Indoor air pollution. Part A. Environmental tobacco smoke (ETS)
Summary of epidemiologic evidence
Updated December 9, 2004

1. Overall summary

This section summarizes epidemiologic evidence cited in the tables below and will be updated as new evidence becomes available. I would appreciate feedback on any errors or omissions. don.wigle@sympatico.ca

Health effect	Level of evidence[a]	Comments
Early fetal deaths (spontaneous abortion)	Maternal exposure Limited Paternal exposure (Inadequate)	A Swedish cohort study found an association between early fetal death and maternal ETS exposure at work but not at home (Ahlborg and Bodin 1991). A case-control study in California found an association between early fetal death among non-smoking women and ETS exposure before gestation week 20 at home or work (Windham et al 1992). A recent California cohort study of non-smoking women enrolled during early pregnancy found a borderline association between early fetal death and maternal ETS exposure at home but not at work; there were relatively strong associations with ETS exposure at home or work among subgroups of women with relatively high intakes of caffeine or alcohol (Windham et al 1999). A literature review concluded that the three available epidemiologic studies provided limited evidence of an association between early fetal death and maternal ETS exposure (Lindbohm et al 2002). An expert panel review concluded that there is limited evidence of a causal association between early fetal death and maternal prenatal ETS exposure but there is uncertainty concerning mechanisms of paternal smoking (e.g., preconceptual germ cell mutations among active male smokers) (California Environmental Protection Agency 2004). A case-control study in California found no association between early fetal death and paternal smoking after adjustment for maternal smoking (Windham et al 1992). A large hospital-based case-control study in Italy found no association between early fetal death and paternal preconceptual or 1st trimester smoking (Chatenoud et al 1998). A recent California cohort study of non-smoking women enrolled during early pregnancy found no association between early fetal death and paternal smoking intensity during the 3 months before conception (Windham et al 1999). A cohort study of nonsmoking women in China found an association between early fetal death and paternal smoking of 20 or more cigarettes daily; this study monitored women for conception using daily urine hCG tests (Venners et al 2004).
Late fetal deaths (stillbirths)	Maternal exposure (Inadequate)	A Swedish cohort study found no association between late fetal death and maternal ETS exposure at work or at home (Ahlborg and Bodin 1991). A retrospective cohort study in California found a statistically non-significant

[a] Sufficient evidence = based on peer-reviewed reports of expert groups or authoritative reviews that concluded that a causal relationship existed; limited evidence = relationships for which several epidemiologic studies, including at least one case-control or cohort study, showed fairly consistent associations and evidence of exposure-risk relationships after control for potential confounders; inadequate evidence = relationships for which epidemiologic studies were limited in number and quality (e.g., small studies, ecologic studies, limited control of potential confounders), had inconsistent results, or showed little or no evidence of exposure-risk relationships. Levels in parentheses are the author's interpretation of available evidence; other levels are based on expert group reviews.

