

## ETS AND BIRTHWEIGHT

1. Over 120 studies, 30 up to 1990<sup>1-30</sup>, 39 from 1990 to 2000<sup>31-69</sup>, 47 from 2001 to 2010<sup>70-116</sup>, and 8 in 2011<sup>117-124</sup> have investigated the possible relationship of birthweight to ETS. Additionally, a review by Liu et al.<sup>125</sup> published in 2009 referred to a meta-analysis which includes 12 citations in Chinese<sup>68,69,126-135</sup>. Only two of these<sup>68,69</sup> are considered in this report. The remaining 10 either proved not to be readily obtainable, or were entirely in Chinese, and have not yet been translated. Smoking by the father has been the most common index of ETS exposure, while other indices that have been used include smoking in the household, smoking at the workplace, the cotinine level of the mother, nicotine levels in the mother and offspring, and expired air carbon monoxide in the parents.
2. Three main endpoints have been used for studying possible effects of ETS exposure on birthweight. One endpoint, used in many of the studies, is the difference in average birthweight between exposed and unexposed mothers. Another endpoint, used in some of the studies, is the risk of having a low birthweight (LBW) infant. This is traditionally defined as less than 2500g<sup>136</sup>. A third endpoint is the risk of having an infant that is “small for gestational age” (SGA). This latter condition has been defined as a birthweight more than 2 SD below the expected age-related mean of birth weight<sup>75</sup>.
3. In view of the known associations between maternal smoking and low birthweight<sup>53,137</sup> and between maternal and paternal smoking<sup>1,138</sup>, most of the studies have restricted attention to nonsmoking mothers. However some studies have based their analyses on all mothers, in most cases making statistical adjustment for smoking.
4. Numerous factors have been linked to low birthweight. These include the sex, parity and gestational age of the child, season of birth, maternal age, the height and weight of the mother and father, socioeconomic and employment status, maternal metabolic genotype, maternal alcohol consumption and nutrition, low

social participation and maternal stress, and exposure to air pollution, pesticides, organic solvents and related compounds<sup>63,72,75,76,81,85,97,98,100,110,113,139,140</sup>. Many of these factors are also related to smoking, and it has been suggested that their effects may explain up to half of the birthweight reduction that is apparently associated with active smoking<sup>72</sup>. The ETS/birthweight studies vary widely in the extent to which these factors have been taken into account. While 24 of these studies<sup>22,27,29,31,41,44,49,51,53,60,63,66,67,70,72,74,96,97,101,105,108,117,119,121</sup> have adjusted for eight or more factors, some of them do not correct for any factors at all. Despite evidence that nutritional factors play a role in birthweight<sup>100,141</sup>, only three ETS/birthweight studies<sup>30,34,85</sup> have reported taking diet into account as a potential confounder.

5. Of 53 studies relating ETS to the risk of having a LBW infant, 12<sup>13,30,57,69,72,83,87,97,108,110,119,121</sup> reported a significant ( $p < 0.05$ ) increase in risk, one reported a reduction that was marginally significant at this level<sup>5</sup>, with the rest reporting no significant association.
6. Of 30 studies relating ETS to the risk of having a SGA infant, ten<sup>33,51,54,74,77,79,86,100,106,116</sup> reported significant increases in at least one analysis, and one<sup>41</sup> a significant decrease.
7. Most of the 92 studies looking for differences in birthweight associated with ETS exposure did not report a statistically significant relationship. However, 29 studies<sup>9,14,18,20,21,25,33,34,36,40,44,45,52,56,66,68,72,73,77,79,87,88,90,91,96,108,112,116,119</sup> have reported a significantly reduced birthweight for at least one index of exposure and two studies<sup>16,47</sup> have reported a significant increase.
8. In addition to the above results, one study<sup>120,142</sup> reported on the effects of an intervention programme to reduce exposure to ETS by the mother during pregnancy and subsequent birthweight of the offspring. Among mothers who were non-smokers as confirmed by serum cotinine, subjects in the intervention group reported significantly less exposure to ETS than in the usual care group,

and the proportions of low birthweight, and very low birthweight, infants in this first group were also lower, although not significantly so<sup>142</sup>.

9. Interpretation of the reported associations is made difficult because:

- although increases in risk of LBW or SGA or reductions in birthweight associated with ETS have been reported in 10<sup>44,51,66,72,74,96,97,108,119,121</sup> of the 24 studies that adjusted for eight or more potential confounding variables, these were generally only in isolated analyses for specific endpoints and exposure indices. In none of these studies did all adjusted analyses show a significant association. Of the remaining 14 studies, 13 did not find any significant relationship at all, and one<sup>41</sup> reported a significantly lower risk of SGA associated with ETS exposure.
- some of the studies that have reported significant associations have not restricted attention to nonsmoking mothers<sup>14,18,51,87</sup> or have accounted for no potential confounding variables<sup>9,21,25,33,45,52,56,57,68,73,79,83,87,90,112,116,119</sup>. In one further study<sup>97</sup>, maternal smoking has not been recorded at all.
- some of the ETS/birthweight studies<sup>11,13,16,32,35,38,44,51,58,63,72,76,79,82,96,107,108,119,121</sup> found that adjustment for potential confounding variables markedly weakened the strength of the reported relationship between ETS and reduced birthweight. In two studies<sup>80,113,116</sup>, the association was strengthened after adjustment.

10. Over 40 studies have presented data relating birthweight to the extent of ETS exposure. Only 14 of these<sup>14,20,30,39,40,68,73,79,80,88,96,101,107,108</sup> found a statistically significant trend. In two studies<sup>20,39</sup>, the claimed effect is limited to the highest ETS exposure group, while in another study<sup>101</sup>, results for the group with an intermediate level of exposure did not follow a dose-response pattern for either endpoint studied. In one study<sup>96</sup>, only the adjusted data showed a significant

dose-response relationship and in one study<sup>108</sup>, dose-response relationships were only seen for certain endpoints. Data by level of exposure was not shown in three of the other studies<sup>14,40,79</sup>. Confounding, and other sources of bias, may contribute to an observed dose-response relationship.

11. Meta-analyses<sup>62,143-145</sup> estimate that ETS exposure is, on average, associated with a decrease in birthweight of 25 to 60g. This modest difference, of about one to two ounces, does not necessarily imply harm to the infant, and can be compared with an estimate of 102g for the reduction in birthweight relating to an elevation in altitude of 1000m<sup>146</sup>.
12. The mechanisms by which ETS may affect birthweight remain unclear. Possibilities include changes in placental morphology and circulation, anti-oestrogenic effects, induction of P450 enzymes, oxidative stress and DNA damage resulting in activation of apoptotic pathways, binding to receptors for placental growth factors resulting in decreased exchange of oxygen and nutrients, and also the direct effects of carbon monoxide and of nicotine<sup>85,91,97,99,103,110,115,118,121,147</sup>. It has also been suggested that the relationships between active and passive smoking and birthweight may be due to different mechanisms<sup>75,91</sup> and this may explain the large reduction in birthweight apparently due to ETS exposure observed in some studies. It has also been noted that many of the constituents of tobacco smoke are present in higher concentrations in sidestream smoke than in mainstream smoke inhaled by the smoker<sup>115</sup>. However, an active smoker would also inhale sidestream smoke, making the effects of this exposure more difficult to determine.
13. Reviewers have noted that in some studies the claimed effects of ETS on birthweight are far greater than would seem biologically plausible and are inconsistent with the results of the remaining studies<sup>148,149</sup>. One study, for example<sup>53</sup>, estimated, based on results for maternal smoking during pregnancy, that a 1000 ng increase in mean urinary cotinine was associated with a 59g reduction in birthweight, and that ETS exposure at home was associated with only a 21 ng increase in urinary cotinine. These results would suggest a

birthweight reduction associated with ETS of about 1g. Similar conclusions have been drawn from other studies<sup>91</sup>. However, some of these studies<sup>9,17-20,45,52,56,73,77,79,80,88,90,106,111</sup> have reported a reduction of 100g or more in some analyses, including one<sup>88</sup> that reported a reduction of over 350g. However, it should be borne in mind that many of these studies are small and take no, or only a few, potential confounding variables into account, and there are also a few studies<sup>16,47,118</sup> which report birthweight increases of 100g or more associated with ETS exposure.

