EPIDEMIOLOGICAL EVIDENCE ON ENVIRONMENTAL TOBACCO SMOKE AND CANCERS OTHER THAN THE LUNG OR BREAST

This report is one of a series that assesses the evidence available on the association between environmental tobacco smoke (ETS) exposure and cancers of various sites. Other reports relate to cancer of the lung [1] and breast cancer [2]. This report describes the evidence available on all other cancers in adults. Cancers in childhood are not reported but possible associations between cancers occurring in adulthood and ETS exposure during childhood are discussed.

41 epidemiological studies have reported results relating ETS exposure in adulthood or childhood to risk of cancers other than the lung or breast in adult non-smokers. Some studies have concentrated on cancers at specific sites, while others have presented results for a range of sites and/or for overall cancer risk. In assessing this evidence, certain general considerations of the data have to be borne in mind:

- Study weaknesses It is notable that the only three studies which have reported results for a wide range of cancer sites are open to criticism for a number of reasons [3]. One study [4-6] had incomplete follow-up and used statistical methods of doubtful validity, another [7-9] used inappropriate controls and had a substantial difference in response rates between cases and controls, while the third [10] is not large enough to provide adequate numbers of cases for many cancer types.

- Categorizing subjects by ETS exposure In many studies, subjects are categorized based on a single source of ETS exposure (e.g. the spouse) or an exposure at a single point in time (e.g. at the time of the questionnaire in some prospective studies) or during a limited period of time (e.g. adulthood). Although it is well documented that marriage to a smoker and working with a smoker are associated with increased overall ETS exposure, as judged by levels of cotinine in blood, urine or saliva [11], and although it is likely that those who are exposed at one point in their life are more likely to be exposed at another point, it is likely

that studies based on a limited assessment of ETS may lack the power to detect any true effect that studies based on a more detailed assessment would have.

In some case-control studies very detailed questions have been asked about multiple sources of ETS over the whole of the subject's lifetime, and analyses have been conducted using those with no reported exposure as the comparison group. The problem with this approach is that everyone is likely to have had some ETS exposure in their life and the estimates of risk are highly dependent on which subjects happen to get classified in the unexposed comparison group. If, among subjects with a relatively low level of ETS exposure, the cases are more likely to report this (in an effort to explain their disease) than are controls, such differential recall may cause substantial bias to the estimated effect of ETS. Limitations caused by inadequate characterization of ETS exposure as well as by small sample sizes in some studies have been pointed to by a recent review [12].

- Confounding Many of the studies, particularly those reporting in the 1980s, made at most only limited adjustment for potential confounding variables. Some studies [7-9,13-17] have adjusted for no other variables at all, not even age.

- Misclassification bias In studies of ETS and lung cancer, considerable attention has been given to estimating the magnitude of bias resulting from the inappropriate inclusion of some misclassified current and former smokers among the target population of lifelong non-smokers. Though it would be expected that bias would also arise for other smoking-associated cancers, this has not been investigated in the literature.

- Publication bias Researchers are more likely to wish to publish, and editors are more likely to accept for publication, results from studies which find a statistically significant association between exposure and disease [18]. As a result the published literature may overstate any true association or produce an apparent association when no true association exists. Two very large prospective studies have reported results relating ETS exposure to lung cancer [19,20] but, with the

exception of a recent publication on breast cancer based on one of these [21], have not reported results for any other cancer site.

- Plausibility As discussed below, some studies have reported associations between ETS and cancers not associated with active smoking. Although it is possible to propose mechanisms by which ETS, but not active smoking, could increase risk of cancer of a specific site [22,23], these are speculative and unsupported. It is far more plausible to believe that they represent associations due to chance or bias.

Bearing these points in mind, it is appropriate to consider the results by site.

Cancer of the nasopharynx, head and neck (Table 1) Five studies have reported results specifically for cancer of the nasopharynx (NPC). Three of the studies [24-26] provided no evidence of an increase in risk with ETS exposure, one of these [26] even reporting a significant negative trend in relation to childhood exposure. In contrast, two recent studies have reported significant positive associations. In one of these [27] a relationship was noted with childhood but not adulthood ETS exposure. The other [28] reported no significant association with any index of ETS exposure in males but reported significant associations and trends with a wide range of indices in females, all the findings being linked to an unusually low number of cases who reported no ETS exposure from any source, the reference group used in all the relative risk calculations. The heterogeneous nature of the findings and the limitations of the analyses make the overall findings difficult to interpret. For example, the authors of the Chinese study [28] reporting significant associations of nasopharyngeal cancer with ETS exposure in females regarded their results as "inconclusive as to whether passive smoking contributes to NPC risk".

Three further studies have also reported results for overall incidence of cancer of the head and neck. Two of these [6,17] reported no significant association of ETS exposure with risk, but one [16], based on analyses which adjusted for no potential confounding variables, and data collected very differently for cases and controls, reported significantly increased risks with ETS exposure at home and at work. Based partly on the evidence from two of these studies [16,17], the Supreme Court of New

South Wales, Australia recently decided that ETS exposure can materially contribute to the development of larynx cancer [29]. Since neither of the studies cited presented results specifically for larynx cancer, since both studies would have involved no more than about 10 larynx cancer cases in non-smokers, since one of the studies [17] found no statistically significant association of ETS with head and neck cancer, and since the one that did [16] had obvious weaknesses, the Supreme Court's decision seems unjustified based on the available data.

Digestive system cancer (Table 2) For most of the studies summarized, the data show no indication of a relationship of ETS exposure with digestive system cancer, either overall or by specific sites. There are four exceptions to this. A study in China reported only as an abstract [30] showed a significantly raised risk of oesophagus cancer and reported the existence of "dose response relations" for cancers of the oesophagus, stomach and liver. Results for colon cancer from another study [31] implausibly reported a significant positive association with ETS exposure in males and a significant negative association with ETS exposure in females. Results for stomach cancer from one study [32] reported a marginally significant ($p=0.03$) positive trend for cancers in the cardia subsite, but no indication of an association for cancers in the distal subsite. Finally, a study giving results for all digestive cancers [33] gives a surprisingly high value for risk. This study also gives an implausibly high value for total cancer risk (see results for Table 8 below). Given that the other studies on digestive system cancer (a considerable number of studies) report no association, the data overall provide little support for the view that ETS exposure affects incidence of digestive system cancer.

Nasosinus cancer (Table 3) All three studies have reported some evidence of an increased risk of nasosinus cancer in association with ETS exposure. Two studies in Japan [4,14] reported no overall significant increase in risk in relation to spousal or household exposure in females, but a significant dose-related trend in relation to extent of exposure. A third study, in the USA [34], reported an increase in risk in relation to spousal smoking in males that was of marginal statistical significance. Limitations of the studies include the small number of cases studied, the failure in the two Japanese studies to control either for the age of the subject or for any of the wide range of factors known to be associated with nasal cancer, and the reliance in the US

study on data collected from next-of-kin. Although some reviewers [12,35] have claimed that ETS exposure is a cause of nasosinus cancer, the evidence does not in fact appear conclusive.

