### EPIDEMIOLOGICAL EVIDENCE ON ENVIRONMENTAL TOBACCO SMOKE AND HEART DISEASE

- 1. Almost 30 epidemiological studies of heart disease and ETS among lifelong non-smokers have been published.
- 2. The overall evidence from these studies does not indicate an increased risk of heart disease in relation to ETS exposure in the workplace, with only one of 17 results reported showing a statistically significant association.
- 3. Although most published estimates for spousal smoking (27out of 40)<sup>1</sup> are not statistically significant, there have been reports of a significant association and dose-response relationship in some studies. However, there are a number of reasons why the findings should not be interpreted as indicating a causal effect of ETS exposure including:
  - the reported results vary markedly with study size. While the reported increase in risk is quite small, less than 10%, in studies involving over 1000 heart disease cases, it is much larger, over 50%, in studies with less than 100 cases.
  - many of the studies fail to consider possible lifestyle confounding factors. There are over 300 different risk factors reported for heart disease<sup>2</sup> and several studies have shown differences in many lifestyle factors between smoking and non-smoking households.<sup>3-9</sup>
  - the studies generally rely on reported rather than objectively measured ETS exposure data. The only study to use serum cotinine as a marker of ETS exposure found no significant relationship between this marker and risk of heart disease.<sup>10</sup>
  - some of the studies<sup>11-13</sup> have relied on unvalidated reports by the subject of current or past heart disease, with no confirmation of the diagnosis.
  - results from by far the largest study,<sup>14</sup> which found no relationship with spousal smoking, have been excluded by some reviewers.<sup>15,16</sup>
  - the studies may have inappropriately included some misclassified current and former smokers. A recent study reported particularly high heart disease mortality among smokers who deny smoking,<sup>17</sup> suggesting the possibility of bias resulting from such misclassification.
- 4. Extrapolation from active smoking data to estimate risk at low exposure lacks scientific credibility. The mechanistic theories that have been proposed to support such extrapolation<sup>15, 18</sup> are speculative.
- 5. Taken as a whole, the epidemiology does not provide strong support to the claim that exposure to ETS causes heart disease in non-smokers.<sup>19</sup>

#### **REFERENCES TO PAPERS CITED ON PAGE 1**

- <sup>1</sup> Based on covariate adjusted data where available; the figure of 27out of 40 applies when spousal current smoking is used as the index of choice, where estimates for both spousal current and spousal ever smoking are available. It would be 29 out of 40 were spousal ever smoking used as the index of choice.
- <sup>2</sup> Hopkins PN and Williams RR "Identification and relative weight of cardiovascular risk factors" Cardiology Clinics: 3-31 (1986).
- <sup>3</sup> Sidney S et al "Dietary intake of carotene in nonsmokers with and without passive smoking at home" Am J Epidemiol 129: 1305-1309 (1989).
- <sup>4</sup> Thompson DH and Warburton DM *'Lifestyle differences between smokers, ex-smokers and non-smokers, and implications for their health* 'Psychology and Health 7: 311-321 (1992).
- <sup>5</sup> Thornton A "Differences between smokers, ex-smokers, passive smokers and non-smokers" J Clin Epidemiol 47: 1143-1162 (1994).
- <sup>6</sup> Cress RD et al "Contraceptive use among women smokers and nonsmokers in the San Francisco Bay area" Preventive Medicine 23: 181-189 (1994).
- <sup>7</sup> Subar AF et al *"Food and nutrient intake differences between smokers and non-smokers in the US"* Am J Public Health 80: 1323-1329 (1990).
- <sup>8</sup> Le Marchand L et al *'Dietary patterns of female nonsmokers with and without exposure to environmental tobacco smoke'* Cancer Causes and Control 2: 11-16 (1991).
- <sup>9</sup> Matanoski G et al "Characteristics of nonsmoking women in NHANES I and NHANES II epidemiologic follow-up study with exposure to spouses who smoke" Am J Epidemiol 142: 149-157 (1995).
- <sup>10</sup> Tunstall-Pedoe H et al "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 49: 139-143 (1995).
- <sup>11</sup> Martin MJ et al *"Increased incidence of heart atacks in non-smoking women married to smokers"* Paper presented at 114<sup>th</sup> Annual Meeting of American Public Health Association (1986).
- <sup>12</sup> Mannino DM et al "Health effects of environmental tobacco smoke exposure in US adults: data from the 1991 National Health Interview Survey" Epidemiology 6: 56S (1995).
- <sup>13</sup> Iribarren C et al *"Exposure to environmental tobacco smoke: association with personal characteristics and self reported health conditions"* J Epidemiol Community Health 55: 721-728 (2001).
- <sup>14</sup> LeVois ME and Layard MW *"Publication bias in the environmental tobacco smoke/coronary heart disease epidemiologic literature"* Regulatory Toxicology and Pharmacology 21: 184-191 (1995).
- <sup>15</sup> Law MR et al "Environmental tobacco smoke exposure and ischaemic heart disease: an evaluation of the evidence" Br Med J 315: 973-980 (1997).
- <sup>16</sup> Wells AJ *"Heart disease from passive smoking in the workplace"* J Am Coll Cardiol 31: 1-9 (1998).
- <sup>17</sup> Suadicani P et al "*Mortality and morbidity of potentially misclassified smokers*" Int J Epidemiol 26: 321-327 (1997).
- <sup>18</sup> Glantz SA and Parmley WW "Passive smoking and heart disease. Mechanisms and risk" JAMA 273: 1047-1053 (1995).
- <sup>19</sup> Lee PN and Roe FJC. "Environmental tobacco smoke exposure and heart disease: a critique of the claims of Glantz and Parmley" HERA 5: 171-218 (1999).