14. Lack of objective measures of actual ETS exposure during gestation, and reliance on unverified paternal smoking as a measure of exposure, are additional flaws in the existing studies, and increase the potential for recall bias. For instance, it has been shown in at least two studies<sup>36,76</sup> that serum cotinine level is a better predictor of low birthweight than self-reported smoking behaviour. Elsewhere, questionnaire responses have revealed that while qualitative information is generally reliable, quantitative data may be less so<sup>72</sup>. Failure to collect information on all sources of ETS exposure may also have led to an under-estimation of its prevalence and altered the apparent associations seen in the studies. Few of the studies collected information on ETS exposure on more than one occasion, which could have implications if the timing of exposure to ETS has an influence on birthweight. Several studies have reported that exposure early in pregnancy may have more pronounced effects than later exposure<sup>36,75</sup>, although elsewhere it has been reported that active smoking by the mother during the third trimester has a bigger effect on birthweight<sup>53,72</sup>. Whether the same is true for ETS exposure is unclear, although one study has shown that tobacco smoke exposures in later pregnancy may cause greater increases in meconium tobacco smoke metabolite concentrations relative to earlier exposures<sup>111</sup>. Other factors that may have an effect on the actual level of fetal exposure include the brand of cigarette smoked, depth of inhalation, and individual differences in the uptake and metabolism of cigarette smoke components<sup>53</sup>. None of the studies appeared to take these factors into account.

15. The evidence, taken as a whole, does not convincingly demonstrate that ETS exposure decreases birthweight or increases risk of LBW or SGA.

## **EPIDEMIOLOGICAL EVIDENCE ON ENVIRONMENTAL TOBACCO SMOKE AND BIRTHWEIGHT**

### **THE DATA**

The tables that follow summarize the key evidence relating birthweight to paternal smoking (Table 1), other questionnaire indices of ETS exposure (Table 2) and biochemical markers of ETS exposure (Table 3). The tables show, for each study providing data, estimates of the birthweight decrease, the relative risk of low birthweight or the relative risk of small for gestational age associated with ETS exposure. 95% confidence levels are also shown, where available, as well as details of statistical significance. The tables, supplemented by Appendix A, also give details of the year each paper was published, the study size, the study design, and how smoking by the mother and potential confounding variables were taken into account.

In each table, results are shown first for those studies restricted to nonsmoking mothers, then for studies of ex-smoking mothers, then for studies which have considered both smoking and nonsmoking mothers and adjusted for maternal smoking in analysis, and finally for studies which have ignored maternal smoking. Within each category of maternal smoking, results are shown in order of the number of potential confounding variables taken into account.

For some studies, the birthweight decrements or the relative risks of low birthweight or of small for gestational age, as well as their 95% confidence intervals, have been estimated from data provided in the source papers.

It should be noted that most of the studies record smoking status and ETS exposure during pregnancy. However for some studies the data collected relate to the period before conception or to the time of interview after birth. The nonsmoking mothers generally include both never and former smokers.

**TABLE 1: Relationship between paternal smoking and birthweight**

Ref	Author	Year	Size <sup>a</sup>	Mother smokes <sup>b</sup>	No. of conf. <sup>c</sup>	End-point <sup>d</sup>	Result <sup>e</sup>	Sig. <sup>f</sup>
74	Mitchell	2002	3	NSM	12	RRS	0.99 (0.72 to 1.37)	No
22	Nakamura	1988	3	NSM	11	RRL	1.40 (0.90 to 2.20)	No
31	Ahlborg	1991	3	NSM	10	RRL	0.84 (0.32 to 2.24)	No
44	Rebagliato	1995	2	NSM	9	BWD	-53g (-110g to 4g)	No
66	Matsubara	2000	3	NSM	9	BWD	11g	No
					9	RRL	0.92 (0.71 to 1.20)	No
					8	RRS	0.95 (0.72 to 1.26)	No
67	Windham	2000	3	NSM	9	BWD	32g (-18g to 81g)	No
108	Tielsch	2009	3	NSM <sup>j</sup>	9	BWD	35g (19g to 51g)	Yes
					9	RRL	1.10 (1.04 to 1.16)	Yes
					9	RRS	1.02 (0.99 to 1.04)	No
70	Jaakkola	2001	2	NSM	8	RRL	1.92 (0.79 to 4.70)	No
					8	RRS	1.41 (0.52 to 3.82)	No
96	Ward	2007	4	NSM	8	BWD	36g (5g to 67g)	Yes
					8	RRL	1.23 (0.96 to 1.58)	No
30	Yan	1990	2	NSM	7	RRL	1.89 (1.23 to 2.91)	Yes
40	Martinez	1994	2	NSM	6	BWD	34g (5g to 63g) per unit <sup>k</sup>	Yes
110	Abu-Baker	2010	2	NSM	5	RRL	1.08 (1.03-1.12) <sup>l</sup>	Yes
37	Zhang	1993	3	NSM	4	BWD	30g (-7g to 66g)	No
					0	RRL	1.07 (0.58 to 1.97)	No
					0	RRS	1.11 (0.83 to 1.48)	No
35	Pan	1992	2	NSM	3	RRS	1.68 (0.69 to 4.10)	No
62	Windham	1999	2	NSM	3	RRS	1.5 <sup>m</sup> (0.64 to 3.4)	No
87	Alonso	2005	3	NSM	0	BWD	70g (16g to 124g)	Yes
	Ojembarrena			AS	3	RRL	1.37 (1.014 to 1.863)	Yes
2	MacMahon	1966	3	NSM	1	BWD	21g (-4g to 47g)	No
3	Ravenholt	1966	3	NSM	1	BWD	33g	No
7	Yerushalmy	1971	3	NSM	1	RRL	0.95	No
64	Haug	2000	4	NSM	1	BWD	1g (-15g to 17g)	No
94	Lee	2007	3	NSM	? <sup>n</sup>	BWD	7g (-19g to 32g)	No
						per hour/day		
1	Yerushalmy	1962	2	NSM	0	RRL	1.09 (0.58 to 2.07)	No
4	Comstock	1967	2	NSM	0	BWD	42g	No
5	Underwood	1967	4	NSM	0	BWD	5g	No
					0	RRL	0.90 (0.82 to 1.00)	p≈0.05
8	Mau	1974	3	NSM	0	RRL	1.27 (0.99 to 1.62)	No
9	Borlee	1978	2	NSM	0	BWD <sup>o</sup>	228g (17g to 439g)	Yes
12	Karakostov	1985	2	NSM	0	BWD	84g (-114g to 282g)	No
17	Schwartz-B.	1987	1	NSM	0	BWD	205g (-32g to 442g)	No
19	Drozd	1988	1	NSM	0	BWD	190g (-160g to 540g)	No
24	Chen	1989	3	NSM	0 <sup>g</sup>	BWD	10g (-89g to 109g)	No
					0 <sup>g</sup>	RRL	1.51 (0.79 to 2.90)	No
26	Kikuchi	1990	2	NSM	0	RRL	1.39 (0.63 to 3.04)	No
33	Saito	1991	3	NSM	0	BWD	33g (0.5g to 66g)	Yes
					0	RRS	1.26 (1.09-1.46)	Yes
68	Liu	1993	3	NSM	0	BWD	294g (224g to 364g)	Yes
71	Kukla	2001	3	NSM	0	BWD	4g <sup>p</sup>	No
						49g <sup>d</sup>	No	
86	Adamek	2005	3	NSM	0	BWD	-10g	No
						RRL	1.08 (0.66 to 1.76)	No
						RRS	0.55 (0.11 to 2.69)	No
16	MacArthur	1987	2	ESM	4	BWD	-123g (-242g to -4g)	Yes
29	Rantakallio	1990	3	AS	20+	RRL	1.18 (0.98 to 1.41)	No
51	Horta	1997	3	AS	7	RRL	1.18 (0.94 to 1.48)	No
					10	RRS	1.33 (1.05 to 1.68)	Yes
11	Magnus	1984	3	AS	7	BWD	5g (-13g to 23g) per unit <sup>f</sup>	No
14	Rubin	1986	2	AS	7	BWD	6.1g (0.2g to 12.0g)/cig	Yes
18	Campbell	1988	2	AS	4	BWD	113g (8g to 216g)	Yes



