EPIDEMIOLOGICAL EVIDENCE ON ENVIRONMENTAL TOBACCO SMOKE AND HEART DISEASE

1. 48 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 disease[1] 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. One[12] of the five studies[13-16] using serum or salivary cotinine and the single study[17] 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 distorted[26]. 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 48 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]

This work was supported by the tobacco industry. The accuracy of the material presented and the interpretation of the findings are solely the responsibility of the authors.

References to text

1. Hopkins PN, Williams RR. Identification and relative weight of cardiovascular risk factors. *Cardiol Clin* 1986;**4**:3-31.

2. Sidney S, Caan BJ, Friedman GD. Dietary intake of carotene in nonsmokers with and without passive smoking at home. *Am J Epidemiol* 1989;**129**:1305-9.

3. Thompson DH, Warburton DM. Lifestyle differences between smokers, ex-smokers and non-smokers, and implications for their health. *Psychol Health* 1992;**7**:311-21.

4. Thornton A, Lee P, Fry J. Differences between smokers, ex-smokers, passive smokers and non-smokers. *J Clin Epidemiol* 1994;**47**:1143-62.

5. Cress RD, Holly EA, Ahn DK, Kristiansen JJ, Aston DA. Contraceptive use among women smokers and nonsmokers in the San Francisco Bay area. *Prev Med* 1994;**23**:181-9.

6. Subar AF, Harlan LC, Mattson ME. Food and nutrient intake differences between smokers and non-smokers in the US. *Am J Public Health* 1990;**80**:1323-9.

7. Le Marchand L, Wilkens LR, Hankin JH, Haley NJ. Dietary patterns of female nonsmokers with and without exposure to environmental tobacco smoke. *Cancer Causes Control* 1991;**2**:11-6.

8. Matanoski G, Kanchanaraksa S, Lantry D, Chang Y. Characteristics of nonsmoking women in NHANES I and NHANES I epidemiologic follow-up study with exposure to spouses who smoke. *Am J Epidemiol* 1995;**142**:149-57.

9. Dallongeville J, Marécaux N, Fruchart J-C, Amouyel P. Cigarette smoking is associated with unhealthy patterns of nutrient intake: a meta-analysis. *J Nutr* 1998;**128**:1450-7.

10. Forastiere F, Mallone S, Lo Presti E, Baldacci S, Pistelli F, Simoni M, *et al*. Characteristics of nonsmoking women exposed to spouses who smoke: epidemiologic study on environment and health in women from four Italian areas. *Environ Health Perspect* 2000;**108**:1171-89.

11. Iribarren C, Friedman GD, Klatsky AL, Eisner MD. Exposure to environmental tobacco smoke: association with personal characteristics and self reported health conditions. *J Epidemiol Community Health* 2001;**55**:721-8.

12. Whincup PH, Gilg JA, Emberson JR, Jarvis MJ, Feyerabend C, Bryant A, *et al*. Passive smoking and risk of coronary heart disease and stroke: prospective study with cotinine measurement. *BMJ* 2004;**329**:200-4.

13. Tunstall-Pedoe H, Brown CA, Woodward M, Tavendale R. Passive smoking by self report and serum cotinine and the prevalence of respiratory and coronary heart disease in the Scottish heart health study. *J Epidemiol Community Health* 1995;**49**:139-43.

14. Chen R, Tavendale R, Tunstall-Pedoe H. Environmental tobacco smoke and prevalent coronary heart disease among never smokers in the Scottish MONICA surveys. *Occup Environ Med* 2004;**61**:790-2.

15. Hamer M, Stamatakis E, Kivimaki M, Lowe GD, Batty GD. Objectively measured secondhand smoke exposure and risk of cardiovascular disease: what is the mediating role of inflammatory and hemostatic factors? *J Am Coll Cardiol* 2010;**56**:18-23.

16. Jefferis BJ, Lawlor DA, Ebrahim S, Wannamethee SG, Feyerabend C, Doig M, *et al*. Cotinine-assessed second-hand smoke exposure and risk of cardiovascular disease in older adults. *Heart* 2010;**96**:854-9.

17. Hedblad B, Engström G, Janzon E, Berglund G, Janzon L. COHb% as a marker of cardiovascular risk in never smokers: results from a population-based cohort study. *Scand J Public Health* 2006;**34**:609-15.

