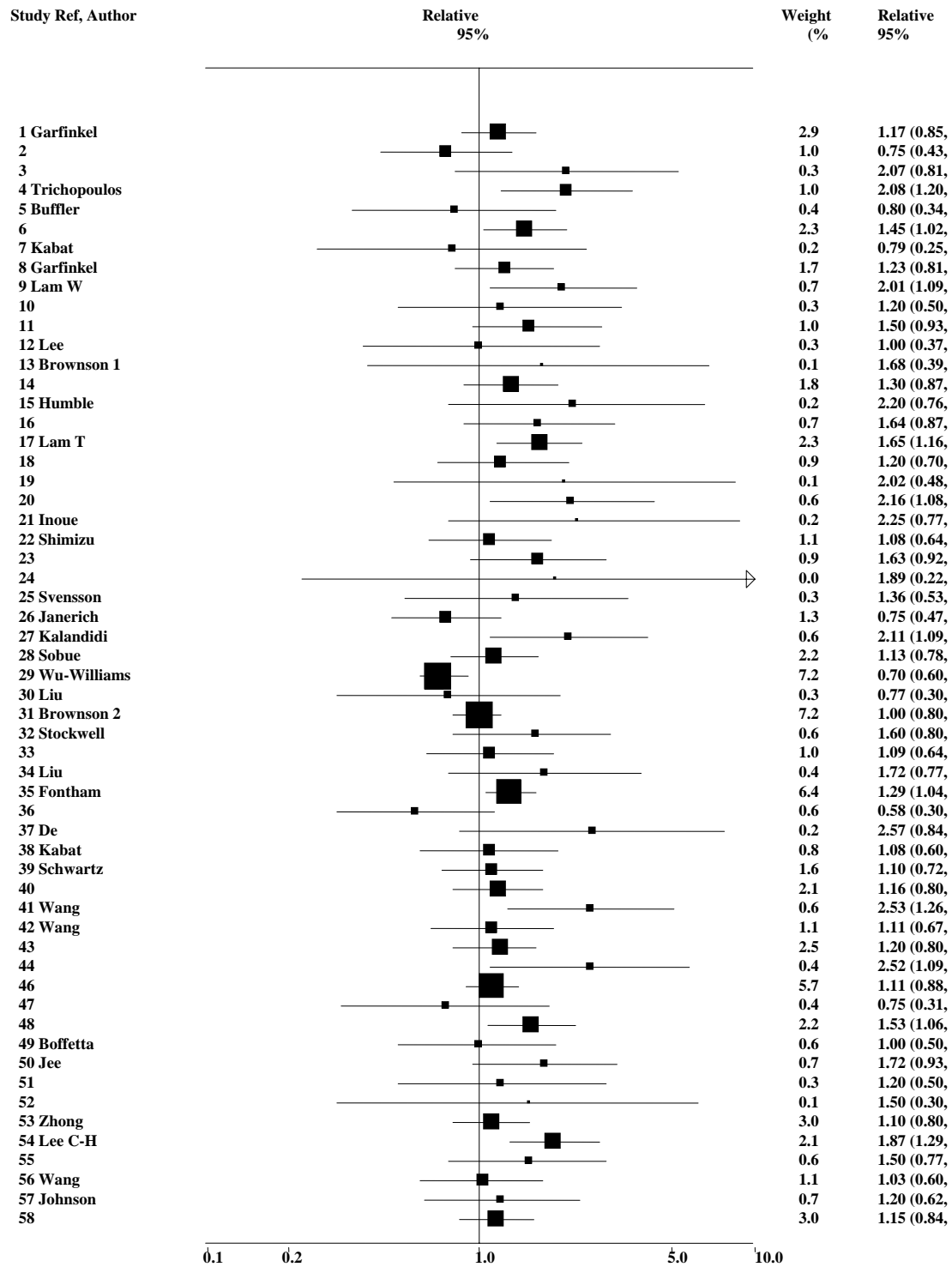
Meta-analyses of these data are available.¹⁰⁻¹²

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References to text

1. Fry JS, Lee PN. Revisiting the association between environmental tobacco smoke exposure and lung cancer risk. I. The dose-response relationship with amount and duration of smoking by the husband. *Indoor Built Environ* 2000;**9**:303-16.
2. Brownson RC, Alavanja MCR, Hock ET, Loy TS. Passive smoking and lung cancer in nonsmoking women. *Am J Public Health* 1992;**82**:1525-30.
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10. Lee PN, Forey BA, Hamling JS. *ETS and lung cancer meta-analyses.* Sutton, Surrey: P N Lee Statistics and Computing Ltd; 2008. www.pnlee.co.uk/reflist.htm [Download LEE2008H]
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12. Lee PN, Forey BA, Hamling JS. *Meta-analyses of the epidemiological evidence relating ETS to lung cancer and heart disease.* Sutton, Surrey: P N Lee Statistics and Computing Ltd; 2008. www.pnlee.co.uk/reflist.htm [Download LEE2008J]

FIGURE 1: Lung cancer and husband's smoking



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FIGURE 1 (continued)

