

EPIDEMIOLOGICAL EVIDENCE ON ENVIRONMENTAL TOBACCO SMOKE AND HEART DISEASE

1. 49 epidemiological studies of heart disease and ETS among lifelong non-smokers have been published.
2. The overall evidence from these studies does not clearly indicate any increased risk of heart disease in relation to workplace ETS exposure. Only one of 22 results reported shows a statistically significant association, and the combined evidence is not significant.
3. Although most published estimates for spousal smoking are not statistically significant, there have been reports of a significant association or 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 fewer than 100 cases.
 - Many of the studies fail to consider possible lifestyle confounding factors. There are over 300 different risk factors reported for heart disease¹ and several studies have shown differences in many lifestyle factors between smoking and non-smoking households.²⁻¹¹
 - The studies generally rely on reported rather than objectively measured ETS exposure data. One¹² of the five studies¹³⁻¹⁶ using serum or salivary cotinine and the single study¹⁷ using carboxyhaemoglobin as a marker of ETS exposure found a significant relationship between the marker and risk of heart disease. However, the combined evidence from these studies does not show a significant relationship.
 - Some of the studies^{11,18-20} 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,²¹ which found no relationship with spousal smoking, have been excluded by some reviewers.^{22,23} Another recent very large study,²⁴ which also found no relationship, has been widely criticised but for reasons which bear little or no relationship to the data presented.²⁵ 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, and biochemical evidence has indicated that self-reporting after a coronary diagnosis is distorted²⁶. A study reporting particularly high heart disease mortality among smokers who deny smoking,²⁷ 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^{22,28} 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.

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 49 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 dose-response 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.²⁹

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.³⁰

The tables are based on results from the sources listed under "References to data sources" which follows the tables. Appendix A explains why results from other specific publications, which might have been thought to cite relevant data, are not included in the tables.

Meta-analyses of these data are available.³¹⁻³³

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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 1	2000	China/Xi'an	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/California	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
34	Qureshi	2005	USA	P	F+NF	CAD	219		
35	Hedblad	2006	Sweden	P	F+NF	IHD+MI			91
36	Stranges	2006	USA	CC	NF	FMI	89		195
37	Teo	2006	52 countries	CC	NF	FMI		6280	
38	Wen	2006	China	P	F	CVD CVD- Stroke	272 115		
39	Eisner	2007	USA	P	F	CVD	718		339
40	Hill 1	2007	New Zealand	P	F	IHD	1299		1272
41	Hill 2	2007	New Zealand	P	F	IHD	1026		654
42	He 2	2008	China/Beijing	CS	NF	IHD	431		
43	Sulo	2008	Albania	CC	NF	ACS		169	
44	Vozoris	2008	Canada	CS	NF	HD		1773	
45	Ding	2009	Hong Kong	CC	NF	IHD	314		

TABLE 1 (continued): 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
46	Gallo (EPIC)	2010	Europe	P	F	CD-Stroke IHD	259	81	140
47	Hamer	2010	England, Scotland	P	F	CVD		96	
48	Jefferis	2010	Britain	P	F+NF	FMI		74	
49	He 3	2012	China/Xi'an	P	F	IHD	22		19

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.

Qureshi (ref 34) reported results for CVD as a whole (defined in that paper as either stroke or coronary artery disease) and for stroke alone. The CAD results reported below were estimated from these separate results.

Wen (ref 38) reported results for CVD as a whole and for stroke alone. The results reported below are for CVD excluding stroke where it was possible to estimate these values from the separate results. Where this was not possible, the results reported are for CVD as a whole.

Jefferis (ref 48) reports combined results for two studies, one in men and the other in women. The study of men is a continuation of that reported by Whincup (ref 32) but the follow-up periods do not overlap.

Hill reported results for two cohorts, one interviewed in 1981 (Hill 1 – ref 40) and one in 1996 (Hill 2 – ref 41).