18. Martin MJ, Hunt SC, Williams RR. Increased incidence of heart attacks in nonsmoking women married to smokers. In: *Presented at 114th Annual Meeting of American Public Health Association, October 1, 1986*. 1986;

19. Mannino DM, Siegel M, Rose D, Etzel R. Health effects of environmental tobacco smoke exposure in US adults: data from the 1991 National Health Interview Survey. *Epidemiology* 1995;**6**:56S.

20. Vozoris N, Lougheed MD. Second-hand smoke exposure in Canada: prevalence, risk factors, and association with respiratory and cardiovascular diseases. *Can Respir J* 2008;**15**:263-9.

21. LeVois ME, Layard MW. Publication bias in the environmental tobacco smoke/coronary heart disease epidemiologic literature. *Regul Toxicol Pharmacol* 1995;**21**:184-91.

22. Law MR, Morris JK, Wald NJ. Environmental tobacco smoke exposure and ischaemic heart disease: an evaluation of the evidence. *BMJ* 1997;**315**:973-80.

23. Wells AJ. Heart disease from passive smoking in the workplace. *J Am Coll Cardiol* 1998;**31**:1-9.

24. Enstrom JE, Kabat GC. Environmental tobacco smoke and tobacco related mortality in a prospective study of Californians, 1960-98. *BMJ* 2003;**326**:1057-61. Full version available at http://bmj.com/cgi/content/full/326/7398/1057

25. Enstrom JE, Kabat GC. *The Lancet*'s call to ban smoking in the UK [Letter]. *Lancet* 2004;**363**:398-9.

26. Woodward M, Tunstall-Pedoe H. Biochemical evidence of persistent heavy smoking after a coronary diagnosis despite self-reported reduction: analysis from the Scottish Heart Health Study. *European Health Journal* 1992;**13**:160-5.

27. Suadicani P, Hein HO, Gyntelberg F. Mortality and morbidity of potentially misclassified smokers. *Int J Epidemiol* 1997;**26**:321-7.

28. Glantz SA, Parmley WW. Passive smoking and heart disease. Mechanisms and risk. *JAMA* 1995;**273**:1047-53.

29. Morris JA, Gardner MJ. Calculating confidence intervals for relative risks (odds ratios) and standardised ratios and rates. *BMJ* 1988;**296**:1313-6.

30. Hamling J, Lee P, Weitkunat R, Ambühl M. Facilitating meta-analyses by deriving relative effect and precision estimates for alternative comparisons from a set of estimates presented by exposure level or disease category. *Stat Med* 2008;**27**:954-70.

31. Lee PN, Forey BA, Hamling JS. *ETS and heart disease meta-analyses*. Sutton, Surrey: P N Lee Statistics and Computing Ltd; 2012. www.pnlee.co.uk/reflist.htm [Download LEE2012C]

32. Lee PN, Forey BA, Hamling JS. *Detailed meta-analysis on ETS and heart disease*. Sutton, Surrey: P N Lee Statistics and Computing Ltd; 2012. www.pnlee.co.uk/reflist.htm [Download LEE2012D]

33. 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; 2012. www.pnlee.co.uk/reflist.htm [Download LEE2012E]

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	259		140
						IHD		81	
47	Hamer	2010	England, Scotland	P	F	CVD		96	
48	Jefferis	2010	Britain	P	F+NF	FMI		74	

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 result 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. B.	Spouse ever smoked 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. B.	Spouse ever smoked 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. B.	Spouse ever smoked in marriage 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. B.	Spouse ever smoked 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. B.	Spouse ever smoked 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. B.	Spouse ever smoked in marriage 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 $\leq$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. B.	Ever lived with smoking spouse 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. B.	Spouse ever smoked 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. B.	Ever lived with a smoker 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. B.	Spouse ever smoked in marriage 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

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	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)	+
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)	+

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 (49).

In study 8 the estimates were given by Wells (50).

In several studies (8, 9, 10, 12, 16, 18, 21, 23, 24, 26, 28, 30, 33, 36, 37, 40, 41, 42, 44, 45, 48) 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
  - 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	

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).

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.

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: 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

In study 21 the estimates were given by Wells (50).

