

## EPIDEMIOLOGICAL EVIDENCE ON ENVIRONMENTAL TOBACCO SMOKE AND HEART DISEASE

1. Over 30 epidemiological studies of heart disease and ETS among lifelong non-smokers have been published.
2. The overall evidence from these studies does not indicate an increased risk of heart disease in relation to ETS exposure in the workplace, with only one of 18 results reported showing a statistically significant association.
3. Although most published estimates for spousal smoking (at least 33 out of 48)\* are not statistically significant, there have been reports of a significant association and dose-response relationship in some studies. However, there are a number of reasons why the findings should not be interpreted as indicating a causal effect of ETS exposure including:
  - the reported results vary markedly with study size. Meta-analyses by study size show quite a small reported increase in risk (less than 10%) in studies involving over 1000 heart disease cases, but a much larger reported increase (over 50%) in studies with less than 100 cases.
  - many of the studies fail to consider possible lifestyle confounding factors. There are over 300 different risk factors reported for heart disease<sup>1</sup> and several studies have shown differences in many lifestyle factors between smoking and non-smoking households.<sup>2-8</sup>
  - the studies generally rely on reported rather than objectively measured ETS exposure data. While one<sup>9</sup> of the three studies<sup>10,11</sup> to use serum cotinine as a marker of ETS exposure found a significant relationship between this marker and risk of heart disease, the combined evidence from these studies does not show a significant relationship.
  - some of the studies<sup>12-14</sup> have relied on unvalidated reports by the subject of current or past heart disease, with no confirmation of the diagnosis.
  - results from one of the very largest studies,<sup>15</sup> which found no relationship with spousal smoking, have been excluded by some reviewers.<sup>16,17</sup> Another recent very large study,<sup>18</sup> which also found no relationship, has been widely criticised but for reasons which bear little or no relationship to the data presented.<sup>19</sup> Whether or not its results are excluded from overall analysis makes little difference to the overall conclusions to be drawn.
  - the studies may have inappropriately included some misclassified current and former smokers. A study reporting particularly high heart disease mortality among smokers who deny smoking,<sup>20</sup> suggests the possibility of bias resulting from such misclassification.
4. Extrapolation from active smoking data to estimate risk at low exposure lacks scientific credibility. The mechanistic theories that have been proposed to support such extrapolation<sup>16,21</sup> are speculative.
5. Taken as a whole, the epidemiology does not provide strong support for the claim that exposure to ETS causes heart disease in non-smokers.

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\* Based on covariate adjusted data where available; the figure of 33 out of 48 applies when spousal current smoking is used as the index of choice, where estimates for both spousal current and spousal ever smoking are available. It would be 35 out of 48 were spousal ever smoking used as the index of choice. For three estimates the significance was unknown.

## THE DATA

The tables and figures that follow summarize the key evidence in relation to heart disease and ETS exposure.

- Table 1 gives details of the 33 studies providing data.
- Table 2 shows the actual indices of spousal smoking (or the nearest equivalent) for which data are available.
- Tables 3 and 5 show, for spousal smoking and for workplace ETS exposure respectively, the individual relative risk estimates and 95% confidence limits for each successive study.
- Tables 4 and 6 show, for spousal smoking and workplace ETS exposure respectively, relative risk estimates by extent of exposure together with the significance of the dose-related trend statistic.
- Table 7 presents data in relation to other indices of ETS exposure.

The term "relative risk" is taken to include direct estimates of the relative risk from prospective studies, and indirect estimates (odds ratios) from case-control or cross-sectional studies. Relative risk estimates and 95% confidence limits in Tables 3 to 7 are adjusted for covariates if adjusted data are available, and otherwise are unadjusted. Where, in some cases, 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.<sup>22</sup>

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 confidence intervals for overall exposure.<sup>23</sup>

The tables are based on results from a total of 33 studies. Appendix A explains why results from certain other publications, which might have been thought to cite relevant data, are not included in the tables.

Meta-analyses of these data are available.<sup>24-26</sup>

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**TABLE 1: Studies providing information on risk of heart disease in relation to ETS exposure in lifelong non-smokers**