Cancer of the cervix (Table 4) Eleven studies have reported results relating ETS exposure to risk of cervix cancer (or, in three studies, to endpoints that also include pre-invasive cervical lesions [36-38]). These consisted of:

- five studies [6,10,36,39,40] reporting no significant increase associated with ETS exposure,
- one study [37] reporting an increased risk in women living with a smoker that was of marginal significance (lower 95% CI stated to be 1.0),
- two studies [7,41] reporting a significantly increased risk associated with spousal smoking,
- one study [42] reporting a significant dose-related trend in relation to hours of ETS exposure,
- one study [38] reporting a significantly increased risk and significant dose-related trend for ETS exposure at home during adulthood and for lifetime exposure, and
- one study [43] showing significantly raised risk in relation to living with a smoker when using data from a 1963 cohort but not when using equivalent data from a 1975 cohort.

While a random-effects meta-analysis based on eleven independent estimates shows a significant elevation in risk (RR = 1.41, 95% CI = 1.16-1.73), there are a number of difficulties in interpreting the findings. One major problem is that none of the estimates have adjusted for human papilloma virus (HPV) infection, known to be the dominant cause of cervical cancer [44], and only three studies [36,37,42] have adjusted for aspects of sexual activity known to be linked to HPV virus infection. Confounding by HPV infection is considered of major importance in the association of active smoking with cervix cancer [35] and could well bias estimates of the risk of cervix cancer with ETS exposure. It has also been noted [45] that non-smoking women married to smokers are significantly less likely to undergo screening for cervical cancer than are non-smoking women married to non-smokers.

Bladder cancer (Table 5) The results from four studies, three conducted in the 1980s [6,13,46] and one in 2002 [47], provide no indication of an effect of ETS on risk of bladder cancer.

Brain cancer (Table 6) Seven studies have reported results relating ETS exposure to brain cancer. Although significant increases have rarely been reported, one study [48] did report a significantly higher risk associated with ETS exposure from the spouse, but not from other cohabitants or co-workers. This study, which also found a significant positive trend for years of exposure to spousal ETS, reported a significant positive association with active smoking for men but a significant negative association with active smoking for women. Two other studies [5,49] have also reported a significant dose-related trend in risk with increasing ETS exposure. However, one of these [5] did not adjust for the age of the subject and the other [49] only reported its results in an abstract with little detail. Few potential confounding variables have been adjusted for in any of the studies. Meta-analysis based on 11 independent estimates shows a marginally significant elevation in risk, the random effects model giving a relative risk estimate of 1.33 (1.00-1.78).

Cancer of other sites (Table 7) The table summarizes the limited results that are available for 10 other cancer sites (or groups of sites). Only three significant differences were reported. One, for kidney cancer in females in relation to hours of ETS exposure at home or work [50], was based on a marginally significant trend statistic where the dose-relationship pattern was actually quite erratic. The second, also for kidney cancer [51], showed a non-significant trend for females but a significant positive trend with years of exposure for males. The third, for endocrine cancer in relation to smoking by the spouse [7], is based on only 13 cases and is unstandardized either for age or sex. These results add little to the evidence on ETS as a potential cause of cancer. Even for kidney cancer, more studies are clearly needed before any assessment can be made.

ETS and total cancer incidence (Table 8) Eleven studies have reported results relating ETS exposure to total cancer risk, smoking-related cancer risk and/or non smoking-related cancer risk. Some of the analyses include lung cancers but they are generally not more than a small fraction of the cancers analysed. Most of the studies

were published before 1990 and only one of the analyses [52] adjusted for more than a very small number of potential confounding variables. The studies can be summarised as follows:

- Two studies [33,53] reported relative risks, of 6.4 for total cancer and 7.0 for smoking-related cancer, that are so high as to be totally implausible bearing in mind the results for individual sites summarized in Tables 1 to 8.
- Two studies from the 1980s [4,7-9], both criticized for weaknesses of design and analysis [3], reported a weaker, but significant association between ETS exposure and total cancer risk. A more recent study in Hong Kong [54] reported a significant association and significant positive trend. However, this study used a strange design that asked the person reporting a cancer death to quantify ETS exposure 10 years earlier for both the case and a living person "who was well known to the informant".
- The other studies [10,39,52,55-57] showed no significant association. One of these [52] used data from a large study, with the analyses adjusted for a wide range of possible confounders.

A meta-analysis of studies reporting ETS and total cancer gave random effects estimates of 1.12 (1.02-1.24) when the extreme relative risk estimate [33] was excluded, and 1.16 (1.03-1.31) when it was included. Results from a well designed, large prospective study adjusting for relevant confounding variables would be needed before any conclusion could be reached regarding the relationship between ETS exposure and total cancer risk. It is notable that neither of the two very large American Cancer Society Cancer Prevention Studies have reported relevant findings here, though they have the potential to do this.

OVERALL CONCLUSIONS

The evidence relating ETS exposure in non-smokers to risk of cancers of any site other than the lung or breast is relatively limited and subject to a number of sources of bias and confounding. For a number of cancer sites, including digestive system, bladder and brain, there is little or no evidence of an association of ETS exposure with risk. Though some studies have reported a relationship with cancers of the cervix and nasopharynx, others have not and the evidence must be regarded as inconclusive. For nasosinus cancer, all three studies have reported a statistically significant relationship with ETS exposure. However, they all suffer from major weaknesses and more evidence is needed to support the existence of a causal relationship. More evidence is also needed for kidney cancer, where the only two studies conducted so far report some evidence of dose-response.

Taken as a whole, the epidemiology does not convincingly demonstrate that, in non-smokers, ETS exposure causes cancers of any of the sites considered.

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ETS AND CANCERS OTHER THAN THE LUNG
THE DATA

The tables that follow summarize the key evidence relating ETS exposure in lifelong non-smokers to risk of cancers other than the lung:-

1. Nasopharynx, head and neck
2. Digestive system
3. Nasosinus
4. Cervix
5. Bladder
6. Brain
7. Other sites
8. Total cancer incidence

The tables show, for each successive study providing data, relative risks and 95% confidence intervals (CIs) relating to various indices of ETS exposure. Unless stated otherwise in the notes to the tables, the reference group comprises subjects unexposed to the source of ETS exposure specified. Where appropriate, and the data are available to do this, relative risks and 95% CIs presented by the authors have been recalculated to this standard reference group. The relative risks are adjusted for the potential confounding variables listed in Appendix A, which also gives fuller details of the studies in question. Where necessary, relative risks and/or 95% confidence intervals have been derived from tabular data presented by the authors, by combining independent relative risks by fixed-effects meta-analysis [58], or by combining non-independent relative risks, e.g. for different exposure levels with the same reference group [59].