- 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 are only available for fatal and non-fatal heart disease combined.
- Disease is indicated by
 - A/E = angina or ECG abnormality,
 - ACS = acute coronary syndrome,
 - AHD = arteriosclerotic heart disease,
 - CAD = coronary artery disease,
 - CD-Stroke = circulatory disease other than cerebrovascular,
 - CVD = cardiovascular disease,
 - CVD-Stroke = CVD other than stroke,
 - 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 lower than this. For studies 16 and 31 (indicated by *) numbers were not given. For studies 18, 28, 30, 37, 43, 44, 47 and 48, and for study 46 for IHD, 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 Ref	Study Author	Exposed Group	Comparison Group
1a	Hirayama	Spouse ever smoked	Spouse never smoked
2	Garland	A. Spouse ever smoked B. Spouse a current smoker	Spouse never smoked Spouse never smoked
3	Lee	Spouse ever smoked in marriage	Spouse never smoked in marriage
4	Martin	A. Spouse ever smoked B. Spouse a current smoker	Spouse never smoked Spouse never smoked
5	Svendsen	Spouse a smoker at entry to study	Spouse non-smoker at entry to study
6	Butler	A. Spouse ever smoked in marriage B. Spouse a current smoker in marriage	Spouse never smoked 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 a 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 B. Spouse a current smoker	Spouse never smoked Spouse never smoked
14	Layard	Any spouse ever smoked	No spouse ever smoked
15	LeVois (CPS-I)	A. Spouse ever smoked B. Spouse a current smoker	Spouse never smoked 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 B. Spouse a current smoker	Spouse never smoked in marriage 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 a 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 1	Spouse smoked in marriage for >5 years	Spouse smoked in marriage for ≤5 years
26	Iribarren	1 hour/week or more current ETS exposure at home	Less than 1 hour/week of such exposure
27	Rosenlund	A. Ever lived with smoking spouse B. Currently living with smoking spouse	Never lived 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 B. Spouse a current smoker	Spouse never smoked Spouse never smoked
30	Chen	Exposed to ETS at home	Not exposed to ETS at home
31	Nishtar	Spouse a smoker	No ETS exposure
33	McGhee	Exposed to ETS at home	Not exposed to ETS at home
34	Qureshi	Spouse a smoker	Spouse not a smoker
36	Stranges	A. Ever lived with a smoker B. Recently lived with a smoker	Never lived with a smoker Did not live with a smoker
37	Teo	1 hour/week or more current ETS exposure from family, friends or co-workers	Less than 1 hour/week of such exposure

TABLE 2 (continued): Smoking by the spouse (or nearest equivalent) – actual index of exposure

Study Ref	Study Author	Exposed Group	Comparison Group
38	Wen	A. Spouse ever smoked in marriage B. Spouse a current smoker	Spouse never smoked in marriage Spouse never smoked in marriage
39	Eisner	Ever exposed to ETS at home	Never exposed to ETS at home
40,41	Hill	Currently living with a smoker	Currently not living with a smoker
42	He 2	Exposed regularly to ETS during the last 10 years, at home or in the workplace	Not so exposed
43	Sulo	Spouse smoked regularly	Spouse did not smoke regularly
44	Vozoris	Exposed to ETS on most days during the past month	Not so exposed
45	Ding	Any family member ever smoked in the household	No family members ever smoked in the household
46	Gallo (EPIC)	Partner smoked one or more cigarettes/day	Partner did not smoke
48	Jefferis	Lived with a smoker	Did not live with a smoker
49	He 3	Exposed to ETS at home and/or at work	No ETS exposure at home or at work

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, 29 and 38 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.

For studies 32, 35 and 47 results are only available for a biochemical index of ETS exposure and are shown in Table 7.

TABLE 3: Smoking by the spouse (or nearest equivalent) – relative risk of heart disease among lifelong non-smokers

Study Ref	Study Author	Sex	Exposure Index	Fatality	Relative risk (95% confidence limits)	Significance
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 (0.58-2.67)	
		F	E	NF	0.93 (0.53-1.64)	
4	Martin	F	E	NF	2.60 (1.20-5.70)	+
		F	C	NF	3.40	?
5	Svendson	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)	+
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)	

TABLE 3 (continued): Smoking by the spouse (or nearest equivalent) – relative risk of heart disease among lifelong non-smokers

Study Ref	Study Author	Sex	Exposure Index	Fatality	Relative risk (95% confidence limits)	Significance
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 1	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)	
34	Qureshi	F	U	F+NF	1.05 (0.81-1.38)	
36	Stranges	M	E	NF	0.98 (0.65-1.50)	
		F	E	NF	1.30 (0.67-2.51)	
		M	C	NF	0.71 (0.40-1.23)	
		F	C	NF	0.94 (0.48-1.82)	
37	Teo	M+F	C	NF	1.37 (1.27-1.48)	+
38	Wen	F	E	F+NF	0.99 (0.72-1.37)	
			C	F+NF	1.19 (0.84-1.67)	
40	Hill 1	M	C	F	1.04 (0.88-1.23)	
		F	C	F	0.98 (0.83-1.17)	
41	Hill 2	M	C	F	1.18 (0.96-1.44)	
		F	C	F	1.27 (0.98-1.66)	
42	He 2	F	T	NF	1.69 (1.31-2.18)	+