Study					Endpoints		Number of heart disease cases in lifelong non-smokers		
Ref	Author	Year	Location	Type	Fatality	Disease	Females	Combined	Males
1a	Hirayama	1984	Japan	P	F	IHD	494		
2	Garland	1985	USA/California	P	F	IHD	19		
3	Lee	1986	England	CC	NF	IHD	77		41
4	Martin	1986	USA/Utah	CS	NF	PHA	23		
5	Svendsen	1987	USA	P	F,NF	IHD,IHD			69
6	Butler	1988	USA/California	P	F	IHD	80		
7	Palmer	1988	USA/?	CC	NF	MI	336		
8	Hole	1989	Scotland	P	F,NF	IHD,A/E	55		65
9	Jackson	1989	New Zealand	CC	F,NF	IHD,MI	73		230
10	Sandler	1989	USA/Maryland	P	F	AHD	988		370
11	Humble	1990	USA/Georgia	P	F	CVD	76		
12	Dobson	1991	Australia	CC	F+NF	IHD+MI	160		183
13	La Vecchia	1993	Italy	CC	NF	FMI	44		69
14	Layard	1995	USA	CC	F	IHD	914		475
15	LeVois (CPS-I)	1995	USA	P	F	AHD	7133		7758
16	Mannino	1995	USA	CS	NF	CVD	*		*
17	Muscat	1995	USA/4 cities	CC	NF	NMI	46		68
18	Tunstall-Pedoe	1995	Scotland	CS	NF	IHD		428	
19	Steenland	1996	USA	P	F	IHD	1325		2494
20	Janghorbani	1997	Iran	CC	NF	IHD	200		
21	Kawachi	1997	USA	P	F+NF	IHD+MI	152		
22	Ciruzzi	1998	Argentina	CC	NF	FMI	180		156
23	McElduff	1998	Australia	CC	F+NF	MI+MI	85		198
24	Spencer	1999	Australia	CC	NF	FMIS			91
25a	He	2000	China	CC	NF	MI/CS	115		
26	Iribarren	2001	USA	CS	NF	HD	1856		2945
27	Rosenlund	2001	Sweden	CC	NF	FMI	135		199
28	Pitsavos	2002	Greece	CC	NF	FMI/UA		279	
29	Enstrom	2003	USA	P	F	IHD	3645		2287
30	Chen	2004	Scotland	CS	NF	IHD		385	
31	Nishtar	2004	Pakistan	CC	NF	CAD	*		*
32	Whincup	2004	Great Britain	P	F+NF	IHD			111
33	McGhee	2005	Hong Kong	CC	F	IHD	225		359

**Notes for Table 1**

McElduff (ref 23) reported results for 3 samples. Only those for Newcastle 1992-94 are included under study 23. Results for Auckland 1986-88 and for Newcastle 1988-89 are additional to earlier reports by Jackson (ref 9) and Dobson (ref 12) and are considered under studies 9 and 12 respectively.

- The study author is usually the first author of the publication providing the data - see references.
- The study year is the year of that publication.
- The study types are CC=case control, CS=cross-sectional and P=prospective.
- Fatality is indicated by F=fatal heart disease and NF=non-fatal heart disease. F + NF implies data only available for fatal and non-fatal heart disease combined.
- Disease is indicated by A/E = angina or ECG abnormality, AHD = arteriosclerotic heart disease, CAD = coronary artery disease, CVD = cardiovascular disease, FMI = first myocardial infarction, FMI/UA = first myocardial infarction or unstable angina, FMIS = first myocardial infarction surviving 28 days, HD = heart disease, IHD = ischaemic (coronary) heart disease, MI = myocardial infarction, MI/CS = myocardial infarction or coronary stenosis, NMI = newly diagnosed myocardial infarction, PHA = previous heart attack.
- Numbers of heart disease cases in lifelong non-smokers are totals in the study; for analyses relating to specific types of exposure numbers may be less than this. For studies 16 and 31 (indicated by \*) numbers were not given. For studies 18, 28 and 30, data were only provided for sexes combined. For study 6, numbers relate to the spouse-pairs cohort only, the AHSMOG cohort including ex-smokers.