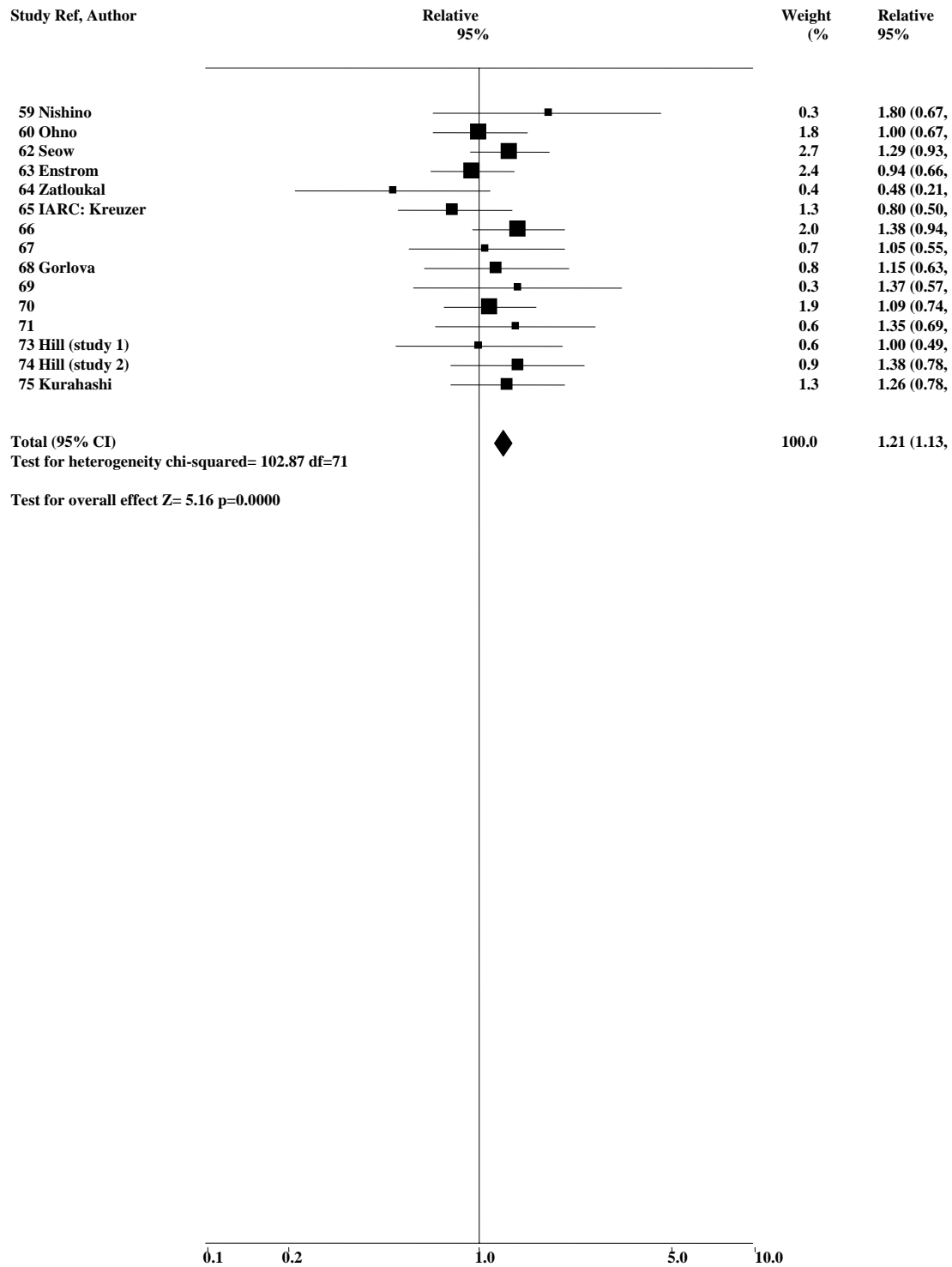


TABLE 1: Relative risk of lung cancer among lifelong nonsmoking women in relation to smoking by the husband

Study					Number of lung cancers	Relative risk (95% confidence limits)	Significance	Notes
Ref	Author	Year	Location	Type				
1	Garfinkel 1	1981	USA	P	153	1.17 (0.85-1.61)		a
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
4	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
6	Hirayama	1984	Japan	P	200	1.45 (1.02-2.08)	+	a
7	Kabat 1	1984	USA	CC	53	0.79 (0.25-2.45)		mr
8	Garfinkel 2	1985	USA	CC	134	1.23 (0.81-1.87)		mr
9	Lam W	1985	Hong Kong	CC	75	2.01 (1.09-3.72)	+	u
10	Wu	1985	USA	CC	31	1.20 (0.50-3.30)		a
11	Akiba	1986	Japan	CC	94	1.50 (0.93-2.76)		ar
12	Lee	1986	UK	CC	32	1.00 (0.37-2.71)		a
13	Brownson 1	1987	USA	CC	19	1.68 (0.39-6.90)		ar
14	Gao	1987	China	CC	246	1.30 (0.87-1.94)		ar
15	Humble	1987	USA	CC	20	2.20 (0.76-6.56)		ar
16a	Koo	1987	Hong Kong	CC	88	1.64 (0.87-3.09)		ar
17	Lam T	1987	Hong Kong	CC	202	1.65 (1.16-2.35)	+	u
18	Pershagen	1987	Sweden	CC	77	1.20 (0.70-2.10)		ar
19	Butler	1988	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	2.25 (0.77-8.85)		a
22	Shimizu	1988	Japan	CC	90	1.08 (0.64-1.82)		mr
23	Choi	1989	Korea	CC	75	1.63 (0.92-2.87)		u
24	Hole	1989	Scotland	P	6	1.89 (0.22-16.12)		uv
25	Svensson	1989	Sweden	CC	38	1.36 (0.53-3.49)		a
26	Janerich	1990	USA	CC	146	0.75 (0.47-1.20)		mrz
27	Kalandidi	1990	Greece	CC	91	2.11 (1.09-4.08)	+	ar
28	Sobue	1990	Japan	CC	144	1.13 (0.78-1.63)		ar
29	Wu-Williams	1990	China	CC	417	0.70 (0.60-0.90)	-	ar
30	Liu Z	1991	China	CC	54	0.77 (0.30-1.96)		ar
31	Brownson 2	1992	USA	CC	432	1.00 (0.80-1.20)		ar
32	Stockwell	1992	USA	CC	210	1.60 (0.80-3.00)		ar
33	Du	1993	China	CC	75	1.09 (0.64-1.85)		dmr
34	Liu Q	1993	China	CC	38	1.72 (0.77-3.87)		r
35a	Fontham	1994	USA	CC	653	1.29 (1.04-1.60)	+	ar
36	Layard	1994	USA	CC	39	0.58 (0.30-1.13)		ar
37	deWaard	1995	Netherlands	CC	23	2.57 (0.84-7.85)		u
38	Kabat 2	1995	USA	CC	69	1.08 (0.60-1.94)		mr
39	Schwartz	1996	USA	CC	185	1.10 (0.72-1.68)		arz
40	Sun	1996	China	CC	230	1.16 (0.80-1.69)		ar
41	Wang S-Y	1996	China	CC	82	2.53 (1.26-5.10)	+	u
42	Wang T-J	1996	China	CC	135	1.11 (0.67-1.84)		m
43a	Cardenas	1997	USA	P	246	1.20 (0.80-1.60)		ar
44	Zheng	1997	China	CC	69	2.52 (1.09-5.85)	+	u
46	Boffetta 1	1998	West Europe	CC	509	1.11 (0.88-1.39)		ar
47	Shen	1998	China	CC	70	0.75 (0.31-1.78)		a
48	Zaridze	1998	Russia	CC	189	1.53 (1.06-2.21)	+	ar
49	Boffetta 2	1999	Europe	CC	66	1.00 (0.50-1.90)		ar
50	Jee	1999	Korea	P	79	1.72 (0.93-3.18)		ar
51	Rapiti	1999	India	CC	41	1.20 (0.50-2.90)		ar
52	Speizer	1999	USA	P	35	1.50 (0.30-6.30)		a
53	Zhong	1999	China	CC	504	1.10 (0.80-1.50)		ar
54	Lee C-H	2000	Taiwan	CC	268	1.87 (1.29-2.71)	+	arv
55	Malats	2000	Europe/Brazil	CC	105	1.50 (0.77-2.91)		arz
56	Wang L	2000	China	CC	200	1.03 (0.60-1.70)		ar
57	Johnson	2001	Canada	CC	71	1.20 (0.62-2.30)		arv
58	Lagarde	2001	Sweden	CC	242	1.15 (0.84-1.58)		artz
59	Nishino	2001	Japan	P	24	1.80 (0.67-4.60)		ar
60	Ohno	2002	Japan	CC	191	1.00 (0.67-1.49)		acr
62	Seow	2002	Singapore	CC	176	1.29 (0.93-1.80)		u
63	Enstrom	2003	USA	P	177	0.94 (0.66-1.33)		ar