**TABLE 1: Relationship between paternal smoking and birthweight (cont'd.)**

Ref	Author	Year	Size <sup>a</sup>	Mother smokes <sup>b</sup>	No. of conf. <sup>c</sup>	End-point <sup>d</sup>	Result <sup>e</sup>	Sig. <sup>f</sup>
<sup>46</sup>	Wilcox	1995	2	AS	2	IBRD	0.046 (-0.042 to 0.134)	No
<sup>43</sup>	Jadsri	1995	1	AS	2	RRL	1.46 (0.79 to 2.69)	No
<sup>15</sup>	Little	1987	2	AS	0	BWD	No sig. effect	No
<sup>6</sup>	Terris	1969	2	I	0	RRL	0.81 (0.43 to 1.53)	No
<sup>122</sup>	L'Abée	2011	3	I	0	RRL	1.24 (0.60 to 2.55)	No

<sup>a</sup> 1,2,3,4 = <100, 100-999, 1000-9999, >10000 infants (see Appendix A)

<sup>b</sup> NSM = nonsmoking mothers ; ESM = ex smoking mothers; AS = adjusted for maternal smoking; I = ignoring smoking

<sup>c</sup> See Appendix A for the confounders considered

<sup>d</sup> BWD = birthweight decrement; IBRD = individual birth ratio decrement; RRL = relative risk of low birthweight; RRS = relative risk of small for gestational age

<sup>e</sup> 95% confidence intervals shown in brackets where available

<sup>f</sup> Yes = significant at p<0.05

<sup>g</sup> Adjustment for confounders stated to have little effect

<sup>h</sup> Data came from reference<sup>150</sup>

<sup>j</sup> Second hand tobacco smoke exposure was defined as "reported smoking by either the mother or father in the household" but less than 1% of pregnant women smoked

<sup>k</sup> Units are 0,1,2,3 = 0,1-10,11-20,21+ cigarettes/day

<sup>l</sup> Per 1 hour increase in average number of hours per week exposed to ETS from husband or other household member in third trimester

<sup>m</sup> RR is for >10 cigs/day. Results for lower amounts and low birthweight showed weaker associations and not presented

<sup>n</sup> Analysis using multiple linear regression but no details of factors included in the model

<sup>o</sup> Includes over 50% malformed births

<sup>p</sup> Husband smokes less than 15 cigarettes daily

<sup>q</sup> Husband smokes more than 15 cigarettes daily (unclear into which category men smoking 15 cigarettes per day were included)

<sup>r</sup> Units are 1,2,3,4 = 0, <10,10-20 and 21 cigarettes/day

**TABLE 2: Relationship between other questionnaire indices of ETS exposure and birthweight**

Ref	Author	Year	Size <sup>a</sup>	Mother smokes <sup>b</sup>	No.of conf. <sup>c</sup>	ETS exposure <sup>d</sup>	End-point <sup>e</sup>	Result <sup>f</sup>	Sig. <sup>g</sup>
60	Sadler	1999	3	NSM	18	Any	BWD	1g (-43g to 41g)	No
					13	Any	RRS	0.82 (0.51 to 1.33)	No
27	Lazzaroni	1990	2	NSM	15	Home or work	BWD	38g (-31g to 107g)	No
63	Chen	2000	2	NSM	14	Home or work	BWD	36g (-19g to 92g)	No
74	Mitchell	2002	3	NSM	12	Home(not father)	RRS	0.83 (0.57 to 1.22)	No
					12	Workplace/social	RRS	1.48 (1.03 to 2.12)	Yes
72	Dejmek	2002	3	NSM	11	Any (5+ cpd)	BWD	53g (24g to 82g)	Yes
							RRL	1.51 (1.02 to 2.26)	Yes
							RRS	1.08 (0.82 to 1.43)	No
31	Ahlborg	1991	3	NSM	10	Home only	RRL	0.69 (0.21 to 2.27)	No
					10	Work	RRL	1.09 (0.33 to 3.62)	No
					10	Home or work	RRL	0.99 (0.45 to 2.21)	No
49	Ahluwalia	1997	4	NSM	10	Home	BWD	4g (-29g to 37g)	No
					10	Home	RRL	1.17 (0.95 to 1.45)	No <sup>h</sup>
41	Chen	1995	2	NSM	9	Any	RRS	0.54 (0.30 to 0.96)	Yes
					9	Work only	RRS	1.02 (0.39 to 2.68)	No
					9	Home only	RRS	0.47 (0.12 to 1.89)	No
					9	Car only	RRS	1.15 (0.22 to 6.00)	No
					9	All three	RRS	0.51 (0.17 to 1.50)	No
44	Rebagliato	1995	2	NSM	9	Work	BWD	61g (3g to 119g)	Yes
					9	Public places	BWD	66g (7g to 126g)	Yes
					9	Others at home	BWD	-43g (-127g to 42g)	No
					9	Any source	BWD	52g (-36g to 141g)	No
66	Matsubara	2000	3	NSM	9	Any	BWD	19g	Yes
					9	Any	RRL	0.99 (0.75 to 1.30)	No
					8	Any	RRS	0.95 (0.71 to 1.26)	No
67	Windham	2000	3	NSM	9	Home or work	BWD	-2g (-45g to 41g)	No
					5	Home or work	RRL	1.1 (0.71 to 1.7)	No
					5	Home or work	RRS	1.01 (0.72 to 1.42)	No
70	Jaakkola	2001	2	NSM	8	Home only	RRL	1.13 (0.34 to 3.78)	No
					8	Work only	RRL	1.43 (0.50 to 4.12)	No
					8	Home and work	RRL	2.08 (0.44 to 9.73)	No
					8	Home only	RRS	1.06 (0.30 to 3.73)	No
					8	Work only	RRS	1.02 (0.31 to 3.31)	No
					8	Home and work	RRS	1.47 (0.23 to 9.32)	No
101	Jaddoe	2008	3	NSM	8	Home and work	BWD	12g (-50g to 74g) <sup>j</sup>	No
					8	Home and work	BWD	12g (-48g to 23g) <sup>k</sup>	No
					8	Home and work	RRL	1.74 (0.74 to 4.10) <sup>j</sup>	No
					8	Home and work	RRL	1.55 (0.90 to 2.67) <sup>k</sup>	No
105	Jedrychowski	2009	2	NSM	8	Home	BWD	46.5g (-34g to 127g) <sup>l</sup>	No
					6	Home or work	BWD	1.5g (-7.3g to 10.2g) per unit <sup>m</sup>	No
119	Crane	2011	4	NSM	8	Any	BWD	53.7g (8.9g to 98.4g)	Yes
					0	Any	RRL	1.65 (1.30 to 2.08)	Yes
121	Khader	2011	3	NSM	8	Home and work	RRL	1.56 (1.31 to 1.89)	Yes
34	Mathai	1992	2	NSM	7	Home	BWD	63g (12g to 114g)	Yes
					0	Home	RRL	0.99 (0.46 to 2.14)	No
113	Slama	2010	2	NSM	7	Any	BWD	28g (-57g to 113g)	No
32	Ogawa	1991	3	NSM	6	Any >2hr/day	RRL	1.0 (0.7 to 1.5)	No
					6	Any >2hr/day	BWD	11g (-11g to 32g)	No
76	Hong	2003	2	NSM	6	Any (1+hr/day)	BWD	52g (-76g to 180g)	No
79	Goel	2004	2	NSM	0	Home	BWD	138g (29g to 247g)	Yes
					6	Home	RRL	1.03 (0.65 to 1.65)	No
					6	Home	RRS	2.10 (1.27 to 3.48)	Yes
54	Dejin-Karlsson	1998	2	NSM	5	Home or work	RRS	3.9 (1.4 to 10.7)	Yes
					0	Home or work	RRL	1.3 (0.7 to 2.5)	No
77	Rashid	2003	2	NSM	5	Home or work	BWD	130g (40g to 220g)	Yes
					5	Home or work	RRS	3.21 (1.06-9.67)	Yes