Where there are reasonable numbers of studies providing independent estimates of risk, fixed-effects and random-effects meta-analysis [58] have been used to derive an overall relative risk estimate. Where a study provides multiple estimates for a given sex, only one has been used in the overall estimate, as indicated in the notes to the table. Preference has been given to estimates relating to adult rather than childhood exposure and to spousal exposure rather than exposure from a cohabitant or co-worker.

TABLE 1 – ETS and Cancer of the Nasopharynx, Head and Neck

Study	Year	Country	Source (timing) of ETS exposure	Sex	Number of cases	Relative risk (95% CI)	Dose response	Notes
Cancer of the nasopharynx								
Yu [24]	1990	China	Spouse (ever)	M+F	72	0.8(0.4-1.9)	-	ac(1)v
			Cohabitant (ever)	M+F	142	0.7(0.4-1.4)	-	ac(1)
			Mother (childhood age 10)	M+F	63	0.7(0.3-1.5)	-	ac(1)v
			Father (childhood age 10)	M+F	109	0.6(0.3-1.2)	-	ac(1)v
			Cohabitant (childhood age 10)	M+F	59	0.7(0.4-1.3)	-	ac(1)v
Vaughan [25]	1996	USA	Cohabitant (adulthood)	M+F	19	No increase	No	ac(1)q
			Cohabitant (childhood)	M+F	19	No increase	No	ac(1)q
Cheng [26]	1999	Taiwan	Cohabitant (adulthood)	M+F	178	0.7(0.5-1.2)	No	ac(4)
			Cohabitant (childhood)	M+F	178	0.6(0.4-1.0)	d1	ac(4)
Armstrong [27]	2000	Malaysia	Cohabitant (adulthood)	M+F	(282)	No association	-	ac(1)s
			Parent (childhood)	M+F	(282)	2.28(1.21-4.28)	-	ac(1)s
Yuan [28]	2000	China	Spouse (adulthood)	F	156	3.09(1.48-6.46)	d2	ac(9)w
				M	17	1.53(0.26-8.93)	No	ac(9)w
			Co-worker (adulthood)	F	139	2.84(1.34-6.00)	d3	ac(9)w
				M	168	1.32(0.63-2.76)	No	ac(9)w
			Cohabitant (adulthood)	F	187	2.88(1.39-5.96)	d4	ac(9)w
				M	63	0.92(0.41-2.03)	No	ac(9)w
			Mother (childhood)	F	44	3.36(1.41-8.05)	d5	ac(9)w
				M	37	1.42(0.56-3.58)	No	ac(9)w
			Father (childhood)	F	151	2.95(1.41-6.19)	d6	ac(9)w
				M	82	1.17(0.54-2.55)	No	ac(9)w
			Cohabitant (childhood)	F	161	2.96(1.42-6.20)	d7	ac(9)w
				M	97	1.26(0.59-2.71)	No	ac(9)w
Head and neck cancer								
Hirayama [6]	1987	Japan	Spouse (ever)	F	22	Not available	No	c(1)
Tan [16]	1997	USA	Spouse (ever)	F	21	7.34(2.44-22.1)	-	ue
				M	22	1.14(0.41-3.23)	-	ue
			Co-worker (ever)	F	18	8.96(2.43-33.0)	-	ue
				M	20	12.0(3.77-38.0)	-	ue
			Spouse or co-worker (ever)	F	21	8.00(2.55-25.1)	-	ue
				M	23	3.78(1.37-10.4)	-	ue
Zhang [17]	2000	USA	Spouse or partner (current)	M+F	13	0.9(0.2-5.2)	-	u
			Cohabitant (ever)	M+F	26	2.03(0.77-5.40)	No	ue
			Co-worker (ever)	M+F	26	1.86(0.68-5.11)	No	ue

(continued)

TABLE 1 – ETS and Cancer of the Nasopharynx, Head and Neck (continued)

Results are not included for six studies [60-65] as the analyses were not restricted to lifelong non-smokers.

Study: described by name of first author of publication – see Appendix A for references.

Year: year of publication of paper reporting results cited.

Number of cases: number among lifelong non-smokers unless in brackets (see note s below)

Relative risk (95% confidence interval = CI): estimated from data provided where necessary – see note e.

Dose response: "-" indicates dose response not studied, "No" indicates dose-response studied but no significant trend seen, "d1", "d2" … "d7" indicate dose-response studied, significant trend with more detailed data as follows:

d1 A significant negative dose-related trend was noted in relation to duration of exposure and cumulative exposure but not in relation to number of smokers in the household (childhood data).

d2 Relative risks 1.0, 3.02, 3.18 for 0, <20, 20+ years lived with smoking spouse (trend p=0.003)

Relative risks 1.0, 3.16, 3.02 for 0, <20, 20+ cigs/day by spouse (trend p=0.004)

Relative risks 1.0, 3.15, 2.45, 6.76 for 0, <20, 20-39, 40+ pack-years by spouse (trend p<0.001)

d3 Relative risks 1.0, 2.47, 3.28 for 0, <3, 3+ hours ETS at work (trend p=0.01)

d4 Relative risks 1.0, 2.65, 2.62, 4.35 for 0, <20, 20-39, 40+ cigs/day by household member (trend p=0.003)

d5 Relative risks 1.0, 2.36, 5.90 for 0, <20, 20+ cigs/day by mother (trend p=0.003)

d6 Relative risks 1.0, 2.46, 3.48 for 0, <20, 20+ cigs/day by father (trend p=0.004)

d7 Relative risks 1.0, 2.33, 3.83, 2.13 for 0, <20, 20-39, 40+ cigs/day by household member (trend p=0.01).

Key to notes

a adjusted for age.

c adjusted for confounding variables other than age (number of confounders given in brackets – see Appendix A for further details).

e estimated from data reported.

q results are for differentiated squamous cell carcinoma.

s number of cases in lifelong non-smokers not known – number given (in brackets) is total for study and includes cancers in smokers.

u unadjusted.

v reference group is never exposed at home from any source.

w reference group is never exposed at home or work from any source.