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

Study		Year	Location	Type	Number of lung cancers	Relative risk (95% confidence limits)	Significance	Notes
Ref	Author							
64	Zatloukal	2003	Czech Republic	CC	84	0.48 (0.21-1.09)		apr
65	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
67	Vineis	2005	Western Europe	P	70	1.05 (0.55-2.02)		arz
68	Gorlova	2006	USA	CC	130	1.15 (0.63-2.10)		ar
69	Rylander	2006	Sweden	CC	31	1.37 (0.57-3.30)		az
70	Wen	2006	China	P	106	1.09 (0.74-1.61)		ar
71	Yu	2006	Hong Kong	CC	200	1.35 (0.69-2.62)		ar
73	Hill (study 1)	2007	New Zealand	P	63	1.00 (0.49-2.01)		ar
74	Hill (study 2)	2007	New Zealand	P	123	1.38 (0.78-2.41)		ar
75	Kurahashi	2008	Japan	P	109	1.26 (0.78-2.03)		ar

Notes for Table 1

Study 45 (Auvinen), which only concerns men, study 61 (Rachtan), which only concerns childhood ETS exposure, and study 72 (Zeka) which only concerns workplace exposure, are not considered in Table 1.

Study 33 (Du) also reported that ETS was not statistically associated with lung cancer in an earlier similar study.

Study 67 (Vineis) 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 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 name of first author in publication from which data extracted, see references.
- Study year is year of that publication.
- Study type: CC case control; P prospective
- Number of lung cancers in lifelong nonsmokers are study totals for females. For specific exposures numbers may be less.
- Where necessary, relative risks and 95% confidence limits were estimated from 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 "Spouse-Pairs Cohort" as "AHSMOG Cohort" not never smokers;
- c based on data for hospital controls. Data for population controls not used as non-response rate very high;
- d based on data for two control groups combined;
- 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 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 and assumed to apply to each sex separately, with confidence intervals weighted according to numbers of subjects by sex.

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

Factors other than age taken account of 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	51	residence; religion
8	hospital	53	income; vitamin C; respondent status;
11	city; vital status; participation in medical examinations		smokiness of kitchen; family history of lung cancer; potentially high risk occupation
13	income; occupation	54	residential area; education; occupation;
14	education		tuberculosis; cooking fumes; fume extractor centre
15	ethnicity	55	
16	live births; years since exposure ceased; schooling	56	ownership of colour TV; number of cattle;
18	vital status		prefecture; childhood ETS exposure
22	hospital	57	province; education; total fruit and vegetables
26	residence; direct/surrogate interview	58	radon; SES; occupation; residence; urban/rural
27	years of schooling; interviewer;	59	alcohol; green and yellow vegetables; fruit;
	total energy intake; fruit consumption		meat; study area; history of respiratory disease
28	education	60	research institution (region)
29	education; study area	61	beer; vodka; milk; butter; margarine; cheese;
30	age of starting to cook; years of cooking		meat; fruit; vegetables; carrots; spinach; siblings
31	history of lung disease		with cancer; tuberculosis; place of residence; any
32	race; education	63	of six defined occupational exposures
33	residence		race; education; exercise; body mass index;
34	education; occupation; living area	64	urbanisation; fruit or fruit juice intake; health status
35	race; area; education; fruits; vegetables and supplemental vitamin index; family history of lung cancer; employment in high risk occupations	65	residence; education
36	race	66	region
38	race; hospital; date of interview; years of education	67	education
39	race	68	country; school years; energy intake; fruit and vegetable consumption; physical activity
40	education	70	race; education; socio-economic status
43	race; education; blue collar employment; vegetable consumption; fat consumption; occupational exposure to asbestos; history of chronic lung disease	71	education; occupation; income; physical activity;
46	study centre		body mass intake; meat; vegetables; fruit
48	education		education; employment; history of lung diseases;
49	centre		family history of lung cancer; radon, kerosene use;
50	socio-economic status; residence; husband's vegetable consumption; husband's occupation	73	firewood use; incense burning; mosquito coil use;
		74	years of cooking; orange/yellow vegetables; dark green vegetables; meats; citrus fruits; salted fish;
		75	pickled vegetables; multivitamins; coffee; tea
			ethnicity
			ethnicity; marital status; SES; household car access; tenure; small-area deprivation index
			study area; alcohol; family history of lung cancer;
			menopausal status

TABLE 1 (continued 3) Relative risk of lung cancer among lifelong nonsmoking women in relation to smoking by the husband**Indices of ETS exposure used other than husband smoked**