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.

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: 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

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.

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

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

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		**ETS exposure from spouse and/or work**		
		F	Neither Home Work Both	1.00 2.07 2.53 4.18	+
26	Iribarren		**ETS exposure in small spaces**		
		M	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	+
			ETS exposure in large indoor areas		
		M	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	
			Total ETS exposure		
		M	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		**ETS exposure from spouse and/or work**		
		M+F	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		**ETS exposure at home or work**		
		M	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	+
			ETS exposure at home and work		
		M+F	Neither Both	1.00 2.56 (1.65-3.96)	
29	Enstrom		**Spouse smoked pipe/cigar**		
		F	No Yes	1.00 0.97 (0.86-1.10)	
30	Chen		**Total ETS exposure**		
		M+F	None A little Some A lot	1.00 1.30 1.50 1.80	+
			Serum cotinine (ng/ml)		
		M+F	0 >0-1.05 1.06-3.97 3.98-17.49	1.00 0.70 1.00 1.10	
			Self-reported ETS and cotinine combined		
		M+F	I II III IV V VI VII	1.00 1.30 1.60 1.50 1.70 1.80 2.60	+
			ETS exposure other than at home and/or work		
		M+F	No Yes	1.00 1.00 (0.40-2.30)	
			Duration of total daily ETS exposure (hours)		
		M+F	0 >0-2 3-5 ≥6	1.00 1.20 1.60 1.70	
31	Nishtar		**Any ETS exposure**		
		M+F	No Yes	1.00 2.87 (1.28-6.42)	+
			Daily ETS exposure		
		M+F	No Yes	1.00 3.87 (1.68-8.86)	+
32	Whincup		**Serum cotinine (ng/ml)**		
		M	≤0.7 0.8-1.4 1.5-2.7 2.8-14.0	1.00 1.54 1.89 1.67	+
35	Hedblad		**Blood carboxyhaemoglobin (%)**		
		M	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	1.00 1.33 2.00	+
			Per unit increase in log cotinine,	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	1.00 0.91 0.99 0.94	
			Per doubling of cotinine	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.

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.

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.

References to data sources

1a Hirayama T. Lung cancer in Japan: effects of nutrition and passive smoking. In: Mizell M, Correa P, editors. *Lung cancer: causes and prevention, Proceedings of the International Lung Cancer Update Conference, New Orleans, Louisiana, March 3-5, 1983*. Deerfield Beach, Florida: Verlag Chemie International, Inc, 1984;175-95.

1b Hirayama T. Passive smoking [Letter]. *N Z Med J* 1990;**103**:54.

2 Garland C, Barrett-Connor E, Suarez L, Criqui MH, Wingard DL. Effects of passive smoking on ischemic heart disease mortality of non-smokers. *Am J Epidemiol* 1985;**121**:645-50. Erratum appears in Am J Epidemiol 1985;122:1112.

3 Lee PN, Chamberlain J, Alderson MR. Relationship of passive smoking to risk of lung cancer and other smoking-associated diseases. *Br J Cancer* 1986;**54**:97-105.

4 Martin MJ, Hunt SC, Williams RR. Increased incidence of heart attacks in nonsmoking women married to smokers. In: *114th Annual Meeting of American Public Health Association, October 1, 1986*. 1986;1p.

5 Svendsen KH, Kuller LH, Martin JM, Ockene JK. Effects of passive smoking in the Multiple Risk Factor Intervention Trial. *Am J Epidemiol* 1987;**126**:783-95.

6 Butler TL. *The relationship of passive smoking to various health outcomes among Seventh day Adventists in California* [Thesis]. Los Angeles: University of California; 1988.

7 Palmer JR, Rosenberg L, Shapiro S. Passive smoking and myocardial infarction in women [Abstract]. *CVD Newsletter* 1988;**43**:29.

8 Hole DJ, Gillis CR, Chopra C, Hawthorne VM. Passive smoking and cardiorespiratory health in a general population in the west of Scotland. *BMJ* 1989;**299**:423-7.

9 Jackson RT. *The Auckland Heart Survey* [Thesis]. Auckland, New Zealand: University of Auckland; 1989.

10 Sandler DP, Comstock GW, Helsing KJ, Shore DL. Deaths from all causes in non-smokers who lived with smokers. *Am J Public Health* 1989;**79**:163-7.