TABLE 2 – ETS and Digestive System Cancers

Study	Year	Country	Source (timing) of ETS exposure	Sex	Number of cases	Relative risk (95% CI)	Dose response	Notes
Cancer of the oesophagus								
Hirayama [6]	1987	Japan	Spouse (ever)	F	58	Not available	No	c(1)
You [30]	2003	China	Unspecified	M+F	84	1.72 (1.0-3.1)	d2	c(?)
Stomach cancer								
Hirayama [4]	1984	Japan	Spouse (ever)	F	854	1.01(0.87-1.18)	No	c(2)e
Jee [40]	1999	Korea	Spouse (ever)	F	197	0.94(0.68-1.29)	No	ac(5)e
Nishino [10]	2001	Japan	Spouse (current)	F	83	0.98(0.59-1.60)	-	ac(6)
			Cohabitant (current)	F	83	0.87(0.54-1.40)	-	ac(6)
Mao [32]	2002	Canada	Cohabitant or	M	31C	4.01(0.90-17.94)	d1	ac(7)e
			Co-worker (ever)	M	101D	0.83(0.48-1.45)	-	ac(7)e
You [30]	2003	China	Unspecified	M+F	85	1.33 (0.8-2.3)	d2	c(?)
Colon cancer								
Hirayama [6]	1987	Japan	Spouse (ever)	F	142	Not available	No	c(1)
Sandler II [31]	1988	USA	Cohabitant (ever)	F	215	0.74(0.56-0.97)	-	a
				M	49	2.99(1.77-5.04)	-	a
Nishino [10]	2001	Japan	Spouse (current)	F	48	1.10(0.54-2.40)	-	ac(5)
			Cohabitant (current)	F	48	1.10(0.58-2.20)	-	ac(5)
Cancer of the rectum								
Hirayama [6]	1987	Japan	Spouse (ever)	F	112	Not available	No	c(1)
Nishino [10]	2001	Japan	Spouse (current)	F	31	1.90(0.87-4.20)	-	ac(5)
			Cohabitant (current)	F	31	1.60(0.75-3.40)	-	ac(5)
Liver cancer								
Hirayama [6]	1987	Japan	Spouse (ever)	F	226	Not available	No	c(1)
Jee [40]	1999	Korea	Spouse (ever)	F	83	0.74(0.46-1.17)	No	ac(5)e
Nishino [10]	2001	Japan	Spouse (current)	F	20	1.20(0.45-3.20)	-	a
You [30]	2003	China	Unspecified	M+F	79	1.13 (0.6-1.9)	d2	c(?)
Gall bladder cancer								
Hirayama [6]	1987	Japan	Spouse (ever)	F	91	Not available	No	c(1)
Nishino [10]	2001	Japan	Spouse (current)	F	23	0.66(0.24-1.90)	-	a

(continued)

TABLE 2 – ETS and Digestive System Cancers (continued)

Study	Year	Country	Source (timing) of ETS exposure	Sex	Number of cases	Relative risk (95% CI)	Dose response	Notes
Pancreas cancer								
Hirayama [6]	1987	Japan	Spouse (ever)	F	127	Not available	No	c(1)
Nishino [10]	2001	Japan	Spouse (current)	F	19	1.20(0.45-3.10)	-	a

Villeneuve [66]	2004	Canada	Cohabitant or co-worker:					
			(childhood only)	M+F	23	1.37 (0.46-4.07)	-	ac(4)
			(adult only)	M+F	33	1.01 (0.41-2.50)	-	ac(4)
			(childhood and adult)	M+F	81	1.21 (0.60-2.44)	-	ac(4)
			(combined)	M+F	105	1.18 (0.60-2.35)	No	ac(4)e
All digestive cancers								
Sandler I [8]	1985	USA	Mother (childhood)	M+F	13	0.7(0.1-5.6)	-	ue
			Father (childhood)	M+F	12	1.3(0.4-4.2)	-	ue
Miller II [33]	1990	USA	Cohabitant (ever) or long-term exposure outside home	F	29	10.8 (1.46-79.1)	-	aex

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Results are not included for three studies [67-69] as the analyses were not restricted to lifelong non-smokers.

Study: described by name of first author of publication – see Appendix A for references.

Year: year of publication of paper reporting results cited.

Number of cases: number among lifelong non-smokers; C indicates cardia, D distal.

Relative risk (95% confidence interval = CI): estimated from data provided where necessary – see note e.

Dose response: "-" indicates dose response not studied, "No" indicates dose-response studied but no significant trend, "d" indicates dose-response studied, significant trend with more detailed data as follows:

d1 Relative risks were 1.0, 3.5, 2.8, 5.8 for 0, 1-22, 23-42, 43+ residential plus occupational years exposed (trend p=0.03)

d2 Relative risks not specified but paper states "There are dose-response relations between total years of ETS exposure and the risk of these three cancers." (i.e. oesophagus, stomach and liver cancers).

Key to notes

a adjusted for age.

c adjusted for confounding variables other than age (number of confounders given in brackets – see Appendix A for further details).

e estimated from data reported.

u unadjusted.

x results relate to unemployed wives only because no separation by ETS exposure for employed wives.

TABLE 3 – ETS and Nasosinus Cancer

Study	Year	Country	Source (timing) of ETS exposure	Sex	Number of cases	Relative risk (95% CI)	Dose Response	Notes
Hirayama [4]	1984	Japan	Spouse (ever)	F	28	1.63(0.61-4.35)	d1	c(1)e
Fukuda [14]	1990	Japan	Cohabitant (?)	F	35	1.96(0.84-4.57)	d2	uet
				M	9	No association	No	rt
Zheng [34]	1993	USA	Spouse (ever)	M	28	3.0(1.0-8.9)	-	ac(1)
				M	<28	4.8(0.9-24.7)	No	ac(1)x

Study: described by name of first author of publication – see Appendix A for references.

Year: year of publication of paper reporting results cited.

Number of cases: number among lifelong nonsmokers.

Relative risk (95% confidence interval = CI): estimated from data provided where necessary – see note e.

Dose response: "-" indicates dose response not studied, "No" indicates dose-response studied but no significant trend seen, "d1", "d2" indicates dose-response studied, significant trend with more detailed data as follows:

d1 Relative risks were 1.00, 1.67, 2.02, 2.55 for 0, 1-14, 15-19, 20+ cigs/day smoked by the husband (one-tailed trend p=0.025).

d2 Relative risks were 1.00, 1.40, 5.73 for 0, 1, 2+ smokers in the household (trend p<0.05).

Key to notes

c adjusted for confounding variables other than age (number of confounders given in brackets – see Appendix A for further details).

e estimated from data reported.

r smoker in the household not included as a significant factor in multiple regression analysis after adjustment for sinusitis and/or polyps and woodworking.

t the source paper does not make clear the time period the ETS exposure relates to.

u unadjusted.

x results are for maxillary cancer only.