Study	Index	Study	Index
5	Household smoker smokes regularly	57	Exposed at home
13	Presence of persons smoking 4+ hours/day	58	Exposed at home
24	Household smoker ever smoked	62	Exposed at home at least weekly
25	Exposure at home and/or at work as an adult	64	Exposed at home and/or work >3 hrs/day
30	Smoker in household	66	Exposed at home
37	Urinary cotinine >9.2 ng/mg creatinine	67	Exposed at home and/or work
39	Exposed at home	68	Exposed at home
41	Exposed at home and/or work	69	Exposed at home
44	Household exposure	71	Exposed at home and/or work
47	Any exposure	73	Living in a smoking household
52	Exposure in adulthood	74	Living in a smoking household
56	Exposed at home		

FIGURE 2: Lung cancer and wife's smoking

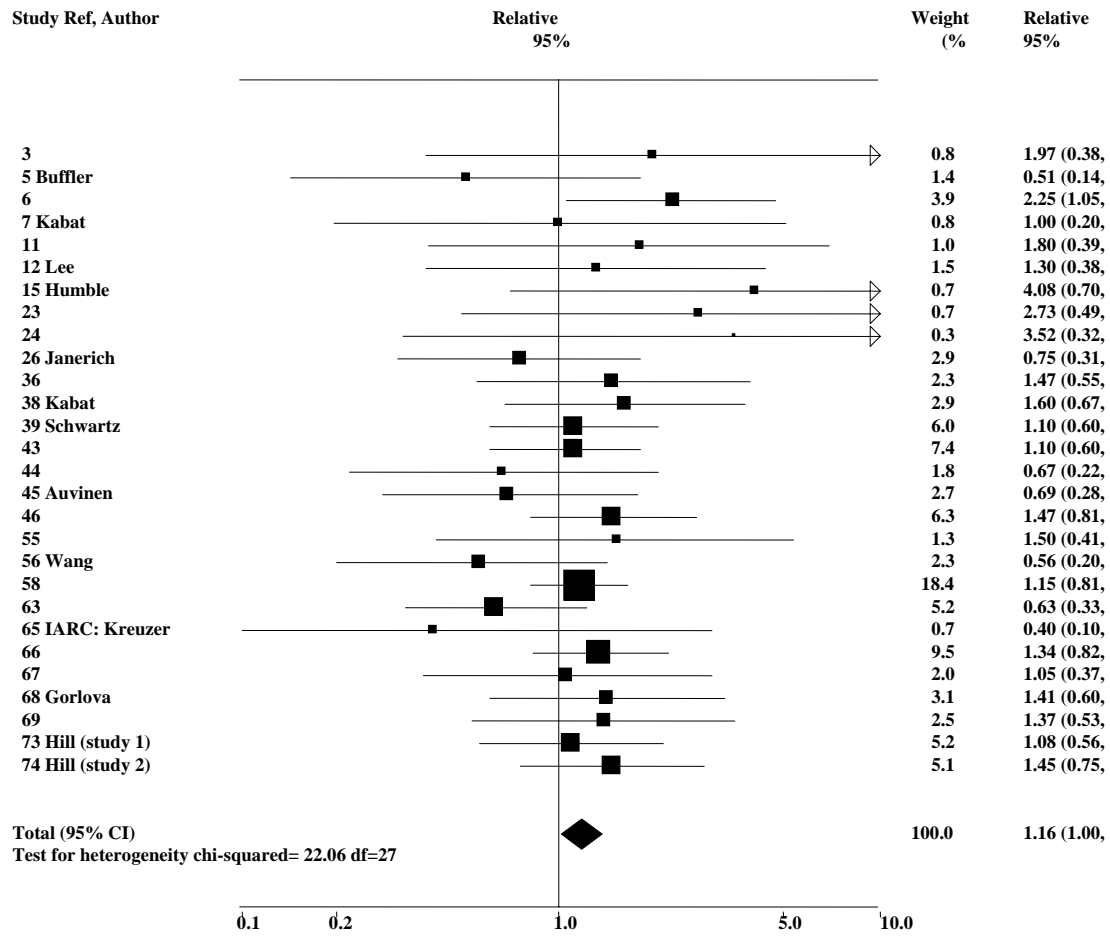


TABLE 2: Relative risk of lung cancer among lifelong nonsmoking men in relation to smoking by the wife

Study		Year	Location	Type	Number of lung cancers	Relative risk (95% confidence limits)	Significance	Notes
Ref	Author							
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	P	64	2.25 (1.05-4.76)	+	a
7	Kabat 1	1984	USA	CC	25	1.00 (0.20-5.07)		mr
11	Akiba	1986	Japan	CC	19	1.80 (0.39-6.96)		ar
12	Lee	1986	UK	CC	15	1.30 (0.38-4.39)		a
15	Humble	1987	USA	CC	8	4.08 (0.70-23.91)		ar
23	Choi	1989	Korea	CC	13	2.73 (0.49-15.21)		u
24	Hole	1989	Scotland	P	3	3.52 (0.32-38.65)		u
26	Janerich	1990	USA	CC	45	0.75 (0.31-1.78)		mrz
36	Layard	1994	USA	CC	21	1.47 (0.55-3.94)		ar
38	Kabat 2	1995	USA	CC	41	1.60 (0.67-3.82)		mr
39	Schwartz	1996	USA	CC	72	1.10 (0.60-2.03)		arz
43a	Cardenas	1997	USA	P	116	1.10 (0.60-1.80)		ar
44	Zheng	1997	China	CC	25	0.67 (0.22-2.04)		u
45	Auvinen	1998	Finland	CC	44	0.69 (0.28-1.74)		as
46	Boffetta 1	1998	West Europe	CC	141	1.47 (0.81-2.66)		ar
55	Malats	2000	Europe/Brazil	CC	17	1.50 (0.41-5.43)		arz
56	Wang L	2000	China	CC	33	0.56 (0.20-1.40)		ar
58	Lagarde	2001	Sweden	CC	191	1.15 (0.81-1.63)		artz
63	Enstrom	2003	USA	P	79	0.63 (0.33-1.22)		ar
65	IARC: Kreuzer	2004	Germany	CC	23	0.40 (0.10-3.00)		u
66	McGhee	2005	Hong Kong	CC	145	1.34 (0.82-2.17)		ar
67	Vineis	2005	Western Europe	P	27	1.05 (0.37-3.01)		arz
68	Gorlova	2006	USA	CC	63	1.41 (0.60-3.30)		ar
69	Rylander	2006	Sweden	CC	18	1.37 (0.53-3.53)		az
73	Hill (study 1)	2007	New Zealand	P	84	1.08 (0.56-2.09)		av
74	Hill (study 2)	2007	New Zealand	P	111	1.45 (0.75-2.81)		aw

Notes for Table 2

Study 33 (Du) also reported that ETS was not statistically associated with lung cancer in an earlier similar study

Study 67 (Vineis) 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 name of first author in publication from which data extracted, see references.
- Study year is 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.
- Where necessary, relative risks and 95% confidence limits were estimated from data presented.
- 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;
- r adjusted or matched for other risk factors (see Table 1);
- s adjusted for sex; data 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 and assumed to apply to each sex separately, with confidence intervals weighted according to numbers of subjects by sex.