11 Humble C, Croft J, Gerber A, Casper M, Hames CG, Tyroler HA. Passive smoking and 20-year cardiovascular disease mortality among non-smoking wives, Evans County, Georgia. *Am J Public Health* 1990;**80**:599-601.

12 Dobson AJ, Alexander HM, Heller RF, Lloyd DM. Passive smoking and the risk of heart attack or coronary death. *Med J Aust* 1991;**154**:793-7.

13 La Vecchia C, D'Avanzo B, Franzosi MG, Tognoni G. Passive smoking and the risk of acute myocardial infarction [Letter]. *Lancet* 1993;**341**:505-6.

14 Layard MW. Ischemic heart disease and spousal smoking in the National Mortality Followback Survey. *Regul Toxicol Pharmacol* 1995;**21**:180-3.

15 LeVois ME, Layard MW. Publication bias in the environmental tobacco smoke/coronary heart disease epidemiologic literature. *Regul Toxicol Pharmacol* 1995;**21**:184-91.

16 Mannino DM, Siegel M, Rose D, Etzel R. Health effects of environmental tobacco smoke exposure in US adults: data from the 1991 National Health Interview Survey. *Epidemiology* 1995;**6**:56S.

17 Muscat JE, Wynder EL. Exposure to environmental tobacco smoke and the risk of heart attack. *Int J Epidemiol* 1995;**24**:715-9.

18 Tunstall-Pedoe H, Brown CA, Woodward M, Tavendale R. Passive smoking by self report and serum cotinine and the prevalence of respiratory and coronary heart disease in the Scottish heart health study. *J Epidemiol Community Health* 1995;**49**:139-43.

19 Steenland K, Thun M, Lally C, Heath C, Jr. Environmental tobacco smoke and coronary heart disease in the American Cancer Society CPS-II cohort. *Circulation* 1996;**94**:622-8.

20 Janghorbani M, Sadeghi-Golmakani N. Passive smoking and the risk of coronary heart disease among married non-smoking women. *Medical Journal of the Islamic Republic of Iran* 1997;**11**:203-8.

21 Kawachi I, Colditz GA, Speizer FE, Manson JE, Stampfer MJ, Willett WC, *et al*. A prospective study of passive smoking and coronary heart disease. *Circulation* 1997;**95**:2374-9.

22 Ciruzzi M, Pramparo P, Esteban O, Rozlosnik J, Tartaglione J, Abecasis B, *et al*. Case-control study of passive smoking at home and risk of acute myocardial infarction. *J Am Coll Cardiol* 1998;**31**:797-803.

23 McElduff P, Dobson AJ, Jackson R, Beaglehole R, Heller RF, Lay-Yee R. Coronary events and exposure to environmental tobacco smoke: a case-control study from Australia and New Zealand. *Tob Control* 1998;**7**:41-6.

24 Spencer CA, Jamrozik K, Lambert L. Do simple prudent health behaviours protect men from myocardial infarction? *Int J Epidemiol* 1999;**28**:846-52.

25a He Y, Lam TH, Li LS, Li LS, Du RY, Jia GL, *et al*. Passive smoking from husbands as a risk factor for coronary heart disease in women in Xi'an, China, who have never smoked. In: Lu R, Mackay J, Niu S, Peto R, editors. *Tobacco: the growing epidemic, Proceedings of the Tenth World Conference on Tobacco or Health, 24-28 August 1997, Beijing, China*. London, Berlin, Heidleberg: Springer-Verlag, 2000;153-5.

25b He Y, Lam TH, Li LS, Du RY, Jia GL, Huang JY, *et al*. Passive smoking at work as a risk factor for coronary heart disease in Chinese women who have never smoked. *BMJ* 1994;**308**:380-4.

26 Iribarren C, Friedman GD, Klatsky AL, Eisner MD. Exposure to environmental tobacco smoke: association with personal characteristics and self reported health conditions. *J Epidemiol Community Health* 2001;**55**:721-8.

27 Rosenlund M, Berglind N, Gustavsson A, Reuterwall C, Hallqvist J, Nyberg F, *et al*. Environmental tobacco smoke and myocardial infarction among never-smokers in the Stockholm Heart Epidemiology Program (SHEEP). *Epidemiology* 2001;**12**:558-64.