**TABLE 2: Relationship between other questionnaire indices of (cont/d. 1) ETS exposure and birthweight**

Ref	Author	Year	Size <sup>a</sup>	Mother smokes <sup>b</sup>	No.of conf. <sup>c</sup>	ETS exposure <sup>d</sup>	End-point <sup>e</sup>	Result <sup>f</sup>	Sig. <sup>g</sup>
81	Jedrychowski	2004	2	NSM	5	Home	BWD	32g (-91.5g to 155.6g)	No
85	Perera	2004	2	NSM	5	Home	RRL	0.98 (0.94 to 1.02)	No
91	Hegaard	2006	3	NSM	5	Outside home	BWD	23.6g (-29.4g to 76.7g)	No
					5	Home	BWD	-49.3g (-184.9g to 86.3g)	No
					5	Any	BWD	78.9g (14.1g to 143.7g)	Yes
					5	Any (<2 hr/day)	BWD	23.2g (-31.0g to 77.4g)	No
					5	Any (>2 hr/day)	BWD	54.9 (-4.0g to 113.9g)	No
59	Hanke	1999	3	NSM	3	Any	BWD	13g (-37g to 63g)	No
					5	Any	RRS	0.98 (0.67 to 1.45)	No
110	Abu-Baker	2010	2	NSM	5	Work	RRL	1.33 (1.05-1.68) <sup>n</sup>	Yes
						Outside	RRL	1.15 (1.06-1.26) <sup>o</sup>	Yes
13	Martin	1986	3	NSM	3	Home/wk>2hr/day	BWD	24g (-13g to 60g)	No
					4	Home/wk>2hr/day	RRLT	2.17 (1.05 to 4.50)	Yes
23	Brooke	1989	3	NSM	4	Home	BWD	18g	No
28	Mathai	1990	2	NSM	0	Home	BWD	66g (-79g to 211g)	No
					4	Home	BPD	4.1% (-4.8% to 13.0%)	No
38	Fortier	1994	3	NSM	4	Home only	RRS	0.98 (0.67 to 1.44)	No
					4	Work only	RRS	1.18 (0.90 to 1.56)	No
					4	Home and work	RRS	0.94 (0.60 to 1.49)	No
					4	Home or work	RRS	1.09 (0.85 to 1.39)	No
39	Mainous	1994	3	NSM	0	Any	BWD	37g (-6g to 80g) <sup>p</sup>	No
					4	Any	RRL	1.39 (0.98 to 1.95)	No
62	Windham	1999	2	NSM	4	Home or work	BWD	-14g (-81g to 54g)	No
					3	Home or work	RRL	1.0 (0.52 to 2.1)	No
					3	Home or work	RRLT	1.8 (0.64 to 4.8)	No
					3	Home or work	RRS	1.4 (0.79 to 2.5)	No
100	Fantuzzi	2008	2	NSM	4	Home	RRSS	1.95 (1.05 to 3.62)	Yes
35	Pan	1992	2	NSM	3	Home	RRS	0.87 (0.42 to 1.78)	No
					3	Work	RRS	0.63 (0.31 to 1.31)	No
106	Krol	2009	1	NSM	0	Any	BWD	193g (-144g to 530g)	No
					2	Any	RRS <sup>q</sup>	0.89 (0.15 to 5.38)	No
107	Pogodina	2009	3	NSM	2	Home	RRL	1.15 (0.91 to 1.44)	No
47	Eliopoulos	1996	1	NSM	0	Home or work	BWD	-260g (-513g to -7g)	Yes
					1	Home or work	BPD	-15.2% (-29.2% to -1.2%)	Yes
116	Varvarigou	2010	3	NSM	0	Indoors	BWD	47g (5g to 89g)	Yes
					1	Indoors	RRS	1.49 (1.10 to 1.91)	Yes
69	Yuan	1997	3	NSM	? <sup>r</sup>	Not stated	RRL	1.94 (1.10 to 3.43)	Yes
94	Lee	2007	3	NSM	? <sup>r</sup>	Any	BWD	-8g (-16g to 1g)	No
							per hour/day		
21	Hamada	1988	2	NSM	0	Home or work	BWD	182g (110g to 254g)	Yes
					0	Home or work	RRS	0.89 (0.35 to 2.25)	No
24	Chen	1989	3	NSM	0 <sup>s</sup>	Home	BWD	11g (-79g to 101g)	No
					0 <sup>s</sup>	Home	RRL	1.33 (0.64 to 2.75)	No
25	Ueda	1989	2	NSM	0	Any	BWD	No association	No
68	Liu	1993	3	NSM	0	Not stated	BWD	123g (47g to 198g)	Yes
45	Roquer	1995	1	NSM	0	Home or work	BWD	192g (19g to 365g)	Yes
					0	Home or work	RRS	1.86 (0.57 to 6.06)	No
52	Lodrup	1997	2	NSM	0	Home	BWD	100g (2g to 198g)	Yes
56	Luciano	1998	1	NSM	0	Home or work <sup>t</sup>	BWD	253g (68g to 438g)	Yes
57	Nafstad	1998	2	NSM	0 <sup>l</sup>	Home or work	RRL	0.82 (0.35 to 1.95)	No
					0 <sup>l</sup>	Home and work	RRL	1.39 (0.44 to 4.41)	No
55	Janghorbani	1998	2	NSM	0	Home or work	BWD	22g (-52g to 96g)	No
					0	Home or work	RRL	0.75 (0.44 to 1.18)	No
61	Steuerer	1999	2	NSM	0	Any	BWD	No significant reduction	No