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

Indices of ETS exposure used other than wife smoked

Study	Index
5	Household member smokes regularly
24	Household member ever smoked
39	Exposed at home
44	Household exposure
45	Passive smoking
56	Exposed at home
58	Exposed at home
66	Exposed at home
67	Exposed at home and/or work
73	Living in a smoking household
74	Living in a smoking household

FIGURE 3: Lung cancer and workplace ETS exposure

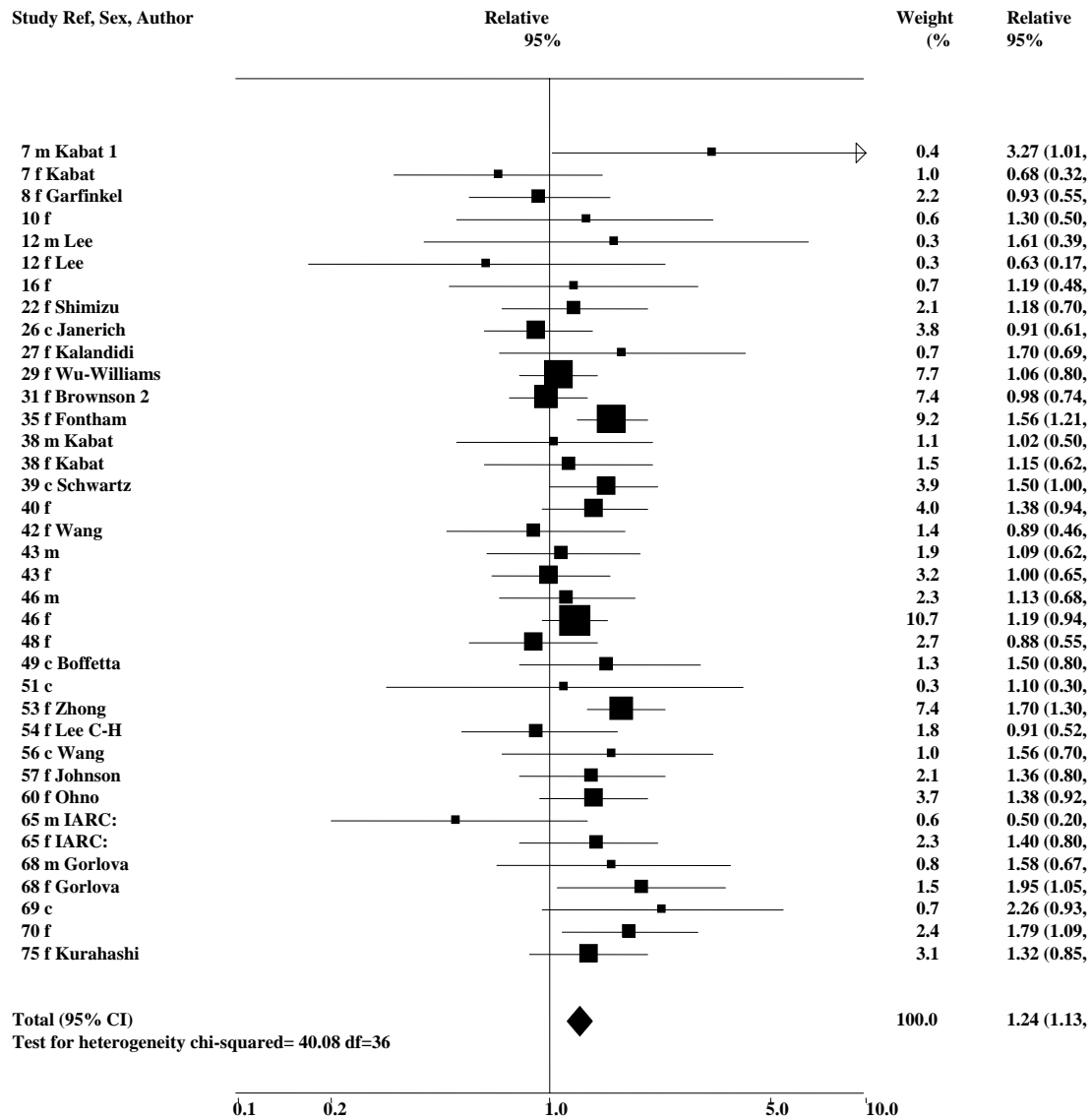


TABLE 3: Relative risk of lung cancer among lifelong nonsmokers in relation to ETS exposure in the workplace