TABLE 4 – ETS and Cancer of the Cervix in women

Study	Year	Country	Source (timing) of ETS exposure	Number of cases	Relative risk (95% CI)	Dose Response	Notes
Sandler I [7]	1985	USA	Spouse (ever)	56	2.1 (1.2-3.9)	-	um
Sandler I [8]	1985	USA	Mother (childhood)	40	0.7 (0.2-2.5)	-	ue
			Father (childhood)	34	1.7 (0.8-3.6)	-	ue
Hirayama [6]	1987	Japan	Spouse (ever)	273	Not available	No	ac(1)
Butler [39]	1988	USA	Spouse (in marriage)	10	2.57 (0.70-9.44)	-	ac(1)my
Slattery [42]	1989	USA	Total (last 5 years)	81	1.7 (0.8-3.7)	d1	ac(3)e
			Cohabitant (last 5 years)	81	1.2 (0.7-2.2)	d2	ac(3)em
			Outside home (last 5 years)	81	1.6 (0.7-3.4)	No	ac(3)e
Coker [36]	1992	USA	Spouse (ever)	36	0.9 (0.3-2.4)	-	ac(5)em
			Cohabitant (ever)	36	0.9 (0.3-2.3)	-	ac(5)e
			Co-worker (ever)	36	0.9 (0.3-2.3)	-	ac(5)e
			Parent (ever)	36	0.3 (0.1-0.9)	-	ac(5)e
Hirose [41]	1996	Japan	Spouse (current)	415	1.30 (1.07-1.59)	d3	ac(1)m
Jee [40]	1999	Korea	Spouse (ever)	203	0.90 (0.65-1.24)	No	ac(5)em
Scholes [37]	1999	USA	Cohabitant (current)	315	1.4 (1.0-2.0)	-	ac(2)m
Nishino [10]	2001	Japan	Spouse (current)	11	1.10 (0.26-4.50)	-	am
Wu [38]	2003	Taiwan	Cohabitant (adult)	89	2.73 (1.31-5.67)	d4	ac(4)m
			Co-worker (adult)	89	1.56 (0.83-2.92)	No	ac(4)
			Cohabitant (childhood)	89	0.99 (0.54-1.83)	No	ac(4)
			Co-worker (childhood)	89	1.03 (0.47-2.26)	No	ac(4)
			Lifetime exposure (pack-years)	89	2.30 (0.91-5.84)	d5	ac(4)e
Trimble [43]	2005	USA	Spouse (baseline) 1963[z]	81	2.0 (1.2-3.3)	-	ac(3)m
			Spouse (baseline) 1975[z]	49	1.6 (0.8-3.2)	-	ac(2)m
			Any cohabitant (baseline) 1963	94	2.1 (1.3-3.3)	-	ac(3)
			Any cohabitant (baseline) 1975	55	1.4 (0.8-2.4)	-	ac(2)
			Cohabitant but not spouse (baseline) 1963	43	2.3 (1.1-4.9)	-	ac(3)
			Cohabitant but not spouse (baseline) 1975	41	1.3 (0.6-3.2)	-	ac(2)
Meta-analyses based on 11 estimates			Fixed effects		1.34 (1.18-1.52)		h
			Random effects		1.41 (1.16-1.73)		

(continued)

TABLE 4 – ETS and Cancer of the Cervix in women (continued)

Results are not included for five studies [70-74] as the analyses were not restricted to lifelong non-smokers.

Study: described by name of first author of publication – see Appendix A for references.

Year: year of publication of paper reporting results cited.

Number of cases: number among lifelong non-smokers.

Relative risk (95% confidence interval = CI): estimated from data provided where necessary – see note e.

Dose response: "-" indicates dose response not studied, "No" indicates dose-response studied but no significant trend seen, "d" indicates dose-response studied, significant trend with more detailed data as follows:

d1 Relative risks 1.00, 1.14, 1.57, 3.43 for 0, 0.1-0.9, 1.0-2.9 3.0+ hours/day total ETS exposure (trend p=0.0179)

d2 Relative risks 1.00, 0.62, 2.66 for 0, 0.1-1.5, 1.6+ hours/day ETS exposure at home (trend p=0.0362).

d3 Relative risks 1.00, 1.00, 1.55 for 0, <20, 20+ cigs/day smoked by husband.

d4 Relative risks 1.00, 2.13, 3.97 for 0, 1-10, >10 cigs/day smoked at home (trend p=0.002).

d5 Relative risks 1.00, 1.90, 2.99 for 0, 1-20, >21 pack-years ETS exposure (trend p=0.02).

Key to notes

a adjusted for age.

c adjusted for confounding variables other than age (number of confounders given in brackets – see Appendix A for further details).

e estimated from data reported.

h heterogeneity chisquared is 16.25 on 10 degrees of freedom (0.05<p<0.1).

m relative risk included in meta-analysis.

u unadjusted.

y adjusted for age and education. Butler [39] also gives 3.01(0.83-10.87) adjusted for age and age married and 2.58(0.70-9.56) adjusted for age and spouse occupation.

z separate results are reported for cohorts established in 1963 and 1975.

TABLE 5 – ETS and Bladder Cancer

Study	Year	Country	Source (timing) of ETS exposure	Sex	Number of cases	Relative risk (95% CI)	Dose Response	Notes
Kabat [13]	1986	USA	Spouse (ever)	F	35	1.21(0.54-2.69)	-	uem
				M	49	0.77(0.38-1.55)	-	uem
			Cohabitant (?)	F	17	0.63(0.18-2.18)	No	uet
				M	23	1.49(0.48-4.62)	No	uet
			Co-worker or in	F	17	2.51(0.63-10.0)	No	uet
			transportation (?)	M	23	0.64(0.23-1.75)	No	uet
Hirayama [6]	1987	Japan	Spouse (ever)	F	49	Not available	No	c(1)x
Burch [46]	1989	Canada	Cohabitant (ever)	F	81	0.75(0.33-1.71)	-	ac(1)m
				M	61	0.94(0.45-1.95)	-	ac(1)m
			Co-worker (ever)	F	81	0.93(0.48-1.79)	-	ac(1)
				M	61	0.97(0.50-1.91)	-	ac(1)
Zeeger [47]	2002	Netherlands	Spouse (ever)	M+F	48	0.89(0.44-1.80)	-	ac(1)em
			Parents (?)	M+F	52	1.20(0.56-2.40)	-	ac(1)e
			Co-worker (?)	M+F	40	1.40(0.70-2.60)	-	ac(1)e
			Cohabitant or co-worker (?)	M+F	41	0.67(0.36-1.25)	No	ac(1)e
Meta-analyses based on 5 estimates				Fixed effects		0.89 (0.64-1.25)		h
				Random effects		0.89 (0.64-1.25)		

Study: described by name of first author of publication – see Appendix A for references.

Year: year of publication of paper reporting results cited.

Number of cases: number among lifelong non-smokers.

Relative risk (95% confidence interval = CI): estimated from data provided where necessary – see note e.

Dose response: "-" indicates dose response not studied, "No" indicates dose-response studied but no significant trend seen.

Key to notes

a adjusted for age.

c adjusted for confounding variables other than age (number of confounders given in brackets – see Appendix A for further details).

e estimated from data reported.

h heterogeneity chisquared is 0.91 on 4 degrees of freedom ($p>0.1$).

t the source paper does not make clear the time period the ETS exposure relates to.

u unadjusted.

x data are for cancer of the urinary organs.