**TABLE 2: Relationship between other questionnaire indices of (cont/d. 2) ETS exposure and birthweight**

Ref	Author	Year	Size <sup>a</sup>	Mother smokes <sup>b</sup>	No.of conf. <sup>c</sup>	ETS exposure <sup>d</sup>	End-point <sup>e</sup>	Result <sup>f</sup>	Sig. <sup>g</sup>
65	Hrubá	2000	3	NSM	0	Any	BWD	46g (-31g to 124g)	No
						Home only	BWD	45g (-68g to 158g)	No
						Work only	BWD	52g (-55g to 159g)	No
						Home and work	BWD	35g (-162g to 233g)	No
						Any	RRL	0.95 (0.63 to 1.45)	No
						Home only	RRL	1.09 (0.61 to 1.93)	No
						Work only	RRL	0.88 (0.48 to 1.61)	No
						Home and work	RRL	0.84 (0.32 to 2.21)	No
73	Kutlu	2002	1	NSM	0	Not stated	BWD	397g (256g to 538g)	Yes
78	Ciesla	2004	2	NSM	0	Any	RRS	1.57 (0.81 to 3.04)	No
83	Nakamura	2004	2	NSM	0	Home or work	BWD	70g (-13g to 153g)	No
						Home or work	RRL	2.13 (1.06 to 4.26)	Yes
90	Gomolka	2006	2	NSM	0	Not stated	BWD	281g (89g to 473g)	Yes
92	Steyn	2006	3	NSM	0	Home	BWD	12.2g (-39.7g to 64.1g)	No
						Home	RRS	0.81 (0.53 to 1.23)	No
						Home or work	BWD	18g (-64 to 100g)	No
93	Adamek	2007	2	NSM	0	Any	BWD	70g	No
99	Aycicek	2008	1	NSM	0	Any	RRL	1.01 (0.46 to 2.21)	No
						Any	BWD	50g	No
103	Tsui	2008	2	NSM	0	Home or work	BWD	34g (-49g to 117g)	No
104	Fenercioglu	2009	2	NSM	0	Home <sup>u</sup>	BWD	66g (-138g to 271g)	No
109	Wdowiak	2009	2	NSM	0	Work	RRL	1.08 (0.26 to 4.49)	No
112	Newman	2010	3	NSM	0	Home	BWD	84g (20g to 148g)	Yes
							RRS	1.38 (0.95 to 2.01)	No
114	Sochaczewska	2010	1	NSM	0	Any	BWD	30g (-134g to 194g)	No
115	Subramoney	2010	2	NSM	0	Home	BWD	11g	No
							RRL	1.01 (0.74 to 1.39)	No
118	Aycicek	2011	1	NSM	0	Any	BWD	-140g	No
123	Lee	2011	2	NSM	0	Any	BWD	53g (-102g to 208g)	No
124	Stankovic	2011	2	NSM	0	Home	BWD	19g (-75g to 113g)	No
50	Frisbie	1997	3	AS	17	Not stated	RRS	1.10 (0.90 to 1.20)	No
102	Mirahmadizadeh	2008	3	AS <sup>v</sup>	5	Any	RRL	1.42 (0.92 to 2.21)	No
84	Ojima	2004	2	AS	7	Home	RRL	1.26 (0.86 to 1.86)	No
						Work	RRL	1.06 (0.63 to 1.79)	No
75	Dejin-Karlsson	2003	2	AS	4	Home or work	RRS	2.60 (0.99 to 6.86) <sup>j</sup>	No
						Home or work	RRS	1.27 (0.64 to 2.49) <sup>k</sup>	No
48	Jedrychowski	1996	3	AS	3	Home or work	BWD	58g (-3g to 119g)	No <sup>w</sup>
						Home or work	RRL	1.46 (0.83 to 2.60)	No
97	Wu II	2007	3	I	11	Home only	BWD	30g (-20g to 80g)	No
						Home only	RRL	1.54 (1.03 to 2.28)	Yes
89	Ramesh	2005	2	I	1	Home or work	BWD	80g (49g to 111g)	No
95	Sanyal	2007	1	I	0	Not stated	BWD	No association	No
120	El-Mohandes	2011	2	I	0	Any <sup>x</sup>	RRL	0.96 (0.64 to 1.45)	No

<sup>a</sup> 1,2,3,4 = <100, 100-999, 1000-9999, >10000 infants (see Appendix A for numbers)

<sup>b</sup> NSM = nonsmoking mothers; AS = adjusted for maternal smoking, I = ignoring smoking

<sup>c</sup> See Appendix A for the confounders considered

<sup>d</sup> Exposures relate to period of pregnancy except for Ueda where this is unclear

<sup>e</sup> BPD = adjusted birthweight percentile decrement; BWD = birthweight decrement; RRL = relative risk of low birthweight; RRLT = relative risk of low birthweight at term; RRS = relative risk of small for gestational age; RRSS = relative risk of severe small for gestational age

<sup>f</sup> 95% confidence intervals shown in brackets where available

<sup>g</sup> Yes= significant at p<0.05

<sup>h</sup> Ahluwalia reported that in mothers aged 30+ there was a significant (p<0.001) RRL of 2.42 (1.51 to 3.87); results cited are for all ages

<sup>j</sup> ETS exposure in early pregnancy

<sup>k</sup> ETS exposure in late pregnancy

<sup>l</sup> Data came from reference<sup>151</sup>

<sup>m</sup> Units are 0,1,2,3 = 0, <5, 6-10, >10 cigarettes per day

<sup>n</sup> Per one hour increase in average exposure per week during second trimester

- o Per one hour increase in average exposure per week during third trimester
- p For high and moderate versus low and very low ETS exposure
- q Birth weight below 10<sup>th</sup> percentile
- r Analysis using multiple linear regression but no details of factors included in model were given
- s Adjustment for confounders stated to have little effect
- t Significant exposure (1+ packs per day)
- u At least one household member who smoked >10 cigarettes per day inside the house
- v Adjusted for waterpipe smoking
- w Stated as significant at  $p = 0.004$  but data given as 57.9 with SE 31.1 which is not significant even at  $p < 0.05$
- x Information came from reference <sup>142</sup>

**TABLE 3: Relationship between birthweight and biochemical markers of ETS exposure in nonsmoking mothers**

Ref	Author	Year	Size <sup>a</sup>	No. of conf. <sup>b</sup>	Marker/restriction <sup>c</sup>	End-point <sup>d</sup>	Result <sup>e</sup>		Sig. <sup>f</sup>
53	Wang	1997	2	12	URC (none)	BWD	0.0-30.9 ng/ml: 31-100 ng/ml:	comparison group 57g (-29g to 143g)	No
44	Rebagliato	1995	2	9	SAC (<14 ng/ml)	BWD	0.0 to 0.5 ng/ml: 0.6 to 0.8 ng/ml: 0.9 to 1.1 ng/ml: 1.2 to 1.7 ng/ml: >1.7 ng/ml	comparison group 42g (-39g to 122g) 53g (-37g to 143g) -54g (-142g to 35g) 87g (1g to 174g)	No No No Yes
117	Almeida	2011	2	9	MHC (>0.2 ng/mg)	RRS	<0.03 ng/mg 0.03 to <0.2 ng/mg	comparison group 1.66 (0.81 to 3.42)	No
						BWD	<0.03 ng/mg: 0.03 to <0.2 ng/mg	14g (-125g to 97g) comparison group	No
						BWZ	per ng/mg:	0.05 (-0.16 to 0.25)	No
					MHN (none)	BWZ	per ng/mg:	-0.04 (-0.17 to 0.09)	No
70	Jaakkola	2001	2	8	MHN (none)	RRL	<0.75 µg/g 0.75 to <4.00 µg/g ≥4.00 µg/g per µg/g	comparison group 1.28 (0.59 to 2.60) 1.55 (0.55 to 4.43) 1.06 (0.96 to 1.17)	No No No
						RRS	<0.75 µg/g 0.75 to <4.00 µg/g ≥4.00 µg/g per µg/g	comparison group 1.05 (0.44 to 2.49) 1.18 (0.34 to 4.19) 1.04 (0.92 to 1.19)	No No No
42	Eskenazi	1995	3	7	SEC (<10 ng/ml)	BWD	<2.0 ng/ml: 2.0+ ng/ml:	comparison group 45g (-36g to 126g)	No
				0		RRL	<2.0 ng/ml: 2.0+ ng/ml:	comparison group 1.35 (0.60 to 3.03)	No
111	Braun	2010	2	7	MEN (>10 ng/g)	BWD	<0.946ng/g: 0.946 to 10 ng/g:	comparison group 136g (-24g to 295g)	No
					MEC (>5 ng/g)	BWD	<0.070 ng/g: 0.070 to 5 ng/g:	comparison group 27g (-120g to 175g)	No
					M3HC (>10 ng/g)	BWD	<0.092 ng/g: 0.092 to 10 ng/g:	comparison group 100g (-46g to 246g)	No
					SEC (>3 ng/g)				
					Mean:	BWD	<0.015 ng/ml: 0.015 to 3 ng/ml:	comparison group 112g (-41g to 264g)	No
					16 weeks:	BWD	<0.015 ng/ml: 0.015 to 3 ng/ml:	comparison group 20g (-132g to 173g)	No
					26 weeks:	BWD	<0.015 ng/ml: 0.015 to 3 ng/ml:	comparison group -20g (-175g to 135g)	No
					Birth:	BWD	<0.015 ng/ml: 0.015 to 3 ng/ml:	comparison group 97g (-54g to 248g)	No