Study				Relative risk (95% confidence limits)	Significance	Notes
Ref	Author	Location	Sex			
7	Kabat 1	USA	Males Females	3.27 (1.01-10.62) 0.68 (0.32-1.47)	+	mr mr
8	Garfinkel 2	USA	Females	0.93 (0.55-1.55)		mr
10	Wu	USA	Females	1.30 (0.50-3.30)		a
12	Lee	UK	Males Females	1.61 (0.39-6.60) 0.63 (0.17-2.33)		u u
16b	Koo	Hong Kong	Females	1.19 (0.48-2.95)		u
22	Shimizu	Japan	Females	1.18 (0.70-2.01)		mr
26	Janerich	USA	Combined	0.91 (0.61-1.35)		mrx
27	Kalandidi	Greece	Females	1.70 (0.69-4.18)		uy
29	Wu-Williams	China	Females	1.06 (0.80-1.40)		arw
31	Brownson 2	USA	Females	0.98 (0.74-1.31)		arz
35b	Fontham	USA	Females	1.56 (1.21-2.02)	+	ar
38	Kabat 2	USA	Males Females	1.02 (0.50-2.09) 1.15 (0.62-2.13)		mr mr
39	Schwartz	USA	Combined	1.50 (1.00-2.20)	?	ar
40	Sun	China	Females	1.38 (0.94-2.04)		ar
42	Wang T-J	China	Females	0.89 (0.46-1.73)		m
43b	Cardenas	USA	Males Females	1.09 (0.62-1.91) 1.00 (0.65-1.54)		ar ar
46	Boffetta 1	West Europe	Males Females	1.13 (0.68-1.86) 1.19 (0.94-1.51)		ar
48	Zaridze	Russia	Females	0.88 (0.55-1.41)		ar
49	Boffetta 2	Europe	Combined	1.50 (0.80-3.00)		ar
51	Rapiti	India	Combined	1.10 (0.30-4.10)		ar
53	Zhong	China	Females	1.70 (1.30-2.30)	+	ar
54	Lee C-H	Taiwan	Females	0.91 (0.52-1.62)		ar
56	Wang L	China	Combined	1.56 (0.70-3.30)		arh
57	Johnson	Canada	Females	1.36 (0.80-2.31)		arv
60	Ohno	Japan	Females	1.38 (0.92-2.05)		ar
65	IARC: Kreuzer	Germany	Males Females	0.50 (0.20-1.30) 1.40 (0.80-2.20)		u ar
68	Gorlova	USA	Males Females	1.58 (0.67-3.70) 1.95 (1.05-3.62)	+	ar ar
69	Rylander	Sweden	Combined	2.26 (0.93-5.48)		a
70	Wen	China	Females	1.79 (1.09-2.93)	+	ar
75	Kurahashi	Japan	Females	1.32 (0.85-2.04)		ar

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

Notes for Table 3

The Stockwell study (32) also reported finding no association but gave no detailed results.

An additional study by Zeka (72) 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:

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

- Study author is name of first author in publication from which data 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:

- | | |
|--|---|
| <ul style="list-style-type: none"> 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; r adjusted or matched for other risk factors (see Table 1); u unadjusted for age or other factors; | <ul style="list-style-type: none"> v 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; z 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

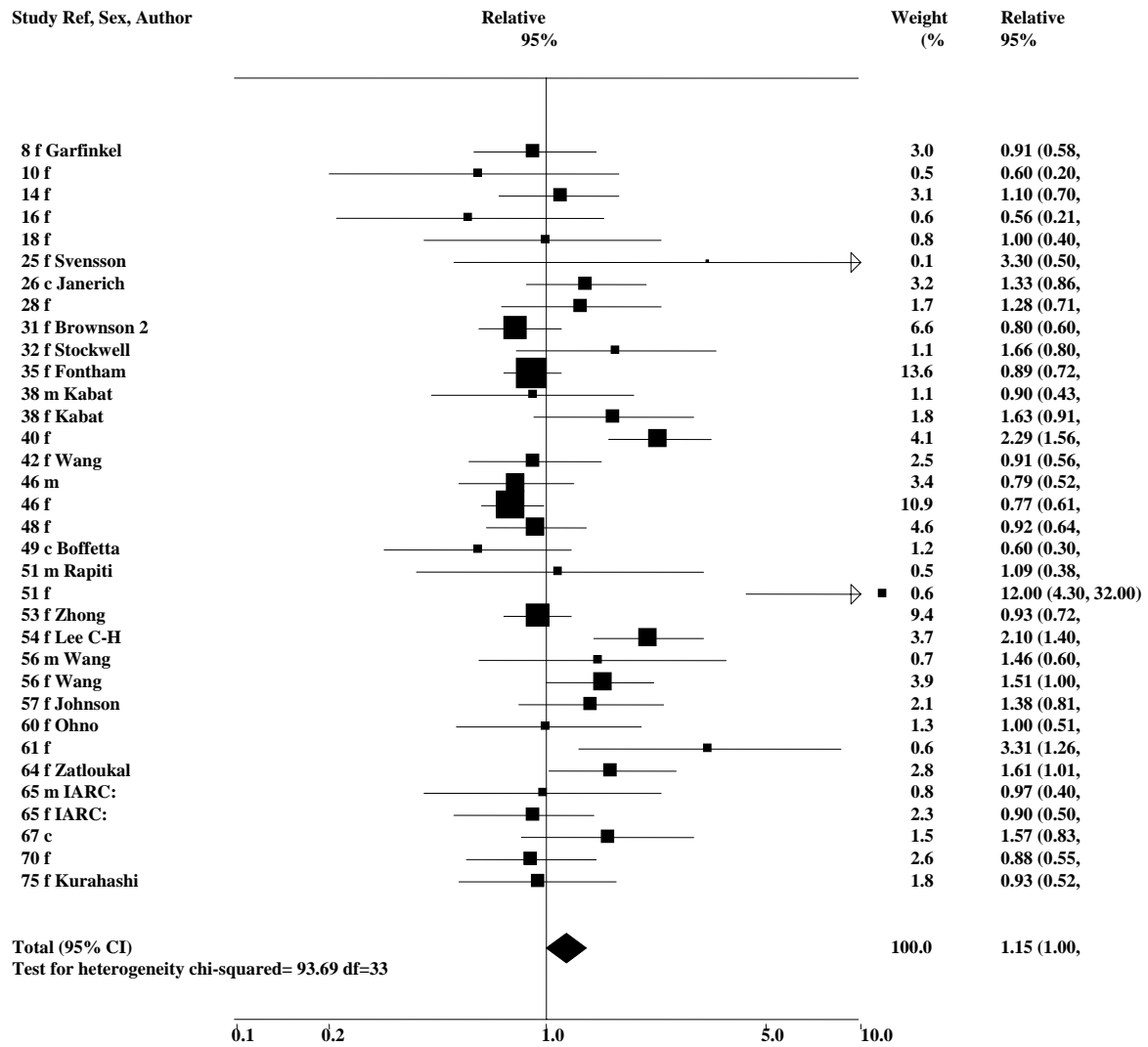


TABLE 4: Relative risk of lung cancer among lifelong nonsmokers in relation to ETS exposure in childhood