28 Pitsavos C, Panagiotakos DB, Chrysohoou C, Skoumas J, Tzioumis K, Stefanadis C. Association between exposure to environmental tobacco smoke and the development of acute coronary syndromes: the CARDIO2000 case-control study. *Tob Control* 2002;**11**:220-5.

29 Enstrom JE, Kabat GC. Environmental tobacco smoke and tobacco related mortality in a prospective study of Californians, 1960-98 [Abridged version]. *BMJ* 2003;**326**:1057-61. Full version available at http://bmj.com/cgi/content/full/326/7398/1057

30 Chen R, Tavendale R, Tunstall-Pedoe H. Environmental tobacco smoke and prevalent coronary heart disease among never smokers in the Scottish MONICA surveys. *Occup Environ Med* 2004;**61** :790-2.

31 Nishtar S, Wierzbicki AS, Lumb PJ, Lambert-Hammill M, Turner CN, Crook MA, *et al*. Waist-hip ratio and low HDL predict the risk of coronary artery disease in Pakistanis. *Curr Med Res Opin* 2004;**20**:55-62.

32 Whincup PH, Gilg JA, Emberson JR, Jarvis MJ, Feyerabend C, Bryant A, *et al*. Passive smoking and risk of coronary heart disease and stroke: prospective study with cotinine measurement. *BMJ* 2004;**329**:200-4.

33 McGhee SM, Ho SY, Schooling M, Ho LM, Thomas GN, Hedley AJ, *et al*. Mortality associated with passive smoking in Hong Kong. *BMJ* 2005;**330**:287-8.

34 Qureshi AI, Suri MFK, Kirmani JF, Divani AA. Cigarette smoking among spouses. Another risk factor for stroke in women. *Stroke* 2005;**36**:e74-e76.

35 Hedblad B, Engström G, Janzon E, Berglund G, Janzon L. COHb% as a marker of cardiovascular risk in never smokers: results from a population-based cohort study. *Scandinavian Journal of Public Health* 2006:**34**:609-615.

36 Stranges S, Bonner MR, Fucci F, Cummings KM, Freudenheim JL, Dorn JM *et al*. Lifetime exposure to secondhand smoke and risk of myocardial infarction in never smokers: results from the Western New York health study, 1995-2001. *Archives of Internal Medicine* 2006:**166**:1961-1967.

37 Teo KK, Ounpuu S, Hawken S, Pandey MR, Valentin V, Hunt D, *et al*. Tobacco use and risk of myocardial infarction in 52 countries in the INTERHEART study: a case-control study. *Lancet* 2006;**368**:647-58.

38 Wen W, Shu XO, Gao Y-T, Yang G, Li Q, Li H, *et al*. Environmental tobacco smoke and mortality in Chinese women who have never smoked: prospective cohort study. *BMJ* 2006;**333**:376-9.

39 Eisner MD, Wang Y, Haight TJ, Balmes J, Hammond SK, Tager I. Secondhand smoke exposure, pulmonary function, and cardiovascular mortality. *Annals of Epidemiology* 2007:**17**:364-373.

40,41 Hill SE, Blakely T, Kawachi I, Woodward A. Mortality among lifelong nonsmokers exposed to secondhand smoke at home: cohort data and sensitivity analyses. *American Journal of Epidemiology* 2007:**165**:530-540.

42 He Y, Lam TH, Jiang B, Wang J, Sai X, Fan L, *et al*. Passive smoking and risk of peripheral arterial disease and ischemic stroke in Chinese women who never smoked. *Circulation* 2008;**118**:1535-40.

43 Sulo G, Burazeri G, Dehghan A, Kark JD. Partner's smoking status and acute coronary syndrome: population-based case-control study in Tirana, Albania. Croat Med J 2008;49:751-6.

44 Vozoris N, Lougheed MD. Second-hand smoke exposure in Canada: prevalence, risk factors, and association with respiratory and cardiovascular diseases. *Can Respir J* 2008;**15**:263-9.