### EPIDEMIOLOGICAL EVIDENCE ON ENVIRONMENTAL TOBACCO SMOKE AND HEART DISEASE

### 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 27 studies providing data.

Table 2 shows the actual indices of spousal smoking (or the nearest equivalent) for which data are available.

Tables 3 and 5 show, for spousal smoking and for workplace ETS exposure respectively, the individual relative risk estimates and 95% confidence limits for each successive study.

Tables 4 and 6 show, for spousal smoking and workplace ETS exposure respectively, relative risk estimates by extent of exposure together with the significance of the dose-related trend statistic.

Table 7 presents data in relation to other indices of ETS exposure.

Relative risk estimates and 95% confidence limits in Tables 3 to 7 are adjusted for covariates if adjusted data are available, and otherwise are unadjusted. Where, in some cases, the source publication provides more than one adjusted estimate, the data that are normally presented are those adjusted for most covariates. Where studies present appropriate data on numbers of cases and controls (or populations at risk) unadjusted relative risks and 95% confidence limits are calculated, or checked, using the CIA program described by Morris and Gardner.<sup>20</sup>

Some studies reported adjusted relative risks and confidence intervals only by level of the exposure of interest. These adjusted risks and intervals were used to estimate corresponding "effective numbers" of cases and controls (or subjects at risk) at each level, which could then be combined to allow estimation of risks and intervals for overall exposure.<sup>21</sup>

<sup>&</sup>lt;sup>20</sup> Morris JA and Gardner MJ "Calculating confidence intervals for relative risks (odds ratios) and standardised ratios and rates" Br Med J 296:1313-1316 (1988).

<sup>&</sup>lt;sup>21</sup> Fry JS and Lee PN "Revisiting the association between environmental tobacco smoke exposure and lung cancer risk. I. The dose-response relationship with amount and duration of smoking by the husband" Indoor Built Environ 9:303-316 (2000).

Study	,				Endpoints		Number of lifelong not	heart disease on-smokers	cases in
Ref	Author	Year	Location	Туре	Fatality	Disease	Females	Combined	Males
1	Hirayama	1984	Japan	Р	F	IHD	494		
2	Garland	1985	USA/California	Р	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	Р	F,NF	IHD,IHD			69
6	Butler	1988	USA/California	Р	F	IHD	80		
7	Palmer	1988	USA/?	CC	NF	MI	336		
8	Hole	1989	Scotland	Р	F,NF	IHD,A/E	55		65
9	Jackson	1989	New Zealand	CC	F,NF	IHD,MI	73		230
10	Sandler	1989	USA/Maryland	Р	F	AHD	988		370
11	Humble	1990	USA/Georgia	Р	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	Р	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	Р	F	IHD	1325		2494
20	Janghorbani	1997	Iran	CC	NF	IHD	200		
21	Kawachi	1997	USA	Р	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
25	He	2000	China	CC	NF	MI/CS	115		
26	Rosenlund	2001	Sweden	CC	NF	FMI	135		199
27	Iribarren	2001	USA	CS	NF	HD	1856		2945
28	Pitsavas	2002	Greece	CC	NF	FMI/UA		279	

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

Footnotes

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

The study year is the year of that publication.