**TABLE 3: Relationship between birthweight and biochemical markers of ETS (cont'd.) exposure in nonsmoking mothers**

Ref	Author	Year	Size <sup>a</sup>	No. of conf. <sup>b</sup>	Marker/restriction <sup>c</sup>	End-point <sup>d</sup>	Result <sup>e</sup>	Sig. <sup>f</sup>						
20	Haddow	1988	3	6	SEC (<10 ng/ml)	BWD	<0.5 ng/ml:	-4g (-73g to 65g)	No					
							0.5-1.0 ng/ml:	comparison group						
							>1.0 ng/ml:	104g (35g to 173g)	Yes					
						RRL	≤1.0 ng/ml:	comparison group						
							>1.0 ng/ml:	1.29	?					
76	Hong	2003	2	6	URC (none)	BWD	<120 µg/ml:	comparison group						
							≥120 µg/ml:	76g (-92g to 243g)	No					
82	Kharrazi	2004	3	6	SEC (<10ng/ml)	BWD	<0.026ng/ml:	comparison group						
							0.026 to 0.053 ng/ml:	-22.9g (-76.6g to 30.8g)	No					
							0.054 to 0.096 ng/ml:	16.1g (-37.7g to 69.9g)	No					
							0.097 to 0.235 ng/ml:	18.2g (-36.1g to 72.5g)	No					
							0.236+ ng/ml:	39.7g (-16.3g to 95.7g)	No					
										5	RRL	<0.026 ng/ml:	comparison group	
												0.026 to 0.053 ng/ml:	1.18 (0.40 to 3.44)	No
												0.054 to 0.096 ng/ml:	1.76 (0.66 to 4.75)	No
				0.097 to 0.235 ng/ml:	1.40 (0.51 to 3.88)	No								
							0.236+ ng/ml:	1.76 (0.65 to 4.81)	No					
105	Jedrychowski	2009	2	6	CBC	BWD		12.3g (-66g to 91g) per unit	No					
85	Perera	2004	2	5	PLC (≤15ng/ml)	RRL	0.0 to 0.0435 ng/ml:	comparison group						
							>0.0435 ng/ml:	0.98 (0.93 to 1.03)	No					
58	Peacock	1998	2	4	SEC (<15 ng/ml)	BRD <sup>g</sup>	0 to 0.180 ng/ml:	comparison group						
							0.180 to 0.291 ng/ml:	0.001 (-0.025 to 0.027)	No					
							0.292 to 0.480 ng/ml:	0.003 (-0.022 to 0.028)	No					
							0.481 to 0.795 ng/ml:	-0.004 (-0.030 to 0.022)	No					
							0.796+ ng/ml:	0.002 (-0.024 to 0.028)	No					
36	Bardy	1993	3	3	SEC (none)	BWD	Per 1 µg/l:	1.29g (0.55g to 2.02g)	Yes					
80	Hanke	2004	2	3	SEC (<10ng/ml)	BWD	0.0 to <2 µg/ml:	comparison group						
							2 to <10 ng/ml:	100g (-17.5g to 218.5g)	No					
				0	URC <sup>h</sup> (<100µg/ml)	BWD	0.0 to <2 µg/ml:	comparison group						
							2 to 100 µg/ml:	negative relationship	?					
88	Gomez	2005	2	3	PCM <sup>i</sup> (none)	BWD	0 to 5 ppm:	comparison group						
							6 to 10 ppm:	62g (-49g to 173g)	Yes					
							11 to 20 ppm:	237g (133g to 341g)	Yes					
							>20 ppm:	356g (234g to 478g)						
10	Hauth	1984	2	0	UCT (none)	BWD	No relationship of UCT to birthweight in women exposed to ETS at home or work (r = 0.02) or those unexposed to ETS (r = 0.15)		No					
25	Ueda <sup>j</sup>	1989	2	0	SEC (none)	RBW	<9 ng/ml:	102.4%						
							>9 ng/ml:	96.2%	Yes					
57	Nafstad	1998	2	0 <sup>k</sup>	MHN (none)	RRL	<0.75 µg/g	comparison group						
							0.75 to 4.00 µg/g	3.35 (1.31 to 8.60)	Yes					
							>4.00 µg/g	2.08 (0.43 to 10.1)	No					
					OHN (none)	RRL	undetectable	comparison group						
							detectable	2.62 (0.85 to 8.08)	No					
95	Sanyal	2007	1	0	URC (none)	BWD	No relationship of URC to birthweight in women exposed to ETS		No					
						URN (none)	BWD	No relationship of URN to birthweight in women exposed to ETS		No				

- <sup>a</sup> 1,2,3,4 = <100, 100-999, 1000-9999, >10000 infants (see Appendix A)
- <sup>b</sup> See Appendix A for the confounders considered
- <sup>c</sup> CBC = cord blood cotinine, MCM = maternal expired air carbon monoxide, MEC = meconium cotinine, MEN = meconium nicotine, MHC = maternal hair cotinine, M3HC = meconium 3HC, MHN = maternal hair nicotine, OHN = offspring hair nicotine, PCM = paternal expired air carbon monoxide, PLC = plasma cotinine, SAC = saliva cotinine, SEC = serum cotinine, UCT = umbilical cord thiocyanate, URC = urinary cotinine, URN = urinary nicotine; analysis limited to those with levels below cut-point stated in brackets
- <sup>d</sup> BRD = decrement in adjusted birthweight ratio; BWD = birthweight decrement; BWZ = birthweight for gestational age Z score, RBW = birthweight relative to national standard for gestational age; RRL = relative risk of low birthweight; RRS = relative risk of small for gestational age
- <sup>e</sup> 95% confidence limits shown in brackets where available
- <sup>f</sup> Yes = significant at  $p < 0.05$ ; ? = significance cannot be estimated
- <sup>g</sup> A BRD of 0.001 corresponds to a BWD of about 3.35g in this study
- <sup>h</sup> Data came from reference <sup>152</sup>
- <sup>j</sup> Analysis restricted to women who had CO between 0 and 5 ppm, so may have included some smokers.
- <sup>k</sup> Adjustment for confounders stated to have little effect