TABLE 3 (continued/2): Smoking by the spouse (or nearest equivalent) – relative risk of heart disease among lifelong non-smokers

Study Ref	Study Author	Sex	Exposure Index	Fatality	Relative risk (95% confidence limits)	Significance
43	Sulo	M	C	NF	1.68 (0.81-3.47)	
		F	C	NF	1.19 (0.25-5.64)	
44	Vozoris	M+F	C	NF	1.00 (0.80-1.20)	
45	Ding	F	E	NF	1.52 (1.01-2.27)	+
46	Gallo	M+F	C	F	1.99 (0.92-4.29)	
48	Jefferis	M+F	C	F+NF	2.41 (1.04-5.59)	+
49	He 3	M	2	F	2.24 (0.76-6.59)	
		F	2	F	2.10 (0.69-6.33)	

Notes for Table 3

This table shows results for the indices of exposure listed in Table 2 (for each study, reporting results for the exposure index identified for that study).

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 (50).

In study 8 the estimates were given by Wells (51).

In several studies (8, 9, 10, 12, 16, 18, 21, 23, 24, 26, 28, 30, 33, 36, 37, 40, 41, 42, 44, 45, 48, 49) the index of exposure is actually based not on spousal smoking but on the nearest equivalent index (see Table 2).

For study 39, results are only available per 10 years of living with a smoker and are included in Table 4.

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
 - T = in the last 10 years
 - 2 = for at least 2 years in the previous 18 years
 - 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: Smoking by the spouse (or nearest equivalent) – dose-response results among lifelong non-smokers

Study Ref	Study Author	Sex	Exposure grouping	Relative risks by grouping	Significance (trend)
1a	Hirayama	F	0 1-19 20+ (cigs/day)	1.00 1.10 1.31	+
5	Svendsen	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 1	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 1 2+ smokers in the home	1.00 1.26 1.68	+
37	Teo	M+F	<1 1-7 8-14 15-21 22+ (hours/week)	1.00 1.32 1.52 1.73 1.49	+
38	Wen	F	0 <8.8 8.8-17.9 18.0+ (pack-years)	1.00 1.10 1.12 1.22	
39	Eisner	M+F	Per 10 years exposure	1.10	
42	He 2	F	0 1-9 10-19 20+ (cigs/day)	1.00 1.41 1.85 1.77	+
			0 1-20 21-40 41+ (minutes/day)	1.00 1.46 1.78 1.86	+

TABLE 4 (continued): Smoking by the spouse (or nearest equivalent) – dose-response results among lifelong non-smokers

Study Ref	Study Author	Sex	Exposure grouping	Relative risks by grouping	Significance (trend)
45	Ding	F	0 <1 1+ (packs/day)	1.00 1.14 1.69	+
			0 <5 5+ (years)	1.00 1.26 1.52	+
			0 <4 4+ (hours/day)	1.00 1.28 1.82	+
			0 <5 5+ (pack-years)	1.00 1.44 1.53	+
			0 <20 20+ (hour-years)	1.00 1.22 1.61	+
46	Gallo	M+F	0 0.5 1.0 1.5+ (packs/day)	1.00 1.87 1.89 2.46	
49	He 3	M+F	None Low Moderate High	1.00 1.74 2.25 3.79	+

Notes for Table 4

This table shows dose-response results for the indices of exposure listed in Table 2 (for each study, reporting dose-response results for the exposure index identified for that study, if available).

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 -).

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.

For study 38 the results relate to CVD as a whole rather than to CVD excluding stroke.

For study 49 the index of exposure was a combination of exposure at home (four categories of pack-years) and exposure at work (four categories of pack-years x hours/day).

TABLE 5: Workplace ETS exposure – relative risk of heart disease among lifelong non-smokers

Study Ref	Study Author	Sex	(95% confidence limits)	Significance
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 1	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)	
36	Stranges	M	0.97 (0.64-1.48)	
		F	0.96 (0.60-1.55)	
38	Wen	F	1.21 (0.74-2.01)	
46	Gallo	M	0.93 (0.46-1.90)	
		F	0.76 (0.47-1.24)	

Notes for Table 5

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 -).

In study 21 the estimates were given by Wells (51).

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.