The study types are CC=case control, CS=cross-sectional and P=prospective.

Fatality is indicated by F=fatal heart disease and NF=non-fatal heart disease. F + NF implies data only available for fatal and non-fatal heart disease combined.

Disease is indicated by A/E = angina or ECG abnormality, AHD = arteriosclerotic heart disease, CVD = cardiovascular disease, FMI = first myocardial infarction, FMI/UA = first myocardial infarction or unstable angina, FMIS = first myocardial infarction surviving 28 days, HD = heart disease, IHD = ischaemic (coronary) heart disease, MI = myocardial infarction, MI/CS = myocardial infarction or coronary stenosis, MNI = newly diagnosed myocardial infarction, PHA = previous heart attack.

Numbers of heart disease cases in lifelong non-smokers are totals in the study; for analyses relating to specific types of exposure numbers may be less than this. For study 16 (indicated by \*) numbers were not given. For study 18, data were only provided for sexes combined. For study 6, numbers relate to the spouse-pairs cohort only, the AHSMOG cohort including ex-smokers. For study 12, numbers also exclude ex-smokers.

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.

Study	1	_		
Ref	Author		Exposed Group	Comparison Group
1	Hirayama		Spouse ever smoked	Spouse never smoked
2	Garland	A. B.	Spouse ever smoked Spouse 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 current smoker	Spouse never smoked Spouse never smoked
5	Svendsen		Spouse smoker at entry to study	Spouse non-smoker at entry to study
6	Butler	A. B.	Spouse ever smoked in marriage Spouse 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 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 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 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 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 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
25	Не		Spouse smoked in marriage for >5 years	Spouse smoked in marriage for $\leq 5$ years
26	Rosenlund	A. B.	Ever lived with smoking spouse Currently living with smoking spouse	Never lived with smoking spouse Not currently living with smoking spous
27	Iribarren		1 hr/wk or more current ETS exposure at home	Less than 1 hr/wk current ETS exposure at home
28	Pitsavas		ETS exposure only at home	No ETS exposure at home or work

#### TABLE 2: Smoking by the spouse - Actual index of exposure

\* 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 current smoker"

For studies 2, 4, 6, 13, 15, 19 and 26 data were presented separately for never, ex- and current smoking spouses so relative risks could be calculated for both indicated comparisons