TABLE 6 – ETS and Brain Cancer

Study	Year	Country	Source (timing) of ETS exposure	Sex	Number of cases	Relative risk (95% CI)	Dose Response	Notes
Sandler I [8]	1985	USA	Mother (childhood)	M+F	11	0.9 (0.1-7.3)	-	um
			Father (childhood)	M+F	9	1.7 (0.4-6.5)	-	u
Hirayama [5]	1985	Japan	Spouse (ever)	F	34	2.93 (0.82-10.5)	d1	c(1)em
Ryan [75]	1992	Australia	Spouse/partner (ever)	F	(50G)	1.14 (0.50-2.59)	-	ams
				M	(60G)	2.01 (0.45-9.04)	-	ams
				F	(48M)	2.54 (0.94-6.89)	-	ams
				M	(12M)	2.85 (0.24-33.7)	-	ams
Hurley [76]	1996	Australia	Cohabitant (adulthood)	M+F	172G	0.97 (0.61-1.53)	-	ac(2)m
Blowers [15]	1997	USA	Spouse (ever)	F	(94G)	0.7 (0.4-1.4)	-	ums
			Parent (ever)	F	(94G)	1.7 (0.8-3.7)	-	us
Johnson [49]	1999	Canada	Cohabitant or co-worker	F	(210)	1.96 (0.99-3.9)	d2	nms
			(ever)	M	(339)	0.97 (0.5-1.7)	No	nms
Phillips [48]	2005	USA	Spouse (10+ years earlier)	M+F	95M	2.0 (1.1-3.5)	d3	ac(2)m
			Cohabitant, not spouse (10+ years earlier)	M+F	95M	0.7 (0.4-1.1)	No	ac(2)
			Co-worker (10+ years earlier)	M+F	95M	0.7 (0.4-1.2)	No	ac(2)
Meta-analyses based on 11 estimates				Fixed effects		1.28 (1.01-1.60)		h
				Random effects		1.33 (1.00-1.78)		

Study: described by name of first author of publication – see Appendix A for references.

Year: year of publication of paper reporting results cited.

Number of cases: number among lifelong non-smokers unless in brackets (see note s below); G indicates glioma, M meningioma

Relative risk (95% confidence interval = CI): estimated from data provided where necessary – see note e.

Dose response: "-" indicates dose response not studied, "No" indicates dose-response studied but no significant trend seen, "d" indicates dose-response studied, significant trend with more detailed data as follows:

d1 Relative risks 1.00, 3.28, 4.92 for husband non-smoker, ex or 1-19/day and 20+/day (trend p=0.002)

d2 Relative risks 1.00, 1.42, 2.20, 2.67 for 0, 1-24, 25-45 and 46+ years of ETS exposure (trend p=0.001)

d3 Relative risks 1.0, 1.4, 2.3, 2.7 for 0, <13, 13-28, >28 years exposure to spousal ETS (trend p=0.02).

Key to notes

a adjusted for age.

c adjusted for confounding variables other than age (number of confounders given in brackets – see Appendix A for further details).

e estimated from data reported.

h heterogeneity chisquared is 13.89 on 10 degrees of freedom (p>0.1).

m relative risk estimate included in meta-analyses.

n not known whether estimate adjusted for confounding variable or not.

s numbers of cases in lifelong non-smokers not known – number given (in brackets) is total for study and includes cancers in smokers.

u unadjusted.

TABLE 7 – ETS and Cancer of Other Sites

Study	Year	Country	Source (timing) of ETS exposure	Sex	Number of cases	Relative risk (95% CI)	Dose response	Notes
Bone cancer								
Sandler I [8]	1985	USA	Mother (childhood)	M+F	19	1.0 (0.2-4.6)	-	ue
			Father (childhood)	M+F	20	0.6 (0.2-1.6)	-	ue
Hirayama [6]	1987	Japan	Spouse (ever)	F	17	Not available	No	c(1)
Skin cancer								
Hirayama [6]	1987	Japan	Spouse (ever)	F	23	Not available	No	c(1)
Cancer of the endometrium/corpus uteri								
Hirose [41]	1996	Japan	Spouse (current)	F	125	1.09 (0.76-1.57)	No	ac(1)
Nishino [10]	2001	Japan	Spouse (current)	F	13	1.30 (0.40-3.90)	-	a
Cancer of the ovary								
Hirayama [6]	1987	Japan	Spouse (ever)	F	54	Not available	No	c(1)
Nishino [10]	2001	Japan	Spouse (current)	F	15	1.70 (0.58-5.20)	-	a
Goodman [77]	2003	USA	Cohabitant (childhood)	F	351	0.98 (0.72-1.35)	-	ac(6)
Cancer of the kidney								
Kreiger [50]	1993	Canada	Cohabitant or co-worker	F	72	0.87 (0.50-1.49)	d1	ac(1)er
			(current)	M	47	1.09 (0.57-2.09)	No	ac(1)er
Hu [51]	2005	Canada	Residential and/or	F	171	1.75 (0.99-3.08)	d2	ac(6)e
			occupational (lifetime)	M	89	2.55 (0.99-6.58)	d3	ac(6)e
Female genital cancer								
Sandler I [8]	1985	USA	Mother (childhood)	F	72	1.0 (0.4-2.4)	-	ue
			Father (childhood)	F	59	1.3 (0.7-2.4)	-	ue
Endocrine gland cancer								
Sandler I [7]	1985	USA	Spouse (ever)	M+F	13	4.4 (1.2-17.4)	-	u
Sandler I [8]	1985	USA	Mother (childhood)	M+F	11	1.9 (0.4-9.3)	-	ue
			Father (childhood)	M+F	11	1.6 (0.5-5.4)	-	ue
Malignant lymphoma								
Hirayama [6]	1987	Japan	Spouse (ever)	F	85	Not available	No	c(1)

(continued)

TABLE 7 – ETS and Cancer of Other Sites (continued)

Study	Year	Country	Source (timing) of ETS exposure	Sex	Number of cases	Relative risk (95% CI)	Dose response	Notes
Leukaemia								
Hirayama [6]	1987	Japan	Spouse (ever)	F	51	Not available	No	c(1)
All haematopoietic								
Sandler I [8]	1985	USA	Mother (childhood)	M+F	19	2.3 (0.7-7.5)	-	ue
			Father (childhood)	M+F	17	2.4 (0.9-6.7)	-	ue

Results are not included for three studies [78-80] as the analyses were not restricted to lifelong non-smokers.

Study: described by name of first author of publication – see Appendix A for references.

Year: year of publication of paper reporting results cited.

Number of cases: number among lifelong nonsmokers.

Relative risk (95% confidence interval = CI): estimated from data provided where necessary – see note e.

Dose response: "-" indicates dose response not studied, "No" indicates dose-response studied but no significant trend.