In study 36 the estimates are for lifetime exposure: estimates for recent exposure are:
0.67 (0.43-1.03) for males and
1.03 (0.50-2.14) for females

For study 39, results are only available per 10 years of working with a smoker and are included in Table 6.

TABLE 6: Workplace ETS exposure – dose-response results among lifelong non-smokers

Study Ref	Study Author	Sex	Exposure grouping	Relative risk by grouping	Significance (trend)
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	
38	Wen	F	0 <10 10-24 >24 years	1.00 0.86 0.96 0.93	
39	Eisner	M+F	Per 10 years exposure	1.04	

Notes for Table 6

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

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

The study author is usually the first author of the publication providing the data, see references.

For study 38 the results relate to CVD as a whole rather than to CVD excluding stroke.

TABLE 7: Other indices of ETS exposure – dose-response results among lifelong non-smokers

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

TABLE 7 (continued): Other indices of ETS exposure – dose-response results among lifelong non-smokers

Study Ref	Study Author	Sex	Exposure grouping	Relative risk by grouping (95% confidence limits)	Significance
25b	He	F	ETS exposure from spouse and/or work Neither Home Work Both	1.00 2.07 2.53 4.18	+
26	Iribarren	M	ETS exposure in small spaces 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	ETS exposure in large indoor areas 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	Total ETS exposure 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	ETS exposure from spouse and/or work 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	ETS exposure at home or work None Occasional Regular	1.00 1.25 1.47	+
		F	None Occasional Regular	1.00 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	ETS exposure at home and work Neither Both	1.00 2.56 (1.65-3.96)	
29	Enstrom	F	Spouse smoked pipe/cigar No Yes	1.00 0.97 (0.86-1.10)	
30	Chen	M+F	Total ETS exposure None A little Some A lot	1.00 1.30 1.50 1.80	+
		M+F	Serum cotinine (ng/ml) 0 >0-1.05 1.06-3.97 3.98-17.49	1.00 0.70 1.00 1.10	
		M+F	Self-reported ETS and cotinine combined I II III IV V VI VII	1.00 1.30 1.60 1.50 1.70 1.80 2.60	+
		M+F	ETS exposure other than at home and/or work No Yes	1.00 1.00 (0.40-2.30)	
		M+F	Duration of total daily ETS exposure (hours) 0 >0-2 3-5 ≥6	1.00 1.20 1.60 1.70	
31	Nishtar	M+F	Any ETS exposure No Yes	1.00 2.87 (1.28-6.42)	+
		M+F	Daily ETS exposure No Yes	1.00 3.87 (1.68-8.86)	+
32	Whincup	M	Serum cotinine (ng/ml) ≤0.7 0.8-1.4 1.5-2.7 2.8-14.0	1.00 1.54 1.89 1.67	+
35	Hedblad	M	Blood carboxyhaemoglobin (%) 0.13-0.49 0.50-0.57 0.58-0.66 0.67-5.47 (quartiles)	1.00 1.26 1.77 3.71	+

TABLE 7 (continued/2): Other indices of ETS exposure – dose-response results among lifelong non-smokers

Study Ref	Study Author	Sex	Exposure grouping	Relative risk by grouping (95% confidence limits)	Significance	
36	Stranges	Cumulative lifetime ETS exposure at home, work and in public settings				
		M	Tertile: 1 2 3		1.00 0.93 1.40	
		F	Tertile: 1 2 3		1.00 0.50 0.67	
		ETS exposure at home, work and in public settings				
		M+F	Low High (see notes)		1.00 0.96 (0.60-1.55)	
		ETS exposure in public settings during life				
		M	No Yes		1.00 0.63 (0.10-3.81)	
		F	No Yes		1.00 0.78 (0.10-6.44)	
		Recent ETS exposure in public settings				
		M	No Yes		1.00 0.75 (0.48-1.18)	
F	No Yes		1.00 0.50 (0.30-0.83)			
38	Wen	Childhood exposure				
		F	No Yes		1.00 1.49 (1.01-2.22)	+
			0 <20 20+ years		1.00 1.21 1.36	
46	Gallo	Childhood exposure				
		M	No Yes		1.00 1.11 (0.72-1.69)	
		F	No Yes		1.00 1.18 (0.88-1.57)	
		ETS exposure at home				
		M+F	0 <1 1-2 3+ hours/day		1.00 1.39 2.08 1.94	+
47	Hamer	Salivary cotinine (ng/ml)				
		M+F	≤0.05 0.06-0.70 0.71-14.99 Per unit increase in log cotinine,		1.00 1.33 2.00 1.60 (1.11-2.31)	+
48	Jefferis	Serum cotinine (ng/ml)				
		M+F	≤0.05 0.06-0.19 0.20-0.70 0.71-15 Per doubling of cotinine		1.00 0.91 0.99 0.94 1.00 (0.86-1.16)	

Notes for Table 7

Table 4 shows dose-response results for the indices of exposure listed in Table 2 (for each study, reporting dose-response results for the exposure index identified for that study). Table 6 shows dose-response results for workplace exposure. This table shows the other dose-response results reported.