Study				Relative risk (95% confidence limits)	Significance	Notes
Ref	Author	Location	Sex			
8	Garfinkel 2	USA	Females	0.91 (0.58-1.42)		mr
10	Wu	USA	Females	0.60 (0.20-1.70)		a
14	Gao	China	Females	1.10 (0.70-1.70)		ar
16a	Koo	Hong Kong	Females	0.56 (0.21-1.50)		ar
18	Pershagen	Sweden	Females	1.00 (0.40-2.30)		ar
25	Svensson	Sweden	Females	3.30 (0.50-18.80)		a
26	Janerich	USA	Combined	1.33 (0.86-2.06)		mr
28	Sobue	Japan	Females	1.28 (0.71-2.31)		ar
31	Brownson 2	USA	Females	0.80 (0.60-1.10)		ar
32	Stockwell	USA	Females	1.66 (0.80-3.44)		ar
35a	Fontham	USA	Females	0.89 (0.72-1.10)		ar
38	Kabat 2	USA	Males Females	0.90 (0.43-1.89) 1.63 (0.91-2.92)		mr mr
40	Sun	China	Females	2.29 (1.56-3.37)	+	ar
42	Wang T-J	China	Females	0.91 (0.56-1.48)		m
46	Boffetta 1	West Europe	Males Females	0.79 (0.52-1.21) 0.77 (0.61-0.98)	-	ar ar
48	Zaridze	Russia	Females	0.92 (0.64-1.32)		ar
49	Boffetta 2	Europe	Combined	0.60 (0.30-1.20)		ar
51	Rapiti	India	Males Females	1.09 (0.38-3.18) 12.0 (4.30-32.0)	+	ar ar
53	Zhong	China	Females	0.93 (0.72-1.20)		ar
54	Lee C-H	Taiwan	Females	2.10 (1.40-3.14)	+	ar
56	Wang L	China	Males Females	1.46 (0.60-3.70) 1.51 (1.00-2.20)	+	arh arh
57	Johnson	Canada	Females	1.38 (0.81-2.34)		arv
60	Ohno	Japan	Females	1.00 (0.51-1.98)		acr
61	Rachtan	Poland	Females	3.31 (1.26-8.69)	+	ar
64	Zatloukal	Czech Republic	Females	1.61 (1.01-2.57)	+	apr
65	IARC: Kreuzer	Germany	Males Females	0.97 (0.40-2.30) 0.90 (0.50-1.40)		ar ar
67	Vineis	Western Europe	Combined	1.57 (0.83-2.95)		ar
70	Wen	China	Females	0.88 (0.55-1.43)		ar
75	Kurahashi	Japan	Females	0.93 (0.52-1.66)		ar

TABLE 4 (continued) Relative risk of lung cancer among lifelong nonsmokers in relation to ETS exposure in childhood

Notes for Table 4

Two other studies, Correa (3) and Akiba (11), reported finding no association but gave no detailed results.

Study 67 (Vineis) provided results from only one type of analysis of ETS exposure in childhood - an analysis of the whole cohort using Cox's proportional hazards model.

- Where study only provided relative risk estimates for individual sources of ETS exposure, that for maternal smoking was used.
- Where study provided relative risk estimates for different time points, that for the earliest was used.
- Study author is name of first author in publication from which data 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.
- 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) - results not 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.

Varela (1987, USA, ref A21) - results superseded by 1990 Janerich paper (ref 26).

Axelson (1988, Sweden, ref A22) - 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 A23) – results already given in 1984 paper (ref 6).

Katada (1988, Japan, ref A24) - 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 A25) – review presenting results for three studies already considered, Chan (ref 2), Koo (ref 16) and Lam T (ref 17).

Pershagen (1988, Sweden, ref A26) - results already given in 1987 paper (ref 18).

Svensson (1988, Sweden, ref A27) - results superseded by 1989 paper (ref 25).

Hirayama (1989, Japan, ref A28) – 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 A29) - results not presented for never smokers.

Sandler (1989, US, ref A30) - results presented only for cancers of smoking-related sites and not for lung cancer.

Wang (1989, China, ref A31) – index of ETS exposure not given, not stated whether results referred to never smokers, and relative risk not given.

Chen (1990, Taiwan, ref A32) - results seem not to be presented for never smokers, and no details given of index of ETS exposure used.

Hirayama (1990, Japan, refs A33, A34) - results already given in 1984 paper (ref 6).

Kabat (1990, USA, ref A35) - results superseded by 1995 paper (ref 38).

Liu (1990, China, ref A36) – results superseded by 1991 paper (ref 30).

Miller (1990, US, ref A37) - results concern respiratory, not lung cancer and only include three cases in spousal smoking analyses.

Sobue (1990, Japan, ref A38) - results given in other 1990 paper (ref 28).

Stellman (1990, USA, ref A39) – results already given in 1985 Garfinkel paper (ref 8).

Ye (1990, China, ref A40) - results not presented for never smokers.

Fontham (1991, USA, ref A41) - results superseded by 1994 paper (ref 35a).

He (1991, China, ref A42) - results given in 1991 Liu paper (ref 30).

Holowaty (1991, Canada, ref A43) - results not presented for never smokers.

Jöckel (1991, Germany, ref A44) – results mainly included as part of Boffetta 1 study (ref 46).

Stockwell (1991, USA, ref A45) – results superseded by 1992 paper (ref 32).

Ger (1992, China, ref A46) - results not presented for never smokers.

Hirayama (1992, Japan, ref A47) – results already given in 1984 paper (ref 6).

Jöckel (1992, Germany, ref A48) - results mainly included as part of Boffetta 1 study (ref 46).

Fontham (1993, USA, refs A49, A50) - results superseded by 1994 paper (ref 35a).

Ger (1993, China, ref A51) - results not presented for never smokers.

Järholm (1993, Sweden, ref A52) - only six lung cancers in never smoking women and cited odds ratio for ETS inconsistent with data presented.

Lan (1993, China, ref A53) - 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 A54) - review paper of lung cancer risk in food-service workers, data generally relating to smokers and non-smokers combined.

Wang (1993, China, ref A55) – believed to be based on a subset of subjects from Wu-Williams study (ref 29).