45 Ding D, Fung JW-H, Zhang Q, Yip GW-K, Chan C-K, Yu C-M. Effect of household passive smoking exposure on the risk of ischaemic heart disease in never-smoke female patients in Hong Kong. *Tob Control* 2009;**18**:354-7.

46 Gallo V, Neasham D, Airoldi L, Ferrari P, Jenab M, Boffetta P, *et al*. Second-hand smoke, cotinine levels, and risk of circulatory mortality in a large cohort study of never-smokers. *Epidemiology* 2010;**21**:207-14.

47 Hamer M, Stamatakis E, Kivimaki M, Lowe GD, Batty GD. Objectively measured secondhand smoke exposure and risk of cardiovascular disease. What is the mediating role of inflammatory and hemostatic factors? *J Am Coll Cardiol* 2010;**56**:18-23.

48 Jefferis BJ, Lawlor DA, Ebrahim S, Wannamethee SG, Feyerabend C, Doig M, *et al*. Cotinine-assessed second-hand smoke exposure and risk of cardiovascular disease in older adults. *Heart* 2010;**96**:854-9.

49 Wells AJ. Passive smoking as a cause of heart disease. *J Am Coll Cardiol* 1994;**24**:546-54.

50 Wells AJ. Heart disease from passive smoking in the workplace. *J Am Coll Cardiol* 1998;**31**:1-9.

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.

References to Appendix

A1 Hirayama T. Non-smoking wives of heavy smokers have a higher risk of lung cancer: a study from Japan. *BMJ* 1981;**282**:183-5.

A2 Gillis CR, Hole DJ, Hawthorne VM, Boyle P. The effect of environmental tobacco smoke in two urban communities in the west of Scotland. *Eur J Respir Dis* 1984;**65(suppl 133)**:121-6.

A3 Hirayama T. Passive smoking and cancer: an epidemiological review. *GANN Monograph on Cancer Research* 1987;**33**:127-35.

A4 Sandler DP, Helsing KJ, Comstock GW. Heart disease mortality in persons living with smokers. In: *Symposium on Indoor Air Quality, Berlin*. 1987;

A5 Helsing KJ, Sandler DP, Comstock GW, Chee E. Heart disease mortality in non-smokers living with smokers. *Am J Epidemiol* 1988;**127**:915-22.

A6 Hirayama T. Health effects of active and passive smoking. In: Aoki M, Hisamichi S, Tominaga S, editors. *Smoking and health 1987, Proceedings of the 6th World Conference on Smoking and Health, Tokyo, 9-12 November 1987*. Amsterdam: Elsevier Science Publishers B.V. (Biomedical Division), 1988;75-86. International Congress Series No. 780.

A7 He Y. Women's passive smoking and coronary heart disease. *Zhonghua Yu Fang Yi Xue Za Zhi* 1989;**23**:19-22.

A8 Butler T. The relationship of passive smoking to various health outcomes among Seventh-Day Adventists in California. In: *Seventh World Conference on Tobacco and Health*. 1990;316.

A9 Hirayama T. Wahrendorf J, editor. *Life-style and mortality: A large scale census based cohort study in Japan. Contributions to epidemiology and biostatistics*. Basle: Karger; 1990. 6.

A10 Hirayama T. Ischemic heart disease; response to Lee [Letter]. *Environ Int* 1990;**16**:181-2.

A11 Ciruzzi M, Esteban O, Rozlosnik J, Montagna H, Caccavo A, De La Cruz Ojeda J, *et al*. Passive smoking and the risk of acute myocardial infarction [Abstract]. *Eur Heart J* 1996;**17**:309.

A12 He Y, Lam TH, Li LS, Li LS, Du RY, Jia GL, *et al*. The number of stenotic coronary arteries and passive smoking exposure from husband in lifelong non-smoking women in Xi'an, China. *Atherosclerosis* 1996;**127**:229-38.

A13 Kawachi I, Colditz GA, Speizer FE, Manson JE, Stampfer MJ, Willett WC, *et al*. A prospective study of passive smoking and coronary heart disease [Abstract]. *Am J Epidemiol* 1996;**143**:S70.

A14 Rosenlund M, Berglind N, Gustavsson A, Reuterwall C, Hallqvist J, Nyberg F, *et al*. Environmental tobacco smoke and non-fatal myocardial infarction among never-smokers [Abstract]. *Epidemiology* 2000;**11**:S103.