**TABLE 2: Smoking by the spouse (or nearest equivalent) - Actual index of exposure**

Study			Exposed Group	Comparison Group
Ref	Author			
1a	Hirayama		Spouse ever smoked	Spouse never smoked
2	Garland	A.	Spouse ever smoked	Spouse never smoked
		B.	Spouse current smoker	Spouse never smoked
3	Lee		Spouse ever smoked in marriage	Spouse never smoked in marriage
4	Martin	A.	Spouse ever smoked	Spouse never smoked
		B.	Spouse current smoker	Spouse never smoked
5	Svendsen		Spouse smoker at entry to study	Spouse non-smoker at entry to study
6	Butler	A.	Spouse ever smoked in marriage	Spouse never smoked in marriage
		B.	Spouse current smoker in marriage	Spouse never smoked in marriage
7	Palmer		Spouse ever smoked*	Spouse never smoked*
8	Hole		Cohabitant ever smoked	Cohabitant never smoked
9	Jackson		Exposed to passive smoking at home	Not exposed to passive smoking at home
10	Sandler		Household smoker at entry to study	No household smoker at entry to study
11	Humble		Spouse current smoker	Spouse never smoked
12	Dobson		Exposed to ETS at home	Not exposed to ETS at home
13	La Vecchia	A.	Spouse ever smoked	Spouse never smoked
		B.	Spouse current smoker	Spouse never smoked
14	Layard		Any spouse ever smoked	No spouse ever smoked
15	LeVois (CPS-I)	A.	Spouse ever smoked	Spouse never smoked
		B.	Spouse current smoker	Spouse never smoked
16	Mannino		Exposed to ETS at home	Not exposed to ETS at home
17	Muscat		Spouse ever smoked	Spouse never smoked
18	Tunstall-Pedoe		Any ETS exposure in last 3 days	No ETS exposure in last 3 days
19	Steenland	A.	Spouse ever smoked in marriage	Spouse never smoked in marriage
		B.	Spouse current smoker	Spouse never smoked in marriage
20	Janghorbani		Spouse ever smoked	Spouse never smoked
21	Kawachi		Current ETS exposure at home	No current ETS exposure at home
22	Ciruzzi		Spouse current smoker	Spouse non-smoker
23	McElduff		Any current ETS exposure	No current ETS exposure
24	Spencer		Exposed to ETS at home in last 10 years	Not exposed to ETS at home in last 10 years
25a	He		Spouse smoked in marriage for >5 years	Spouse smoked in marriage for ≤5 years
26	Iribarren		1 hr/wk or more current ETS exposure at home	Less than 1 hr/wk current ETS exposure at home
27	Rosenlund	A.	Ever lived with smoking spouse	Never lived with smoking spouse
		B.	Currently living with smoking spouse	Not currently living with smoking spouse
28	Pitsavos		ETS exposure only at home	No ETS exposure at home or work
29	Enstrom	A.	Spouse ever smoked	Spouse never smoked
		B.	Spouse current smoker	Spouse never smoked
30	Chen		Exposed to ETS at home	Not exposed to ETS at home
31	Nishtar		Spouse smoker	No ETS exposure
33	McGhee		Exposed to ETS at home	Not exposed to ETS at home

**Notes for Table 2**

\* For study 7 it is probable that the exposed group was as stated, though the wording does not exclude the possibility that the exposed group was “spouse a current smoker”.

For studies 2, 4, 6, 13, 15, 19, 27 and 29 data were presented separately for never, ex- and current smoking spouses so relative risks could be calculated for both indicated comparisons.

For study 30, the analysis was restricted to those in full-time employment and the comparison group was not clearly defined.



**TABLE 3: Relative risk of heart disease among lifelong non-smokers in relation to smoking by the spouse (or nearest equivalent)**

Study		Sex	Exposure Index	Fatality	Relative risk (95% confidence limits)	Significance
Ref	Author					
1a	Hirayama	F	E	F	1.16 (0.94-1.43)	
2	Garland	F	E	F	2.70 (0.63-11.58)	
		F	C(N)	F	2.25 (0.32-15.74)	
3	Lee	M	E	NF	1.24 (0.59-2.59)	
		F	E	NF	0.93 (0.54-1.61)	
4	Martin	F	E	NF	2.60 (1.20-5.70)	+
		F	C	NF	3.40	?
5	Svendsen	M	C	F+NF	1.61 (0.96-2.71)	
6	Butler	F	E	F	1.07 (0.65-1.75)	
		F	C(N)	F	1.40 (0.51-3.84)	
7	Palmer	F	E	NF	1.20	?
8	Hole	M	E	F	1.73 (1.01-2.96)	+
		F	E	F	1.65 (0.79-3.46)	
9	Jackson	M	C	F+NF	1.06 (0.39-2.91)	
		F	C	F+NF	3.74 (1.15-12.19)	+
10	Sandler	M	C	F	1.31 (1.05-1.64)	+
		F	C	F	1.19 (1.04-1.36)	+
11	Humble	F	C(N)	F	1.59 (0.99-2.57)	
12	Dobson	M	C	F+NF	0.97 (0.50-1.86)	
		F	C	F+NF	2.46 (1.47-4.13)	+
13	La Vecchia	M	E	NF	1.09 (0.47-2.53)	
		F	E	NF	1.27 (0.52-3.09)	
		M	C(N)	NF	1.09 (0.39-3.01)	
		F	C(N)	NF	1.36 (0.46-4.05)	
14	Layard	M	E	F	0.97 (0.73-1.28)	
		F	E	F	0.99 (0.84-1.16)	
15	LeVois (CPS-I)	M	E	F	0.97 (0.90-1.05)	
		F	E	F	1.03 (0.98-1.08)	
		M	C(N)	F	0.98 (0.91-1.06)	
		F	C(N)	F	1.04 (0.99-1.09)	
16	Mannino	M+F	C	NF	1.12	?
17	Muscat	M	E	NF	1.38 (0.70-2.75)	
		F	E	NF	1.33 (0.59-2.99)	
18	Tunstall- Pedoe	M+F	C	NF	1.34 (1.07-1.67)	+