**APPENDIX A : Further details of studies**

Ref	Author	Year	Location	Study type <sup>a</sup>	Sample size <sup>b</sup>	Dose-resp. <sup>c</sup>	Confounders accounted for <sup>d</sup>													Others <sup>d</sup>	
							PA	SX	GE	MA	MH	MW	MB	PH	PW	PE	SES	EM	AC		
1	Yerushalmy	1962	USA	PC	606	-															
2	MacMahon	1966	USA	RC	5935	No		+													
3	Ravenholt	1966	USA	RC	1240	No		+													
4	Comstock	1967	USA	RC	238	-															
5	Underwood	1967	USA	RC	24773	No															
6	Terris	1969	USA	CC	214	No															
7	Yerushalmy	1971	USA	PC	6015	-															ET
8	Mau	1974	Germany	PC	3696	Yes															
9	Borlee	1978	Belgium	RC	238	-															
10	Hauth	1984	USA	RC	134	-															
11	Magnus	1984	Norway	PC	3130	No		+			+	+			+	+	+	+			
12	Karakostov	1985	Bulgaria	RC	118	-									+	+	+	+			
13	Martin	1986	USA	PC	2473	-		+		+											ET
14	Rubin	1986	Denmark	RC	500	Yes		+	+		+							+		+	CP,MS
15	Little	1987	USA	PC	377	-															
16	MacArthur	1987	England	RC	180	No		+	+	+		+									
17	Schwartz-B.	1987	Germany	RC	54	-															
18	Campbell	1988	England	RC	518	-		+			+								+		+
19	Drozd	1988	Poland	RC	54	-															
20	Haddow	1988	USA	PC	1231	Yes		+	+		+	+	+			+					
21	Hamada	1988	Japan	RC	734	-															
22	Nakamura	1988	Japan	PC	2005	-		+			+							+	+	+	BP,CP,GR, MD,MS,RH
23	Brooke	1989	UK	PC	1018	-		+	+	+		+									
24	Chen	1989	China	RC	1163	No		+	+		+					+	+				
25	Ueda	1989	Japan	RC	242	-															
26	Kikuchi	1990	Japan	RC	778	-															
27	Lazzaroni	1990	Italy	RC	647	No		+	+	+	+	+	+		+	+	+		+	+	BP,CC,CP,WG, Others
28	Mathai	1990	England	PC	187	-		<sup>f</sup>	<sup>f</sup>	<sup>f</sup>					<sup>f</sup>						

**APPENDIX A : Further details of studies (Cont'd./1)**

Ref	Author	Year	Location	Study type <sup>a</sup>	Sample size <sup>b</sup>	Dose-resp. <sup>c</sup>	Confounders accounted for <sup>d</sup>													Others <sup>d</sup>	
							PA	SX	GE	MA	MH	MW	MB	PH	PW	PE	SES	EM	AC		
29	Rantakallio	1990	Finland	PC	9478	-	+	+		+	+	+		+	+	+	+	+	+	+	AB,CP,MD,MS, PB,PP,PR,RH, SB,Others
30	Yan	1990	China	CC	385	Yes			+		+			+							CP,CX,DI,MM
31	Ahlborg	1991	Sweden	PC	2940	No	+	+	+	+						+			+	+	AB,PP,PR
32	Ogawa	1991	Japan	PC	5336	-	+		+	+											
33	Saito	1991	Japan	RC	2713	-															
34	Mathai	1992	India	RC	994	-	+	+	+	+	+						+				DI <sup>h</sup>
35	Pan	1992	China	PC	253	-															CB,CK,HT
36	Bardy	1993	Finland	PC	1237	-	+	+	+												
68	Liu	1993	China	PC?	1060	Yes															
37	Zhang	1993	China	RC	1785	No	+		+	+										+	
38	Fortier	1994	Canada	RC	4644	No	+						+								CC,PB
39	Mainous	1994	USA	RC	3253	Yes	+			+							+				ET <sup>e</sup>
40	Martinez	1994	USA	RC	907	Yes	+	+	+	+						+					ET
41	Chen	1995	USA	CC	235	No	+			+			+			+			+	+	PC,WG
42	Eskenazi	1995	USA	PC	2243	No	+		+	+			+			+					ET <sup>h</sup> ,WG <sup>h</sup>
43	Jadsri	1995	Thailand	PC?	77	-															CP,PT
44	Rebagliato	1995	Spain	PC	710	No	+	+	+	+	+					+	+				CP
45	Roquer	1995	Spain	RC	74	-															
46	Wilcox	1995	UK	RC	571	-								+	+						
47	Eliopoulos	1996	Canada	RC	58	-			+												
48	Jedrychowski	1996	Poland	RC	1165	-	+	+	+												
49	Ahluwalia	1997	USA	RC	13497	-	+			+			+			+				+	AL,ET,MS,PR, WG
50	Frisbie	1997	USA	RC	8424	-	+	+		+			+			+	+				BP,CP,ET,MAS, MS,PC,SB,SPP, WG
51	Horta	1997	Brazil	RC	5166	-	+			+	+	+				+	+				BI,MS <sup>j</sup> ,PB,PC, SC <sup>j</sup>
52	Lodrup	1997	Norway	RC	588	-															
53	Wang	1997	USA	PC	740	-	+	+	+	+	+					+				+	CP,ET,PT,SB

**APPENDIX A : Further details of studies (Cont'd./2)**

Ref	Author	Year	Location	Study type <sup>a</sup>	Sample size <sup>b</sup>	Dose-resp. <sup>c</sup>	Confounders accounted for <sup>d</sup>													Others <sup>d</sup>
							PA	SX	GE	MA	MH	MW	MB	PH	PW	PE	SES	EM	AC	
69	Yuan	1997	China	PC?	2010	-														No details of adjustment factors given
54	Dejin-Karlsson	1998	Sweden	PC	575	-				+	+	+					+			MN <sup>j</sup>
55	Janghorbani	1998	Iran	RC	702	-	k													
56	Luciano	1998	Italy	PC	89	-														
57	Nafstad	1998	Norway	CC	122	No														
58	Peacock	1998	UK	PC	818	No	+	+	+		+									
59	Hanke	1999	Poland	RC	1751	No	+		+	+	+							+		MS <sup>j</sup>
60	Sadler	1999	USA	PC	2283	No	+	+	+	+			+				+	+	+	ET,HT,MS <sup>h</sup> ,PB,PD <sup>h</sup> ,PE,PM,RE,WG,XS
61	Steuerer	1999	Germany	RC	164	-														
62	Windham	1999	USA	RC	992	No			+										+	CC,ET
63	Chen	2000	China	PC	823	-	+	+	+	+	+						+			OE
64	Haug	2000	Norway	RC	16430	-				+										
65	Hrubá	2000	Czech Republic	RC	1097	-														
66	Matsubara	2000	Japan	PC	6335	No	+	+	+	+	+						+		+	
67	Windham	2000	USA	PC	4454	No	+			+							+		+	CC <sup>h</sup> ,ET,LE,MS <sup>h</sup>
70	Jaakkola	2001	Finland	RC	389	No	+	+		+							+	+	+	MS
71	Kukla	2001	Czech Republic	RC	4165	No														
72	Dejmek	2002	Czech Republic	RC	4309	-	+	+		+	+	+					+		+	ET,PR,SE
73	Kutlu	2002	Turkey	RC	40	Yes														
74	Mitchell	2002	New Zealand	CC	1248	-	+	+	+	+	+	+					+		+	HT,MF,MJ,MS
75	Dejin-Karlsson	2003	Sweden	PC	708	-				+	+						+			MAS,MN
76	Hong	2003	Korea	RC	266	-		+	+	+	+	+								PR