A15 Panagiotakos DB, Pitsavos C, Chrysohoou C, Stefanadis C, Toutouzas P. Risk stratification of coronary heart disease through established and emerging lifestyle factors in a Mediterranean population: CARDIO2000 epidemiological study. *J Cardiovasc Risk* 2001;**8**:329-35.

A16 Panagiotakos DB, Pitsavos C, Chrysohoou C, Stefanadis C, Toutouzas P. Risk stratification of coronary heart disease in Greece: final results from the CARDI2000 epidemiological study. *Prev Med* 2002;**35**:548-56.

A17 Panagiotakos DB, Chrysohoou C, Pitsavos C, Papaioannou I, Skoumas J, Stefanadis C, *et al*. The association between secondhand smoke and the risk of developing acute coronary syndromes, among non-smokers, under the presence of several cardiovascular risk factors: The CARDIO2000 case-control study. *BMC Public Health* 2002;**2**:9.

A18 Pitsavos C, Panagiotakos DB, Chrysohoou C, Tzioumis K, Papaioannou I, Stefanadis C, *et al*. Association between passive cigarette smoking and the risk of developing acute coronary syndromes: the CARDIO2000 study. *Heart Vessels* 2002;**16**:127-30.

A19 Chen R, Tunstall-Pedoe H. Coronary heart disease in relation to passive smoking by self report, serum cotinine and their combination: Scottish MONICA study [Abstract]. Society for Epidemiologic Research 36th Annual Meeting, Atlanta, Georgia, June 11-14, 2003. *Am J Epidemiol* 2003;**157(Suppl)**:S27.

A20 Jabbour S, El-Roueiheb Z, Sibai AM. Nargileh (water-pipe) smoking and incident coronary heart disease: a case-control study [Abstract]. *Ann Epidemiol* 2003;**13**:570.

A21 Sargent RP, Shepard RM, Glantz SA. Reduced incidence of admissions for myocardial infarction associated with public smoking ban: before and after study. *BMJ* 2004;**328**:977-80.

A22 Barone-Adesi F, Vizzini L, Merletti F, Richiardi L. Short-term effects of Italian smoking regulation on rates of hospital admission for acute myocardial infarction. *Eur Heart J* 2006;**27**:2468-72.

A23 Bartecchi C, Alsever RN, Nevin-Wood C, Thomas WM, Estacio RO, Bartelson BB, *et al*. Reduction in the incidence of acute myocardial infarction associated with a citywide smoking ordinance. *Circulation* 2006;**114**:1490-4.

A24 Khuder SA, Milz S, Jordan T, Price J, Silvestri K, Butler P. The impact of a smoking ban on hospital admissions for coronary heart disease. *Prev Med* 2007;**45**:3-8.

A25 Cesaroni G, Forastiere F, Agabiti N, Valente P, Zuccaro P, Perucci CA. Effect of the Italian smoking ban on population rates of acute coronary events. *Circulation* 2008;**117**:1183-8.

A26 Jefferis BJ, Lowe GDO, Welsh P, Lawlor DA, Ebrahim S, Wannamethee SG, *et al*. Secondhand smoke exposure assessed using serum cotinine, associations with myocardial infarction, stroke and cardiovascular risk factors in adult men and women. Society for Social Medicine 53rd Annual Scientific Meeting, 1 October 2009. *J Epidemiol Community Health* 2009;**63(Suppl II)**:A35-A36.

A27 Pope CA, III, Burnett RT, Krewski D, Jerrett M, Shi Y, Calle EE, *et al*. Cardiovascular mortality and exposure to airborne fine particulate matter and cigarette smoke: shape of the exposure-response relationship. *Circulation* 2009;**120**:941-8.

APPENDIX B

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

	Study																								
Risk factor	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
Sex*	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
Marital status**	x			x				x	x					x	x	x	x						
Blood pressure/ hypertension		x			x		x		x	x	x						x	x		x		x	x
Cholesterol	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
Obesity/weight	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
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					
Oestrogen use																				x			
Other			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, FEV_1, height, triglycerides and white cell count
Study 35	Other risk factors considered: triglycerides and FEV_1
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, FEV_1, C-reactive protein, interleukin 6, white cell count