Study						
Ref	Author	Sex	Exposure Index	Fatality	Relative risk (95% confidence limits)	Significance
1	Hirayama	F	Е	F	1.16 (0.94-1.43)	
2	Garland	F	Е	F	2.70 (0.63-11.58)	
		F	C(N)	F	2.25 (0.32-15.74)	
3	Lee	М	Е	NF	1.24 (0.59-2.59)	
		F	Е	NF	0.93 (0.54-1.62)	
4	Martin	F	Е	Ν	2.60 (1.20-5.70)	+
		F	С	Ν	3.40	?
5	Svendsen	М	С	F+NF	1.61 (0.96-2.71)	
6	Butler	F	Е	F	1.07 (0.65-1.75)	
		F	C(N)	F	1.40 (0.51-3.84)	
7	Palmer	F	Е	NF	1.20	?
8	Hole	М	Е	F	1.73 (1.01-2.96)	+
		F	Е	F	1.65 (0.79-3.46)	
9	Jackson	М	С	F+NF	1.06 (0.39-2.91)	
		F	С	F+NF	3.74 (1.15-12.19)	+
10	Sandler	М	С	F	1.31 (1.05-1.64)	+
		F	С	F	1.19 (1.04-1.36)	+
11	Humble	F	C(N)	F	1.59 (0.99-2.57)	
12	Dobson	М	С	F+NF	0.97 (0.50-1.86)	
		F	С	F+NF	2.46 (1.47-4.13)	+
13	La Vecchia	М	Е	Ν	1.09 (0.47-2.53)	
	<ul> <li>6 Butler</li> <li>7 Palmer</li> <li>8 Hole</li> <li>9 Jackson</li> <li>10 Sandler</li> <li>11 Humble</li> <li>12 Dobson</li> <li>13 La Vecchia</li> <li>14 Layard</li> </ul>	F	E	Ν	1.27 (0.52-3.09)	
		М	C(N)	Ν	1.09 (0.39-3.01)	
	<ul> <li>3 Lee</li> <li>4 Martin</li> <li>5 Svendsen</li> <li>6 Butler</li> <li>7 Palmer</li> <li>8 Hole</li> <li>9 Jackson</li> <li>10 Sandler</li> <li>11 Humble</li> <li>12 Dobson</li> <li>13 La Vecchia</li> <li>14 Layard</li> <li>15 LeVois</li> </ul>	F	C(N)	Ν	1.36 (0.46-4.05)	
14	Layard	М	Е	F	0.97 (0.73-1.28)	
		F	Е	F	0.99 (0.84-1.16)	
15		М	Е	F	0.97 (0.90-1.05)	
	(CPS-I)	F	Е	F	1.03 (0.98-1.08)	
		М	C(N)	F	0.98 (0.91-1.06)	
		F	C(N)	F	1.04 (0.99-1.09)	
16	Mannino	M+F	С	NF	1.12	?
17	Muscat	М	Е	NF	1.38 (0.70-2.75)	
		F	Е	NF	1.33 (0.59-2.99)	
18		M+F	С	NF	1.34 (1.07-1.67)	+

# TABLE 3 Relative risk of heart disease among lifelong non-smokers in relation to smoking by the spouse

Study						
Ref	Author	Sex	Exposure		Relative risk	Significance
			index	Fatality	(95% confidence limits	
19	Steenland	М	Е	F	1.09 (0.98-1.21)	
		F	Е	F	1.04 (0.93-1.16)	
		Μ	C(N)	F	1.22 (1.07-1.40)	+
		F	C(N)	F	1.10 (0.96-1.27)	
20	Janghorbani	F	Е	NF	1.38 (0.95-2.01)	
21	Kawachi	F	С	F+NF	1.53 (0.81-2.90)	
22	Ciruzzi	М	С	NF	1.18 (0.55-2.52)	
		F	С	NF	1.73 (0.89-3.36)	
23	McElduff	М	С	F+NF	0.82 (0.55-1.22)	
		F	С	F+NF	2.15 (1.18-3.92)	+
24	Spencer	М	Е	NF	No significant association	
25	Не	F	Е	NF	1.60 (0.94-2.90)	
26	Rosenlund	М	Е	NF	0.96 (0.64-1.44)	
		F	Е	NF	1.53 (0.95-2.44)	
		Μ	C(N)	NF	0.98 (0.57-1.69)	
		F	C(N)	NF	2.59 (1.27-5.29)	+
27	Iribarren	М	С	NF	1.13 (1.00-1.27)	+
		F	С	NF	1.20 (1.09-1.30)	+
28	Pitsavas	M+F	Е	NF	1.33 (0.89-1.99)	

# TABLE 3 (continued)Relative risk of heart disease among lifelong non-smokers in<br/>relation to smoking by the spouse

Footnotes

In nine studies (8,9,10,12,16,18,21,23,24,27) the index of exposure is actually based not on spousal smoking but on the nearest equivalent index (see Table 2).

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).

Fatality F = fatal NF = non-fatal F+NF = fatal and non-fatal combined.

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

See Appendix A for the covariates considered in adjusted analyses.

Significant (p<0.05) positive (negative) relative risks are indicated by + (or -). ? indicates not known if significant or not.

In study 4 (exposure index E) and study 21, the estimates were given by Wells (28).

In study 8 the estimates were given by Wells (29).