**TABLE 3 (continued) Relative risk of heart disease among lifelong non-smokers in relation to smoking by the spouse (or nearest equivalent)**

Study						
Ref	Author	Sex	Exposure index	Fatality	Relative risk (95% confidence limits)	Significance
19	Steenland	M	E	F	1.09 (0.98-1.21)	+
		F	E	F	1.04 (0.93-1.16)	
		M	C(N)	F	1.22 (1.07-1.40)	
		F	C(N)	F	1.10 (0.96-1.27)	
20	Janghorbani	F	E	NF	1.38 (0.95-2.01)	
21	Kawachi	F	C	F+NF	1.53 (0.81-2.90)	
22	Ciruzzi	M	C	NF	1.18 (0.55-2.52)	
		F	C	NF	1.73 (0.89-3.36)	
23	McElduff	M	C	F+NF	0.82 (0.55-1.22)	+
		F	C	F+NF	2.15 (1.18-3.92)	
24	Spencer	M	E	NF	No significant association	
25a	He	F	E	NF	1.60 (0.94-2.90)	
26	Iribarren	M	C	NF	1.13 (1.00-1.27)	+
		F	C	NF	1.20 (1.09-1.30)	+
27	Rosenlund	M	E	NF	0.96 (0.64-1.44)	
		F	E	NF	1.53 (0.95-2.44)	
		M	C(N)	NF	0.98 (0.57-1.69)	
		F	C(N)	NF	2.59 (1.27-5.29)	
28	Pitsavos	M+F	E	NF	1.33 (0.89-1.99)	
29	Enstrom	M	E	F	0.93 (0.83-1.04)	
		F	E	F	0.99 (0.92-1.08)	
		M	C(N)	F	0.92 (0.80-1.05)	
		F	C(N)	F	0.97 (0.89-1.06)	
30	Chen	M+F	C	NF	1.20 (0.70-2.20)	
31	Nishtar	M+F	U	NF	2.38 (1.04-5.42)	+
33	McGhee	M	P	F	1.30 (0.88-1.93)	
		F	P	F	1.39 (0.95-2.04)	

**Notes for Table 3**

In study 1, estimates are adjusted for the age of the husband. Alternative estimates, adjusted for the age of the subject are also given by Hirayama (1b), and are very similar.

In study 4 (exposure index E) and study 21, the estimates were given by Wells (34).

In study 8 the estimates were given by Wells (35).

In several studies (8,9,10,12,16,18,21,23,24,26,28,30,33) the index of exposure is actually based not on spousal smoking but on the nearest equivalent index (see Table 2).

See Appendix B for the covariates considered in adjusted analyses.

- The study author is usually the first author of the publication providing the data – see references.
- Exposure index: E = ever smoked (compared to never smoked); C(N) = current smoker (compared to never smoked); C = current exposure (compared to non-current exposure); P = in the past; U = undefined.
- Fatality: F = fatal; NF = non-fatal; F+NF = fatal and non-fatal combined.
- Significant ( $p < 0.05$ ) positive (negative) relative risks are indicated by + (or -). ? indicates not known if significant or not.

**TABLE 4: Relative risk of heart disease among lifelong non-smokers in relation to extent of smoking by the spouse (or nearest equivalent)**