"d" indicates dose-response studied, significant trend with more detailed data as follows (note that d2 shows a trend that is non-significant but is not far from significance):

d1 Relative risks 1.0, 0.6, 1.7 for <3, 3-8, >8 hours/day ETS exposure (trend p=0.03)

d2 Relative risks 1.0, 1.7, 1.7, 1.8 for never, 1-22, 23-42 and ≥43 years exposure (sum of years residential exposure and years occupation exposure) (trend p=0.09)

d3 Relative risks 1.0, 1.5, 2.5, 3.9 for never, 1-22, 23-42 and ≥43 years exposure (sum of years residential exposure and years occupation exposure) (trend p=0.001)

Key to notes

a adjusted for age.

c adjusted for confounding variables other than age (number of additional confounders given in brackets – see Appendix A for further details).

e estimated by us from data reported.

r comparison is of usual exposure 3+ vs <3 hours/day.

u unadjusted.

TABLE 8 – ETS and Total Cancer Incidence

Study	Year	Country	Source (timing) of ETS exposure	Sex	Number of cases	Relative risk (95% CI)	Dose response	Notes
Total cancer (including lung cancer)								
Hirayama [4]	1984	Japan	Spouse (ever)	F	2705(200)	1.14 (1.04-1.25)	d1	c(2)em
Miller I [55]	1984	USA	Spouse (ever)	F	123(5)	0.95 (0.57-1.60)	-	aem
Sandler I [7]	1985	USA	Spouse (ever)	F	192(≤2)	1.96 (1.30-2.97)	-	uenm
				M	39(≤2)	1.53 (0.41-5.68)	-	uenm
Sandler I [9]	1985	USA	Cohabitant (ever)	M+F	157(≤2)	1.78 (1.09-2.91)	d2	uen
Sandler I [8]	1985	USA	Mother (childhood)	M+F	191(1)	1.2 (0.7-2.2)	-	ue
			Father (childhood)	M+F	173(1)	1.2 (0.8-1.8)	-	ue
Reynolds [53]	1987	USA	Spouse (ever)	F	73(1)	1.68 (1.04-2.71)	d3	ac(1)em
Butler [39]	1988	USA	Spouse (in marriage)	F	321(8)	1.20 (0.94-1.54)	-	am
Sandler II [56]	1989	USA	Cohabitant (ever)	F	501(?)	1.00 (0.82-1.21)	-	ac(3)m
				M	115(?)	1.01 (0.66-1.53)	-	ac(3)m
Miller II [33]	1990	USA	Cohabitant (ever) or long-term exposure outside home	F	82(3)	6.40 (2.34-17.5)	-	aexk
Iribarren [52]	2001	USA	Cohabitant (current)	F	1220(?)	0.94 (0.82-1.08)	No	ac(10)m
				M	239(?)	0.93 (0.65-1.31)	No	ac(10)m
			Total (current)	F	1220(?)	0.95 (0.84-1.08)	No	ac(10)
				M	239(?)	1.28 (0.94-1.75)	No	ac(10)
Nishino [10]	2001	Japan	Spouse (current)	F	426(24)	1.10 (0.92-1.40)	-	am
McGhee [54]	2005	Hong Kong	Cohabitants (10 years earlier)	F	764(179)	1.35 (1.03-1.76)	-	ac(1)
				M	851(145)	1.16 (0.85-1.60)	-	ac(1)
				M+F	1615(324)	1.27 (1.03-1.55)	d4	ac(2)m
Meta-analysis based on 12 estimates (excluding Miller II)				Fixed effects		1.11 (1.04-1.17)		hk
				Random effects		1.12 (1.02-1.24)		
Smoking related cancer (including lung cancer)								
Sandler II [8]	1985	USA	Mother (childhood)	M+F	47(1)	0.8 (0.3-2.4)	-	ue
			Father (childhood)	M+F	41(1)	1.7 (0.9-3.3)	-	ue
Reynolds [53]	1987	USA	Spouse (ever)	F	<73(1)	7.01 (0.73-67.5)	d5	ac(1)e
Butler [39]	1988	USA	Spouse (in marriage)	F	41(8)	1.22 (0.61-2.44)	-	a
Sandler II [56]	1989	USA	Cohabitant (ever)	F	76(?)	1.45 (0.88-2.40)	-	ac(3)
				M	32(?)	0.96 (0.43-2.16)	-	ac(3)
Nishino [10]	2001	Japan	Spouse (current)	F	56(20)	1.70 (0.94-2.90)	-	a

(continued)

TABLE 8 – ETS and Total Cancer Incidence (continued)

Study	Year	Country	Source (timing) of ETS exposure	Sex	Number of cases	Relative risk (95% CI)	Dose response	Notes

Smoking-related cancer (excluding lung cancer)								
Butler [39]	1988	USA	Spouse (in marriage)	F	33 (0)	1.06 (0.47-2.36)	-	a
Cancer other than the lung								
Gillis [57]	1984	Scotland	Cohabitant (current)	F	43 (0)	1.26 (0.62-2.56)	-	a
				M	8 (0)	0.50 (0.10-2.48)	-	a
Cancer other than smoking-related								
Sandler I [8]	1985	USA	Mother (childhood)	F	144 (0)	1.3 (0.7-2.5)	-	ue
			Father (childhood)	M	132 (0)	1.1 (0.7-1.7)	-	ue
Sandler II [56]	1989	USA	Cohabitant (ever)	F	425 (0)	0.93 (0.76-1.54)	-	ac(3)
				M	83 (0)	1.03 (0.40-2.62)	-	ac(3)

Study: described by name of first author of publication – see Appendix A for references.

Year: year of publication of paper reporting results cited.

Number of cases: number among lifelong non-smokers. Bracketed numbers indicate lung cancers. (?) indicates the number of lung cancers was not known.

Relative risk (95% confidence interval = CI): estimated from data provided where necessary – see note e.

Dose response: "-" indicates dose response not studied, "No" indicates dose-response studied but no significant trend.
"d" indicates dose-response studied, with significant trend – more detailed data as follows:

d1 Relative risks 1.00, 1.12, 1.23 for husband non-smoker, ex-smoker or 1-19/day, 20+/day (one-tailed trend p=0.0002).

d2 Relative risks 1.0, 1.5, 2.3, 2.8 for 0, 1, 2, 3+ cohabitants smoking.

d3 A significant trend (p=0.0433) was noted with pack-years ETS exposure but relative risks by level were not given.

d4 Relative risks 1.0, 1.14, 1.74 for 0, 1 and 2+ smoking cohabitants (sexes combined), trend p=0.003.

d5 A significant trend (p=0.0007) was noted with pack-years ETS exposure but relative risks by level were not given.