Study	,				Signifi- cance
Ref	Author	Sex	Exposure grouping	Relative risks by grouping	(trend)
1	Hirayama	F	0 1-19 20+ (cigs/day)	1.00 1.10 1.31	+
5	Svendsen	М	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 F	None Low High (exposure) None Low High (exposure)	$\begin{array}{cccccccccccccccccccccccccccccccccccc$	+
13	La Vecchia	M+F	0 1-14 15+ (cigs/day)	1.00 1.13 1.30	
14	Layard	M F	0 1-14 15-34 35+ (cigs/day) 0 1-14 15-34 35+ (cigs/day)	$\begin{array}{cccccccccccccccccccccccccccccccccccc$	
15	LeVois (CPS-I)	M F	0 1-19 20-39 40+ (cigs/day) 0 1-19 20-39 40+ (cigs/day)	1.00 0.99 0.98 0.72 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 F M F M F	0 1-19 20 21+ (cigs/day) 0 1-19 20 21-39 40+ (cigs/day) 0 1-12 13-21 22-29 30+ (years) 0 1-14 15-25 26-33 34+ (years) 0 1-5 6-14 15-27 28+ (pack years) 0 1-12 13-25 26-33 34+ (pack years)	1.001.331.171.091.001.151.070.991.041.001.141.131.141.251.000.840.991.201.201.001.251.331.131.001.000.831.121.091.26	
20	Janghorbani	F F F	0 1-30 31+ (years) 0 1-19 20+ (cigs/day) 0 1-10 11+ (pack years)	1.00 1.74 0.85 1.00 1.76 1.11 1.00 1.95 1.17	
21	Kawachi	F F	None Occasional Regular <1 1-9 10-19 20-29 30+ (years)	1.00 1.19 2.11 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	
25	Не	F	0 1-10 11-20 21+ (cigs/day) 0-5 6-15 16-30 31+ (years) 0 1-399 400-799 800+ (cigs/day x years)	1.000.931.403.201.000.802.102.301.001.201.903.60	+ + +
26	Rosenlund	M+F M+F M+F	0 1-19 20+ (cigs/day) 0 1-32 33+ (years) 0 1-20 21+ (pack-years)	1.01.021.581.01.111.251.001.091.33	
27	Iribarren	M F	0 1-9 10-39 40+ (hrs/week) 0 1-9 10-39 40+ (hrs/week)	1.01.121.261.201.001.211.311.36	+++

#### TABLE 4Relative risk of heart disease among lifelong non-smokers in relation to extent of smoking by the spouse

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

For study 1 the 1-19 cigs/day group includes ex-smokers.

Relative risks presented are adjusted for covariates (see Appendix A) if adjusted data are available. Significant (p < 0.05) positive (negative) trends are indicated by + (or -).

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

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

<u>Footnotes</u> The study author is usually the first author of the publication providing the data, see references.

See Appendix A for the covariates considered.

Significant (p<0.05) positive (or negative) relative risks are indicated by + (or -).

In study, 21 the estimates were given by Wells (28).

In study 26, 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.

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

Study					Significance			
Ref	Author	Sex	Exposure grouping	Relative risk by grouping	(trend)			
21	Kawachi	F	None occasional regular	1.00 1.49 1.92				
25	F F F		0-5 6-10 11-20 21+ cigs/day 0-5 6-15 16+ years 0 1-2 3 4+ smokers 0 1-2 3-4 5+ hours/day 0 1-2000 2001-4000 4000+	1.00 3.08 1.56 1.00 1.16 5.06 4.11 1.00 0.62 4.03 21.32				
		F	(cigs/day x years x smokers x hours)	1.00 1.00 2.03 9.23	+			
26	Rosenlund	M+F M+F	0 1-31 32+ years 0 1-68 69+ hour years (= hours/day x years)	1.00 1.04 1.30 1.00 0.99 1.48				