Study		Sex	Exposure grouping	Relative risks by grouping	Significance (trend)
Ref	Author				
1a	Hirayama	F	0 1-19 20+ (cigs/day)	1.00 1.10 1.31	+
5	Svensden	M	0 1-19 20+ (cigs/day)	1.00 1.20 1.75	
8	Hole	F	0 1-14 15+ (cigs/day)	1.00 2.09 4.12	+
9	Jackson	M	None Low High (exposure)	1.00 1.30 0.90	
		F	None Low High (exposure)	1.00 2.10 7.50	+
13	La Vecchia	M+F	0 1-14 15+ (cigs/day)	1.00 1.13 1.30	
14	Layard	M	0 1-14 15-34 35+ (cigs/day)	1.00 0.76 1.07 0.92	
		F	0 1-14 15-34 35+ (cigs/day)	1.00 0.85 1.15 1.06	
15	LeVois (CPS-I)	M	0 1-19 20-39 40+ (cigs/day)	1.00 0.99 0.98 0.72	
		F	0 1-19 20-39 40+ (cigs/day)	1.00 1.04 1.06 0.95	
18	Tunstall-Pedoe	M+F	None Little Some A lot (exposure)	1.00 1.2 1.5 1.6	+
19	Steenland	M	0 1-19 20 21+ (cigs/day)	1.00 1.33 1.17 1.09	
		F	0 1-19 20 21-39 40+ (cigs/day)	1.00 1.15 1.07 0.99 1.04	
		M	0 1-12 13-21 22-29 30+ (years)	1.00 1.14 1.13 1.14 1.25	
		F	0 1-14 15-25 26-33 34+ (years)	1.00 0.84 0.99 1.20 1.20	
		M	0 1-5 6-14 15-27 28+ (pack years)	1.00 1.25 1.33 1.13 1.00	
		F	0 1-12 13-25 26-33 34+ (pack years)	1.00 0.83 1.12 1.09 1.26	
20	Janghorbani	F	0 1-30 31+ (years)	1.00 1.74 0.85	
		F	0 1-19 20+ (cigs/day)	1.00 1.76 1.11	
		F	0 1-10 11+ (pack years)	1.00 1.95 1.17	
21	Kawachi	F	None Occasional Regular	1.00 1.19 2.11	+
		F	<1 1-9 10-19 20-29 30+ (years)	1.00 1.19 1.54 1.11 1.50	
22	Ciruzzi	F	0 1-20 21+ (cigs/day)	1.00 0.82 3.00	
25a	He	F	0 1-10 11-20 21+ (cigs/day)	1.00 0.93 1.40 3.20	+
			0-5 6-15 16-30 31+ (years)	1.00 0.80 2.10 2.30	+
			0 1-399 400-799 800+ (cigs/day x years)	1.00 1.20 1.90 3.60	+
26	Iribarren	M	0 1-9 10-39 40+ (hrs/week)	1.00 1.12 1.26 1.20	+
		F	0 1-9 10-39 40+ (hrs/week)	1.00 1.21 1.31 1.36	+
27	Rosenlund	M+F	0 1-19 20+ (cigs/day)	1.00 1.02 1.58	
		M+F	0 1-32 33+ (years)	1.00 1.11 1.25	
		M+F	0 1-20 21+ (pack-years)	1.00 1.09 1.33	
29	Enstrom	M	0 1-9 10-19 20 21-39 40+ (cigs/day)	1.00 0.98 0.82 0.89 1.13 1.24	
		F	0 1-9 10-19 20 21-39 40+ (cigs/day)	1.00 1.03 0.99 1.02 0.88 0.80	
33	McGhee	M+F	0 smokers 1 smoker 2+ smokers in the home	1.00 1.26 1.68	+

**Notes for Table 4**

For study 1 the 1-19 cigs/day group includes ex-smokers. Estimates are adjusted for the age of the husband. Alternative estimates, adjusted for the age of the subject are also given by Hirayama (1b) and are very similar. Relative risks presented are adjusted for covariates (see Appendix B) if adjusted data are available.

- The study author is usually the first author of the publication providing the data – see references.
- Significant ( $p < 0.05$ ) positive (negative) trends are indicated by + (or -).

**TABLE 5: Relative risk of heart disease among lifelong non-smokers in relation to workplace ETS exposure**

Study		Sex	Relative risk (95% confidence limits)	Significance
Ref	Author			
3	Lee	M	0.66 (0.26-1.66)	
		F	0.69 (0.26-1.87)	
5	Svendsen	M	1.40 (0.80-2.50)	
9	Jackson	M	1.80 (0.94-3.46)	
		F	1.55 (0.48-5.03)	
12	Dobson	M	0.95 (0.51-1.78)	
		F	0.66 (0.17-2.62)	
17	Muscat	M	1.20 (0.60-2.20)	
		F	1.00 (0.40-2.50)	
19	Steenland	M	1.03 (0.89-1.19)	
		F	1.06 (0.84-1.34)	
21	Kawachi	F	1.68 (0.81-3.47)	
24	Spencer	M	No significant association	
25b	He	F	1.85 (0.86-4.00)	
27	Rosenlund	M	1.14 (0.78-1.67)	
		F	0.94 (0.59-1.50)	
28	Pitsavos	M+F	1.97 (1.16-3.34)	+
30	Chen	M+F	1.70 (0.90-3.20)	

**Notes for Table 5**

In study 21 the estimates were given by Wells (35).

In study 27 the estimates are for ever exposure: estimates for current exposure are

1.39 (0.86-2.25) for males and

1.31 (0.62-2.79) for females.