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 (or results for log cotinine are given), the relative risk and 95% confidence limits for the exposed group (per unit increase) 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.

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

For study 36, the comparison for the combined sex relative risk is between subjects with high levels (greater than the median) of either distant or recent ETS exposure and subjects with low distant and low recent exposure (less than the median).

For study 38, the results for any childhood exposure (Yes/No) relate to CVD excluding stroke but the results by years exposed relate to CVD as a whole.

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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 (2001, 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.

Note also that this review does not consider various publications (e.g. Sargent, 2004, USA, ref A21; Barone, 2006, ref A22; Bartecchi, 2006, ref A23; Khuder, 2007, ref A24; Cesaro, 2008, ref A25) which compare rates of heart disease before and after introduction of a smoking ban, as they do not provide direct information on effects of ETS exposure in never smokers. Any decline observed, if not due to reasons unrelated to the ban, may occur due to reduced death rates in smokers.

Jefferis (2009, Britain, ref A26) – results not restricted to never-smokers.

Pope (2009, USA, ref A27) – no original results given for 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
Sex	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x		x	x	x	x	x	x	x
Age	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*	x	x	x	x	x	x	x				x		x	x	x				x	x					
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	34	35	36	37	38	39	40	41	42	43	44	45	46	47	48	49
Sex*	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x
Age	x	x	x	x	x	x	x	x	x			x	x	x	x	x	x	x	x	x	x	x	x	x
Marital status**	x			x				x	x					x	x	x	x							x
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			x		x	x	x
Social class/ education/income	x	x		x	x		x	x			x		x	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			x		x	x
Alcohol	x		x		x		x		x	x	x	x					x			x			x	x
Diabetes	x	x	x				x		x	x	x						x	x		x			x	
Family history of heart disease/ hypertension					x												x	x		x				
Race	x			x					x		x				x	x		x						
Exercise	x		x	x			x			x	x	x	x				x	x			x	x	x	x
Housing/urban-rural				x																				
Personal history of heart disease							x			x														
Coffee																								
Personality type	x																					x		
Occupation		x											x		x	x		x						x
Oestrogen use																					x			
Other			x	x	x	x	x			x		x					x	x	x	x	x	x	x	x

Notes

- x Risk factor used as matching or adjustment factor in study
- * Results that are for one sex only are counted as being adjusted for sex
- ** Studies that are restricted to married subjects are counted as having adjusted for marital status
- 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: aspirin use, diuretic use and personal history of arthritis
- Study 21 Other risk factors considered: oral contraceptive use, saturated fat intake, vitamin E intake, menopausal status and use of postmenopausal hormones
- Study 27 Other risk factors considered: 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: employment status and dietary vitamin C and fibre
- Study 31 Other risk factors considered: matched pair (conditional logistic regression was used)
- Study 32 Other risk factors considered: town of residence, FEV₁, height, triglycerides and white cell count
- Study 35 Other risk factors considered: triglycerides and FEV₁
- Study 36 Only the relative risks for cumulative exposure in Table 7 were adjusted for those factors; other relative risks cited were unadjusted
- Study 37 Other risk factors considered: region, consumption of fruits and vegetables
- Study 38 Other risk factors considered: intake of meat, vegetables and fruit
- Study 42 Other risk factors considered: triglycerides, family history of stroke
- Study 43 Other risk factors considered: financial loss in pyramid schemes, emigration of spouse and/or offspring, religious observance
- Study 44 Other risk factors considered: province, immigration status, presence of children younger than 12 years in household
- Study 45 Other risk factors considered: history of stroke, history of gout
- Study 46 Other risk factors considered: study centre
- Study 47 Other risk factors considered: survey location, log C-reactive protein, fibrinogen
- Study 48 Other risk factors considered: region, triglycerides, FEV₁, C-reactive protein, interleukin 6, white cell count
- Study 49 Other risk factor considered: triglycerides