Footnotes

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

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

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

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

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

24	Spencer	М	ETS exposure in cars No Yes	No significant association	
		М	ETS exposure in social venues No Yes	No significant association	
		М	ETS exposure at home, at work, in social venues and/or in cars	Significant increase	+
25a	Не	F	ETS exposure from spouse and/or work Neither Home Work Both	1.00 2.07 2.53 4.18	+
26	Rosenlund	M+F M+F M+F M+F	<b>ETS exposure from spouse and/or work</b> No Yes 0 >16 7-16 1-6 <1 years ago 0 1-12 13-23 24-34 35+ years 0 1-17 18-41 42-89 90+ hour-years (= years x	1.18 (0.87-1.60)1.00 0.92 1.11 1.30 1.391.00 0.72 0.97 1.54 1.481.00 0.70 1.22 1.27 1.55	+ +
27	Iribarren	M F	hols/day) ETS exposure in small spaces 0 1-9 10-39 40+ hrs/wk 0 1-9 10-39 40+ hrs/wk	1.00 1.08 1.12 1.24 1.00 0.97 1.10 1.17	+ +
		M F	<b>ETS exposure in large indoor areas</b> 0 1-9 10-39 40+ hrs/wk 0 1-9 10-39 40+ hrs/wk	1.00 0.94 1.17 1.03 1.00 0.82 0.98 1.28	+
		M F	<b>Total ETS exposure</b> 0 1-9 10-39 40+ hrs/wk 0 1-9 10-39 40+ hrs/wk	1.00 0.90 1.08 1.13 1.00 0.86 1.07 1.17	+ +
28	Pitsavas	M F M+F	ETS exposure at home or work None occasional regular None occasional regular 0 1-4 5-9 10-19 20-29 30-39 40+ years	1.01.251.471.01.291.561.001.071.161.391.752.203.09	+ + +
		M+F	ETS exposure at home and work Neither both	1.00 2.56 (1.65-3.96)	

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

Footnotes

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

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

When two groups only are being compared, the relative risk and 95% confidence limits for the exposed group are shown: when more than two exposure groups are being compared, only the set of relative risks is shown.

Significant (p < 0.05) positive (or negative) differences or trends are indicated by + (or -). ? indicates not known if significant or not.

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

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#### **APPENDIX A**

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

											St	udy																
Risk factor	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28
Age	х	x	х		x	х		x	x	x	х	x	Х	x	x	х	x	х	х	х	x	x	x	x	x	x	x	x
Marital status (in spousal analyses)	X	x	x	x	x	x		n	n	n	x	n	Х	x	x	n		n	x	x	n						n	
Blood pressure/ hypertension		v		v	v			v			v		v				v	v	v		v	v			v	v		v
Cholesterol		X X		Х	X X			X X			X X		X X				Х	X X	Х		X X	X X			X X	Х	x	X X
Social class/ education/income		~			x			x	x	x	A	x	x			x	x	Α	x		~	x	x		A	x	x	x
Obesity/weight		х		х	x			x	x		х	x	x						x		х	x	x			x	x	x
Alcohol				x	x														x		x						x	x
Diabetes				x									х						x			х				х	x	x
Family history of heart disease/				x					x				x									x	x		x			x
hypertension Race														••	••	••	••											
Exercise				v										Х	Х	Х	х		х		v	v					X	v
Housing/urban-rural				Х												v		х	х		х	х					х	х
Personal history of																х		А										
heart disease Coffee										х		X	X						Х									
Personality type																									х			
Occupation																			х		х						х	
Oestrogen use																			х		х							
Other																			х		х							х

Notes

Study 7 No reference was made to any adjustment for confounding in the abstract

Study 12 Data in Tables 3 and 5 only adjusted for age and personal history of heart disease

Study 13 Only data for spouse current smoker are adjusted for risk factors stated

Study 17 Non-smoking cases and controls were matched on age and race. Adjustment for other risk factors noted only applied to analyses of workplace, adulthood and childhood ETS exposure, but not other indices of ETS exposure, including spousal smoking

Study 19 Other risk factors considered were aspirin use, diuretic use and personal history of arthritis

Study 21 Other risk factors considered were oral contraceptive use, saturated fat intake, vitamin E intake, menopausal status and use of postmenopausal hormones

Study 26 Other risk factors considered were hospital/catchment area, job strain and diet

Study 28 Only the relative risks in Table 7 for none/occasional/regular exposure were adjusted for all these factors; other relative risks cited were adjusted only for age, sex, hypertension, cholesterol, diabetes, exercise and family history of heart disease

Study 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

x Risk factor used as matching or adjustment factor in study

n not applicable - spousal smoking not the index (see Table 2).