See Appendix B for the covariates considered.

- The study author is usually the first author of the publication providing the data, see references.
- Significant ( $p < 0.05$ ) positive (or negative) relative risks are indicated by + (or -).

**TABLE 6: Relative risk of heart disease among lifelong non-smokers in relation to extent of workplace ETS exposure**

Study					Significance (trend)
Ref	Author	Sex	Exposure grouping	Relative risk by grouping	
21	Kawachi	F	None occasional regular	1.00 1.49 1.92	
25a	He	F	0-5 6-10 11-20 21+ cigs/day	1.00 0.87 2.95 3.56	+
		F	0-5 6-15 16+ years	1.00 3.08 1.56	
		F	0 1-2 3 4+ smokers	1.00 1.16 5.06 4.11	
		F	0 1-2 3-4 5+ hours/day	1.00 0.62 4.03 21.32	
		F	0 1-2000 2001-4000 4000+ (cigs/day x years x smokers x hours)	1.00 1.00 2.05 9.23	
27	Rosenlund	M+F	0 1-31 32+ years	1.00 1.04 1.30	
		M+F	0 1-68 69+ hour years (= hours/day x years)	1.00 0.99 1.48	

**Notes for Table 6**

The study author is usually the first author of the publication providing the data, see references. Relative risks presented are adjusted for covariates (see Appendix B).

- Significant ( $p < 0.05$ ) positive (negative) trends are indicated by + (or -).

**TABLE 7: Relative risk of heart disease among lifelong non-smokers in relation to other indices of ETS exposure**

Study					
Ref	Author	Sex	Exposure grouping	Relative risk by grouping (95% confidence limits)	Significance
3	Lee		<b>Total ETS exposure</b>		
		M	Score 0-1 2-4 5-12	1.00 0.43 0.43	
		F	Score 0-1 2-4 5-12	1.00 0.59 0.81	
5	Svendsen		<b>Spousal and/or workplace ETS exposure</b>		
		M	Neither Work Spouse Both	1.0 1.0 1.2 1.7	
9	Jackson		<b>ETS exposure at home and/or work</b>		
		M	No Yes	1.14 (0.76-1.70)	
		F	No Yes	1.56 (0.76-3.20)	
12	Dobson		<b>ETS exposure at home and/or work</b>		
		M	No Yes	1.09 (0.72-1.63)	
		F	No Yes	2.24 (1.28-3.91)	+
15	LeVois (CPS-I)		<b>Spouse smoked pipe/cigar</b>		
		F	Never smoked at all Yes	1.06 (0.99-1.14)	
17	Muscat		<b>Childhood exposure</b>		
		M	None 1-17 >17 years	1.0 0.9 0.7	
		F	None 1-17 >17 years	1.0 0.6 0.8	
			<b>Adult exposure at home</b>		
		M	None 1-20 21-30 31+ years	1.0 1.7 1.5 1.1	
		F	None 1-20 21-30 31+ years	1.0 2.0 0.9 1.7	
			<b>Cars</b>		
		M	No Yes	1.00 1.07 (0.50-2.29)	
		F	No Yes	1.00 1.85 (0.68-5.05)	
			<b>Other transportation</b>		
		M	No Yes	1.00 0.95 (0.22-4.11)	
		F	No Yes	1.00 1.09 (0.15-8.08)	
18	Tunstall-Pedoe		<b>Serum cotinine (ng/ml)</b>		
		M+F	0, >0-1.05, 1.06-3.97, 3.98-17.49	1.00 1.00 1.30 1.20	
19	Steenland		<b>ETS exposure other than home and/or work</b>		
		M	No Yes	1.00 1.03 (0.93-1.13)	
		F	No Yes	1.00 0.91 (0.83-1.00)	?
20	Janghorbani		<b>Household members other than spouse smoked</b>		
		F	No Yes	1.00 1.02 (0.65-1.58)	
21	Kawachi		<b>ETS exposure at home and/or work</b>		
		F	No Occasional Regular	1.00 1.58 1.91	+
22	Ciruzzi		<b>One or more children smoke</b>		
		M	No Yes	1.00 1.75 (0.98-3.13)	
		F	No Yes	1.00 1.52 (0.92-2.50)	
			<b>Spouse and/or one or more children smoke</b>		
		M	No Yes	1.00 1.89 (1.13-3.18)	+
		F	No Yes	1.00 1.54 (0.95-2.51)	

**TABLE 7 (continued) Relative risk of heart disease among lifelong non-smokers in relation to other indices of ETS exposure**