**APPENDIX A : Further details of studies (Cont'd./3)**

Ref	Author	Year	Location	Study type <sup>a</sup>	Sample size <sup>b</sup>	Dose-resp. <sup>c</sup>	Confounders accounted for <sup>d</sup>											Others <sup>d</sup>			
							PA	SX	GE	MA	MH	MW	MB	PH	PW	PE	SES		EM	AC	
77	Rashid	2003	Saudi Arabia	RC	868	No	+	+	+	+	+										
78	Ciesla	2004	Poland	CC	178	-															
79	Goel	2004	India	RC	576	Yes	+ <sup>m</sup>				+ <sup>m</sup>					+ <sup>m</sup>					AN <sup>m</sup> ,LI, <sup>m</sup> OCC <sup>m</sup>
80	Hanke	2004	Poland	PC	183	Yes		+ <sup>e</sup>					+ <sup>e</sup>								GU <sup>c</sup>
81	Jedrychowski	2004	USA/ Poland	PC	362	-	+	+	+		+		+								
82	Kharrazi	2004	USA	PC	2777	No	+	+	+ <sup>h</sup>	+											ET,SPP
83	Nakamura	2004	Brazil	RC	608	-															
84	Ojima	2004	Japan	CC	690	-					+						+		+		CP,MAS,PB,TI, DI,ET
85	Perera	2004	USA	PC	214	-		+	+					+							
86	Adamek	2005	Poland	PC	1250	-															
87	Alonso Ojembarrena	2005	Spain	CC	2370	-		+ <sup>e</sup>	+ <sup>e</sup>												MAS <sup>e</sup>
88	Gomez	2005	France	PC	630	Yes	+	+		+											
89	Ramesh	2005	Malaysia	PC	154	-								+							
90	Gomolka	2006	Poland	PC	157	-															
91	Hegaard	2006	Denmark	PC	1612	No	+	+	+	+											
92	Steyn	2006	South Africa	PC	1376	No															
93	Adamek	2007	Poland	PC	338	-															
94	Lee	2007	China	RC	2770	-															No details of adjustment factors given
95	Sanyal	2007	USA	PC	43	-															
96	Ward	2007	UK	RC	10347	Yes	+				+					+		+		+	CP,ET
98	Wu I	2007	Taiwan	PC	358	-															
97	Wu II	2007	China	PC	1388	-			+		+		+								AB,CK,OE
99	Aycicek	2008	Turkey	RC	59	-															
100	Fantuzzi	2008	Italy	CC	240	-															AN,HT,PB,UI
101	Jaddoe	2008	The Neth- erlands	PC	5289	Yes	+	+	+	+						+				+	ET

**APPENDIX A : Further details of studies (Cont'd./4)**

Ref	Author	Year	Location	Study type <sup>a</sup>	Sample size <sup>b</sup>	Dose-resp. <sup>c</sup>	Confounders accounted for <sup>d</sup>													Others <sup>d</sup>	
							PA	SX	GE	MA	MH	MW	MB	PH	PW	PE	SES	EM	AC		
102	Mirahmadi-zadeh	2008	Iran	RC	2808	-					+	+									CP,NP,WS
103	Tsui	2008	Taiwan	PC	359	-															
104	Fenercioglu	2009	Turkey	PC	111	-															
105	Jedrychowski	2009	Poland	PC	467	-	+	+	+	+ <sup>n</sup>	+	+				+ <sup>o</sup>					EP <sup>o</sup> , SEB <sup>o</sup>
106	Krol	2009	Poland	RC	89	-					+										CP
107	Pogodina	2009	USA	RC	1912	Yes <sup>p</sup>												+			MS
108	Tielsch	2009	India	PC	9604	Yes	+														EH,HHO,LD, NB,NC,RE,RM, TV
109	Wdowiak	2009	Poland	RC	150	-															
110	Abu-Baker	2010	Jordan	RC	300	-				+		+	+					+			WG
111	Braun	2010	USA	PC	274	-	+				+						+				DE,ET,MS
112	Newman	2010	USA	PC	1732	-															
113	Slama	2010	Germany	RC	798	-	+	+	+			+	+				+				ST
114	Sochaczewska	2010	Poland	RC	99	-															
115	Subramoney	2010	India	PC	802	-															
116	Varvarigou	2010	Greece	RC	2229	-					+										
117	Almeida	2011	Canada	PC	304	-	+				+	+		+			+	+		+ <sup>q</sup>	BP,LP
118	Aycicek	2011	Turkey	RC	41	-															
119	Crane	2011	Canada	RC	11852	-	+			+	+			+			+		+	+ <sup>q</sup>	LP
120	El-Mohandes	2011	USA	PC	817	-															
121	Khader	2011	Jordan	RC	8490	-	+				+	+					+	+	+		BG,PL
122	L' Abee	2011	The Netherlands	PC	2947	-															
123	Lee	2011	Korea	PC	414	-															
124	Stankovic	2011	USSR	PC	324	-															

<sup>a</sup> CC = case control, PC = prospective cohort (i.e. smoking and ETS data obtained before birth), RC = retrospective cohort (i.e. data obtained after birth)  
<sup>b</sup> Sample size is of nonsmoking mothers except for studies which included smoking mothers in the analysis where sample size is of all mothers  
<sup>c</sup> Yes = significant dose response seen, No = dose response investigated but not significant, - = dose response not investigated

- <sup>d</sup> Abbreviations used for main confounders:  
 PA = parity/previous pregnancies/birth order, SX = sex of child, GE = gestation time at delivery, MA = maternal age, MH = maternal height, MW = maternal weight, MB = maternal body mass, PH = paternal height, PW = paternal weight, PE = parental education, SES = socioeconomic status/income, EM = employment status, AC = alcohol consumption  
 Abbreviations used for other confounders:  
 AB = previous abortions, AL = altitude, AN = anaemia, BG = blood group, BI = birth interval, BP = birth place of mother, CB = coal burning, CC = coffee consumption of mother, CK = cooking time spent, CP = complications of pregnancy/illness of mother, CX = chemical exposures of parents, DE = depression, DI = diet of mother, EH = electricity in household, EP = exposure to particulate matter, ET = ethnicity/race, FA = received financial/other assistance, GR = gestational week at report of pregnancy, GU = gestational week at time of ultrasound, HHO = head of household's occupation, HT = hypertension, LD = location of delivery, LE = life events, LI = number of 'live issues', LP = living with partner, MAS = maternal active smoking, MD = medical history of mother, MF = maternal age at first pregnancy, MJ = marijuana use of mother, MM = maternal medication use in pregnancy, MN = maternal nationality, MS = marital status, NB = maternal night blindness, NC = number of children under 5 years in household, NP = Number of prenatal visits, OCC = occupation, OE = occupational exposures, PB = previous birthweights, PC = prenatal care, PD = placental disorders, PE = preeclampsia/eclampsia, PL = history of preterm birth/low birthweight, PM = passive marijuana, PP = pregnancy planned, PR = place of residence, PT = preterm birth, RE = religion, RH = reproductive history, RM = roof material, SB = previous still births, SC = skin colour, SE = season, SEB = season of birth, SPP = source of payment for prenatal care, ST = study centre, TI = treatment for infertility, TV = television/radio ownership, UI = Urinary tract infection, WG = weight gain in pregnancy, WS = waterpipe smoking, XS = past smoking
- <sup>e</sup> Only accounted for in analyses of low birthweight
- <sup>f</sup> Only accounted for in analyses of birthweight percentile decrement
- <sup>g</sup> Maternal and paternal height were considered as a single variable
- <sup>h</sup> Only accounted for in analyses of birthweight decrement
- <sup>j</sup> Only accounted for in analyses of small-for-gestational-age
- <sup>k</sup> Multivariate analyses carried out but inappropriately included variables such as cranial circumference and length at birth so only unadjusted analyses included in Table 2
- <sup>l</sup> Only accounted for in analyses of low birthweight and birthweight decrement
- <sup>m</sup> Only accounted for in analyses of low birthweight and small-for-gestational age
- <sup>n</sup> Only accounted for in analyses of ETS exposure at home or work
- <sup>o</sup> Only accounted for in analyses of ETS exposure at home
- <sup>p</sup> Includes women who smoked during pregnancy
- <sup>q</sup> Alcohol and drug use

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