Key to notes

a adjusted for age.

c adjusted for confounding variables other than age (number of confounders given in brackets – see Appendix A for further details).

e estimated from data reported.

h heterogeneity chisquared is 20.97 on 11 degrees of freedom ($0.01<p<0.025$)

k meta-analysis additionally including Miller II (based on 13 estimates) gave
Fixed effects: 1.11 (1.05-1.18)
Random effects: 1.16 (1.03-1.31)
with heterogeneity chisquared 32.64 on 12 degrees of freedom ($0.001<p<0.005$)

m relative risk included in meta-analyses.

n there were a total of 2 non-smokers with lung cancer but it was not stated how many there were in each sex or how many provided full data on smoking by cohabitants.

u unadjusted.

x results relate to unemployed wives only because no separation by ETS exposure for employed wives.

APPENDIX A – Studies providing data on ETS and cancer other than the lung or breast

Study [ref]	Year[1]	Location	Design[2]	Cancers	Potential confounding variables adjusted for
Gillis [57]	1984	Scotland	P	Total (not lung)	Age
Hirayama [4-6]	1984[3]	Japan, 6 prefectures	P	Total and 17 sites[4]	Age of husband, occupation of husband[5]
Miller I [55]	1984	USA, Pennsylvania	CC	Total	Age
Sandler I [7-9]	1985	USA, N Carolina	CC	Total and 9 categories[6]	None
Kabat [13]	1986	USA, 18 hospitals	CC	Bladder	None
Reynolds [53]	1987	USA, California	P	Total, smoking-related	Age, income
Butler [39]	1988[7]	USA, California	P	Total, smoking-related, cervix	Age
Sandler II [31,56]	1988	USA, Maryland	P	Total, smoking-related, not smoking-related, colon	Age, housing quality, schooling, marital status
Burch [46]	1989	Canada, Alberta and Ontario	CC	Bladder	Age, area of residence
Slattery [42]	1989	USA, Utah	CC	Cervix	Age, education, church attendance, number of sexual partners
Fukuda [14]	1990	Japan, Hokkaido	CC	Nasal cavity	None
Miller II [33]	1990	USA, Pennsylvania	CC	Total	Age
Yu [24]	1990	China, Guangzhou	CC	Nasopharynx	Age, sex
Coker [36]	1992	USA, N Carolina	CC	Cervix[8]	Age, education, race, number of Pap smears, number of partners, genital warts
Ryan [75]	1992	Australia, Adelaide	CC	Brain	Age
Kreiger [50]	1993	Canada, Ontario	CC	Kidney	Age, body mass index
Zheng [34]	1993	USA, National	CC	Nasal cavity	Age, alcohol use
Hirose [41]	1996	Japan, Nagoya	CC	Cervix, endometrium	Age, year of first visit
Hurley [76]	1996	Australia, Melbourne	CC	Brain	Age, sex, reference date
Vaughan [25]	1996	USA, 5 cancer registries	CC	Nasopharynx	Age, sex
Blowers [15]	1997	USA, California	CC	Brain	None
Tan [16]	1997	USA, Ohio	CC	Head/neck	None
Cheng [26]	1999	Taiwan	CC	Nasopharynx	Age, sex, race, educational level, family history of nasopharynx cancer
Jee [40]	1999	Korea	P	Stomach, liver, cervix	Age, socioeconomic status, residency, husband's age, vegetable consumption, occupation
Johnson I [49]	1999	Canada	CC	Brain	None stated (in abstract)
Scholes [37]	1999	USA, Washington State	CS	Cervix[8]	Age, number of sexual partners, age at first intercourse
Armstrong [27]	2000	Malaysia	CC	Nasopharynx	Diet
Yuan [28]	2000	China, Shanghai	CC	Nasopharynx	Age and 7 others[9]
Zhang [17]	2000	USA[10]	CC	Head/neck	None
Iribarren [52]	2001	USA, California	CS	Cancer/tumour	Age and 10 others[11]
Nishino [10]	2001	Japan, Miyagi	P	Total, smoking-related and 9 sites[12]	Age and others[13]
Mao [32]	2002	Canada	CC	Stomach	Age and 7 others[14]
Zeeger [47]	2002	Netherlands	P	Bladder	Age and sex
Goodman [77]	2003	USA	CC	Ovary	Age, ethnicity, education, study site, use of oral contraceptive pill, parity, tubal ligation

(continued)

APPENDIX A – Studies providing data on ETS and cancer other than the lung (continued)

Study [ref]	Year[1]	Location	Design[2]	Cancers	Potential confounding variables adjusted for
Wu [38]	2003	Taiwan	CC	Cervix[8]	Age, education level, number of pregnancies, age at first intercourse, cooking in the kitchen during ages 20-40
You [30]	2003	China	CC	Oesophagus, stomach, liver	Unspecified but states that "ETS and confounders information was collected …"
Villenueve [66]	2004	Canada	CC	Pancreas	Age, sex, body mass index, income adequacy, province of residence
Hu [51]	2005	Canada	CC	Renal cell	Age, province, education, body mass index, alcohol use, total consumption of meat and of vegetables and fruit
McGhee [54]	2005	Hong Kong	CC	All cancers	Age and education (and sex for sexes-combined analysis)
Phillips [48]	2005	USA, western Washington State	CC	Intracranial meningioma	Age, sex, education
Trimble [43]	2005	USA, Washington County	P	Cervix	Age, education, marital status, religious attendance (1963 only)

Notes:

[1] Year of first publication.

[2] Study design P = prospective CC = case-control CS = cross-sectional.

[3] Also 1987.

[4] Mouth/pharynx, oesophagus, stomach, colon, rectum, liver, gall bladder, pancreas, nasal cavity, bone, skin, cervix, ovary, bladder, brain, malignant lymphoma, leukaemia.

[5] Occupation of husband only adjusted for in analyses of total and stomach cancer.

[6] Smoking related, not smoking related, digestive, bone, brain, cervix, female genital, endocrine and hematopoietic.

[7] Results for spouse-pairs cohort only considered; AHSMOG cohort includes ex-smokers.

[8] Also includes cervical intraepithelial neoplasia that are not cancer.

[9] Education, preserved food intake, oranges/tangerines intake, exposure to smoke from heated rapeseed oil and from burning coal during cooking, occupational exposure to chemical fumes, history of chronic ear and nose conditions, family history of nasopharynx cancer.

[10] Memorial Sloan-Kettering Cancer Centre.

[11] Race/ethnicity, education level, marital status, alcohol consumption, physical activity at work, serum total cholesterol, body mass index, hypertension, diabetes, individual occupational hazards.

[12] Stomach, colon, rectum, liver, gall bladder, pancreas, cervix uteri, corpus uteri, ovary and all smoking-related cancer.

[13] Age only for liver, gall bladder, pancreas, cervix uteri, corpus uteri and ovary. For other sites analyses adjusted for age, study area, alcohol, green and yellow vegetables, fruit. For stomach analyses also adjusted for miso-soup, and pickled vegetables. For colon and rectum analyses also adjusted for meat.

[14] Province, education, social class, meat consumption, vegetable consumption, fruit, juices.

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