Study		Sex	Exposure grouping	Relative risk by grouping (95% confidence limits)	Significance
24	Spencer	M	<b>ETS exposure in cars</b> No Yes	No significant association	
		M	<b>ETS exposure in social venues</b> No Yes	No significant association	
		M	<b>ETS exposure at home, at work, in social venues and/or in cars</b> No Yes	Significant increase	+
25b	He	F	<b>ETS exposure from spouse and/or work</b> Neither Home Work Both	1.00 2.07 2.53 4.18	+
26	Iribarren	M	<b>ETS exposure in small spaces</b> 0 1-9 10-39 40+ hrs/wk	1.00 1.08 1.12 1.24	+
		F	0 1-9 10-39 40+ hrs/wk	1.00 0.97 1.10 1.17	+
		M	<b>ETS exposure in large indoor areas</b> 0 1-9 10-39 40+ hrs/wk	1.00 0.94 1.17 1.03	+
		F	0 1-9 10-39 40+ hrs/wk	1.00 0.82 0.98 1.28	
		M	<b>Total ETS exposure</b> 0 1-9 10-39 40+ hrs/wk	1.00 0.90 1.08 1.13	+
		F	0 1-9 10-39 40+ hrs/wk	1.00 0.86 1.07 1.17	+
27	Rosenlund	M+F	<b>ETS exposure from spouse and/or work</b> No Yes	1.18 (0.87-1.60)	
		M+F	0 >16 7-16 1-6 <1 years ago	1.00 0.92 1.11 1.30 1.39	
		M+F	0 1-12 13-23 24-34 35+ years	1.00 0.72 0.97 1.54 1.48	+
		M+F	0 1-17 18-41 42-89 90+ hour-years (= years x hours/day)	1.00 0.70 1.22 1.27 1.55	+
28	Pitsavos	M	<b>ETS exposure at home or work</b> None Occasional Regular	1.25 1.47	+
		F	None Occasional Regular	1.29 1.56	+
		M+F	0 1-4 5-9 10-19 20-29 30-39 40+ years	1.00 1.07 1.16 1.39 1.75 2.20 3.09	+
		M+F	<b>ETS exposure at home and work</b> Neither Both	1.00 2.56 (1.65-3.96)	
29	Enstrom	F	<b>Spouse smoked pipe/cigar</b> No Yes	1.00 0.97 (0.86-1.10)	
30	Chen	M+F	<b>Total ETS exposure</b> None A little Some A lot	1.00 1.30 1.50 1.80	+
		M+F	<b>Serum cotinine (ng/ml)</b> 0 >0-1.05 1.06-3.97 3.98-17.49	1.00 0.70 1.00 1.10	
		M+F	<b>Self-reported ETS and cotinine combined</b> I II III IV V VI VII	1.00 1.30 1.60 1.50 1.70 1.80 2.60	+
		M+F	<b>ETS exposure other than at home and/or work</b> No Yes	1.00 1.00 (0.40-2.30)	
		M+F	<b>Duration of total daily ETS exposure (hours)</b> 0 >0-2 3-5 ≥6	1.00 1.20 1.60 1.70	
31	Nishtar	M+F	<b>Any ETS exposure</b> No Yes	1.00 2.87 (1.28-6.42)	+
		M+F	<b>Daily ETS exposure</b> No Yes	1.00 3.87 (1.68-8.86)	+

**TABLE 7 (continued/2) Relative risk of heart disease among lifelong non-smokers in relation to other indices of ETS exposure**

Study								
Ref	Author	Sex	Exposure grouping				Relative risk by grouping (95% confidence limits)	Signi- ficance
32	Whincup		<b>Serum cotinine (ng/ml)</b>					
			≤0.7	0.8-1.4	1.5-2.7	2.8-14.0	1.00 1.54 1.89 1.67	+

**Notes for Table 7**

For studies 9 and 12, the data come from ref 23.

Relative risks presented are adjusted for covariates (see Appendix B) if adjusted data are available.

- The study author is usually the first author of the publication providing the data, see references.
- When two groups only are being compared, the relative risk and 95% confidence limits for the exposed group are shown; when more than two exposure groups are being compared, only the set of relative risks is shown.
- Significant ( $p < 0.05$ ) positive (or negative) differences or trends are indicated by + (or -). ? indicates not known if significant or not.



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## APPENDIX A

## STUDIES/ANALYSES NOT INCLUDED IN TABLES

In preparing the tables 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 the 1984 paper (ref 1a).

Gillis (1984, Japan, ref A2) – results superseded by the 1989 Hole paper (ref 8).

Hirayama (1987, Japan, ref A3) – results already presented in 1984 (ref 1a).

Sandler (1987, USA, ref A4) – results superseded by the 1989 paper (ref 10).