Alavanja (1994, USA, ref A56) - results already given in 1992 Brownson paper (ref 31).

Geng (1994, China, ref A57) - results already given in 1988 paper (ref 20).

Kabat (1994, USA, ref A58) - results superseded by 1995 paper (ref 38).

Miller (1994, USA, ref A59) - control group (formed from decedents from all causes of death except lung cancer) contains many with diseases associated with smoking.

Shen (1994, China, ref A60) – results not presented for never smokers, and superseded by 1998 paper (ref 47).

Wang (1994, China, ref A61) - believed to be based on subset of subjects from Wu-Williams study (ref 29).

Zaridze (1994, Russia, ref A62) - results superseded by the 1998 paper (ref 48).

Alavanja (1995, USA, ref A63) - results already given in 1992 Brownson paper (ref 31).

Du (1995, China, ref A64) - results already given in 1993 Du paper (ref 33).

Ellard (1995, UK, ref A65) – gives results for total nicotine metabolites. Results for cotinine already given in deWaard study (ref 37).

Auvinen (1996, Finland, ref A66) - corrected results given in 1998 (ref 45).

Dai (1996, China, ref A67) - exposure to ETS recorded (source unstated) but not significant in regression analysis and relative risk not given.

Du (1996, China, ref A68) - results already given in 1993 Du paper (ref 33).

Lei (1996, China, ref A69) - results already given in 1993 Du paper (ref 33).

Luo (1996, China, ref A70) - results not presented for never smokers.

Shen (1996, China, ref A71) – results superseded by 1998 paper (ref 47).

Shen (1996, China, ref A72) – results not presented for never smokers, and superseded by 1998 paper (ref 47).

Shen (1996, China, ref A73) - results not presented for never smokers.

Wang (1996, China, ref A74) - believed to be based on subset of subjects from Wu-Williams study (ref 29).

Yu S-Z (1996, China, ref A75) - 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 A76) - results not presented for never smokers.

Cardenas (1997, USA, ref A77) – gives corrected age-standardized results for Cardenas study (ref 43), but results used are adjusted for age and other factors.

Dai (1997, China, ref A78) - results not presented for never smokers.

Jöckel (1997, Germany, ref A79) - results mainly included as part of Boffetta 1 study (ref 46).

- Ko (1997, Taiwan, ref A80) – results superseded by Lee C-H report (ref 54).
- Nyberg (1997, Sweden, ref A81) - results mainly included as part of Boffetta 1 study (ref 46).
- Yang (1997, USA, ref A82) - results not presented for never smokers.
- Boffetta (1998, West Europe, refs A83, A84) – results given in 1998 paper cited (ref 46).
- Jöckel (1998, Germany, ref A85) - results mainly included as part of Boffetta 1 study (ref 46).
- Nyberg (1998, Sweden, ref A86) - results mainly included as part of Boffetta 1 study (ref 46).
- Wichmann (1998, Germany, ref A87) – results mainly included as part of Boffetta 1 study (ref 46).
- Zaridze (1998, Russia, ref A88) – results superseded by other 1998 paper (ref 48).
- Zemlianaja (1998, Russia, ref A89) – results superseded by 1998 Zaridze paper (ref 48).
- Bennett (1999, USA, ref A90) - main results already given in 1992 Brownson paper (ref 31).
- Boffetta (1999, West Europe, ref A91) - main results already given by Boffetta 1 (ref 46).
- Brennan (2000, West Europe, ref A92) - main results already given by Boffetta 1 (ref 46).
- Johnson (2000, USA, refs A93, A94) - results superseded by 2001 paper (ref 57).
- Kleinerman (2000, China, ref A95) - results superseded by Wang L paper (ref 56).
- Ko (2000, Taiwan, ref A96) - results superseded by Lee C-H paper (ref 54).
- Kreuzer (2000, Germany, ref A97) - results included as parts of Boffetta 1 study (ref 46) and IARC: Kreuzer study (ref 65).
- Li (2000, China, ref A98) – results not presented for never smokers.
- Zhou (2000, China, ref A99) - results not presented for never smokers.
- Goldoni (2001, Italy, ref A100) – results not presented for never smokers.
- Kreuzer (2001, Germany, ref A101) - results mainly included as part of Boffetta 1 study (ref 46).
- Kubík (2001, Czech Republic, ref A102) – results superseded by 2003 Zatloukal paper (ref 64).
- Lee (2001, Taiwan, ref A103) - results not presented for never smokers. Results for never smokers given in 2000 paper (ref 54).
- Liu (2001, China, ref A104) – proved unobtainable.
- Hu (2002, Canada, ref A105) - similar analyses to those given by Johnson (ref 57), but based on fewer controls.
- Kreuzer (2002, Germany, ref A106) - results mainly included as part of Boffetta 1 study (ref 46).
- Merrill (2002, Morocco, ref A107) – abstract reporting same study as 2002 paper by Sasco (ref A110).
- Miller (2002, USA, ref A108) - abstract with no relative risks cited.
- Rachtan (2002, Poland, ref A109) - results not presented for never smokers. Results for never smokers given in another Rachtan paper (ref 61).

Sasco (2002, Morocco, ref A110) - results not presented for never smokers.

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

Chen (2003, China, ref A112) – results not 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 60).

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 35 and 46).

Cohet (2004, Europe and Brazil, ref A117) – largely same subjects as previously reported in Malats study (ref 55). 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 39).

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 62).

Wenzlaff (2005, USA, refs A123, A124) – believed to be based mainly on a subset of subjects from Schwartz (ref 39).

Yang (2005, USA, ref A125) – results not presented for never smokers.

Boffet (2006, Norway, ref A126) – results not 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) – results not presented for never smokers.

Franco-Marina (2006, Mexico, ref A128) – results not presented for never smokers.

Hemminki (2006, Sweden, ref A129) – results not presented for never smokers.

Spitz (2007, USA, ref A130) – results previously reported by Gorlova (ref 68) using a more detailed ETS exposure index (though based on slightly fewer subjects).

Veglia (2007, Western Europe, ref A131) – results not already reported previously for Vineis (ref 67) are not for never smokers and relate to working in bars or restaurants, not overall workplace ETS exposure.

Aldington (2008, New Zealand, ref A132) – results not presented for never smokers.

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