Helsing (1988, USA, ref A5) – results superseded by the 1989 Sandler paper (ref 10).

Hirayama (1988, Japan, ref A6) – results already presented in 1984 (ref 1a).

He (1989, China, ref A7) – results superseded by the 2000 paper (ref 25a).

Butler (1990, USA, ref A8) – results already presented in 1988 (ref 6).

Hirayama (1990, Japan, refs A9 and A10) – results already presented in 1984 (ref 1a).

Ciruzzi (1996, Argentina, ref A11) – results superseded by the 1998 paper (ref 22).

He (1996, China, ref A12) – results superseded by the 2000 paper (ref 25a).

Kawachi (1996, USA, ref A13) – results superseded by the 1997 paper (ref 21).

Rosenlund (2000, Sweden, ref A14) – results superseded by the 2001 paper (ref 27).

Panagiotakos (2000, Greece, ref A15) – results superseded by the 2002 Pitsavos paper (ref 28).

Panagiotakos (2002, Greece, refs A16 and A17) – results given in the 2002 Pitsavos paper (ref 28).

Pitsavos (2002, Greece, ref A18) – results given in another 2002 paper (ref 28).

Chen (2003, Scotland, ref A19) – results superseded by the 2004 paper (ref 30).

Jabbour (2003, Lebanon, ref A20) – results not restricted to never-smokers.

Sargent (2004, USA, ref A21) – no analysis of never-smokers.

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**APPENDIX B**

**Risk factors used as matching factors or to adjust relative risk estimates**

Risk factor	Study																									
	1a	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25a	
Age	x	x	x		x	x		x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x
Marital status (in spousal analyses)	x	x	x	x	x	x		n	n	n	x	n	x	x	x	n		n	x	x	n					
Blood pressure/hypertension		x		x	x			x			x		x					x	x	x		x	x			x
Cholesterol		x			x			x			x		x						x			x	x			x
Social class/education/income					x			x	x	x		x	x			x	x		x				x	x		
Obesity/weight		x		x	x			x	x		x	x	x						x		x	x	x			
Alcohol				x	x														x		x					
Diabetes				x									x						x		x	x				
Family history of heart disease/hypertension				x					x				x								x	x	x			x
Race														x	x	x	x									
Exercise				x																x		x	x			
Housing/urban-rural																x			x							
Personal history of heart disease										x		x								x						
Coffee													x													
Personality type																										x
Occupation																				x		x				
Oestrogen use																				x		x				
Other																				x		x				

Study									
Risk factor	26	27	28	29	30	31	32	33	
Age	x	x	x	x	x	x	x	x	
Marital status (in spousal analyses)	n				n		n	n	
Blood pressure/hypertension		x			x		x		
Cholesterol	x	x	x		x		x		
Social class/education/income	x	x		x	x		x	x	
Obesity/weight	x	x	x	x	x		x		
Alcohol	x		x		x		x		
Diabetes	x	x	x				x		
Family history of heart disease/hypertension					x				
Race	x			x					
Exercise	x		x	x			x		
Housing/urban-rural				x					
Personal history of heart disease							x		
Coffee									
Personality type	x								
Occupation		x							
Oestrogen use									
Other			x	x	x	x	x		



Notes

- x Risk factor used as matching or adjustment factor in study
- n not applicable – spousal smoking not the index (see Table 2).
- Study 7 No reference was made to any adjustment for confounding in the abstract
- Study 12 Data in Tables 3 and 5 only adjusted for age and personal history of heart disease
- Study 13 Only data for spouse current smoker are adjusted for risk factors stated
- Study 17 Non-smoking cases and controls were matched on age and race. Adjustment for other risk factors noted only applied to analyses of workplace, adulthood and childhood ETS exposure, but not other indices of ETS exposure, including spousal smoking
- Study 19 Other risk factors considered were aspirin use, diuretic use and personal history of arthritis
- Study 21 Other risk factors considered were oral contraceptive use, saturated fat intake, vitamin E intake, menopausal status and use of postmenopausal hormones
- Study 27 Other risk factors considered were hospital/catchment area, job strain and diet
- Study 28 Only the relative risks in Table 7 for none/occasional/regular exposure were adjusted for all these factors; other relative risks cited were adjusted only for age, sex, hypertension, cholesterol, diabetes, exercise and family history of heart disease
- Study 29 Other risk factors considered: fruit or fruit juice intake and health status
- Study 30 Other risk factors considered: sex, employment status and dietary vitamin C and fibre
- Study 31 Other risk factors considered: sex, matched pair (conditional logistic regression was used)
- Study 32 Other risk factors considered: town of residence, FEV<sub>1</sub>, height, triglycerides and white cell count