		association between late fetal deaths and maternal serum cotinine levels during early pregnancy (Kharrazi et al 2004).
Gestation length	Maternal exposure Limited Paternal smoking (Inadequate)	A California birth cohort study of women who did not smoke before or during pregnancy found an association between very preterm birth (gestation length < 35 weeks) and average ETS exposure of 7 hours or more per day at home and work since their last menstrual period; the associations between preterm (gestation length < 37 weeks) and very preterm births occurred mainly among women age 30 years or older (Windham et al 2000). A cohort study in Japan found no association between gestation length and maternal ETS exposure at home and work (hours per week) during pregnancy (Matsubara et al 2000). A small retrospective cohort study of non-smoking women in Finland found a dose-response relationship between preterm birth and maternal hair nicotine levels in segments corresponding to 3rd trimester exposure (Jaakkola et al 2001). A review of epidemiologic studies concluded that there is strong evidence for an association between preterm birth and maternal prenatal ETS exposure (Jaakkola and Jaakkola 2002). Another review concluded that there is limited evidence of an association between preterm birth and maternal ETS exposure (Lindbohm et al 2002). An expert group convened by the State of California concluded that there is limited evidence for an association between preterm birth and maternal prenatal ETS exposure (California Environmental Protection Agency 2004). A retrospective cohort study of non-smoking mothers in India found no association between preterm birth and maternal ETS exposure at home (Goel et al 2004). However, a large retrospective cohort study of non-smoking mothers in California (confirmed by low serum cotinine levels at gestation week 15-19) found an association between preterm birth and 2nd trimester maternal serum cotinine levels (Goel et al 2004). A cohort study in Japan found a borderline inverse association between gestation length and paternal smoking intensity during pregnancy (Matsubara et al 2000).
Birth weight low for gestational age	Maternal exposure Sufficient	A California birth cohort study of women who did not smoke before or during pregnancy found no association between birth weight low for gestational age and average ETS exposure of 7 hours or more per day at home and work since their last menstrual period (Windham et al 2000). A cohort study in Japan found no association between birth weight adjusted for gestation length and maternal ETS exposure at home and work (hours per week) during pregnancy (Matsubara et al 2000). A retrospective birth cohort study in the Czech Republic found no association between term low birth weight and maternal ETS exposure (Hruba and Kachlik 2000). A small retrospective cohort study of non-smoking women in Finland found no association between IUGR and maternal hair nicotine levels in segments corresponding to 3rd trimester exposure (Jaakkola et al 2001). A literature review concluded that there is limited evidence of an association between birth weight low for gestational age and maternal ETS exposure (Lindbohm et al 2002). A retrospective cohort study in China found a borderline inverse association between birth weight and maternal ETS exposure among infants of non-smoking women (Ha et al 2002). A retrospective cohort study in the Czech Republic found associations between IUGR and maternal ETS exposure among infants of both smoking and non-smoking women; the association was stronger among infants of smoking women (Dejmek et al 2002). A prospective cohort study in Sweden found a strong association between birth weight low for gestational age and maternal ETS exposure at home or work; the association occurred among infants of women exposed during early pregnancy but not among those exposed during late pregnancy (after adjustment for exposure during the other time period) (Dejin-Karlsson and Ostergren 2003). A small retrospective cohort study of non-smoking women in Korea found an inverse association between birth weight at term and maternal urinary cotinine levels at delivery among infants of women with the GSTT1 null genotype but

	Paternal smoking (Inadequate)	not among the whole cohort (Hong et al 2003). A small retrospective cohort study in Spain found inverse associations between birth weight and head circumference (adjusted for gestation length) and maternal hair nicotine levels in segments corresponding to the gestation period (Pichini et al 2003). An expert group convened by the State of California concluded that there is sufficient evidence of causal associations between maternal prenatal ETS exposure and reduced birth weight, including birth weights below 2500g; they found limited evidence for an association between IUGR and maternal prenatal ETS exposure (California Environmental Protection Agency 2004). A literature review concluded that there is an inverse dose-response between birth weight and prenatal maternal smoking, independent of gestation length (DiFranza et al 2004). A small cohort study in Poland found a borderline inverse association between birth weight adjusted for gestation length and maternal serum cotinine levels at gestation week 20-24 among infants of non-smoking mothers (Hanke et al 2004). A small cohort study of non-smoking Dominican and African American women in New York City found no association between birth weight and self-reported household ETS exposure, maternal or cord plasma cotinine or cord blood BaP-DNA adduct levels; there was an inverse association between head circumference at birth and self-reported household ETS exposure but not with maternal or cord plasma cotinine or cord blood BaP-DNA adduct levels (Perera et al 2004). A retrospective cohort study of non-smoking mothers in India found an association between IUGR and maternal ETS exposure at home (Goel et al 2004). A large retrospective cohort study of non-smoking mothers in California (confirmed by low serum cotinine levels at gestation week 15-19) found borderline associations between term low birth weight and birth weight adjusted for gestation length and maternal 2nd trimester serum cotinine levels; the inverse association between birth weight and maternal serum cotinine levels was statistically significant when they were analyzed as continuous variables (Goel et al 2004). A small cohort study of non-smoking women in New York City and Krakow (Poland) found an inverse association between birth weight adjusted for gestation length and maternal 2nd trimester personal $PM_{2.5}$ levels (note: indoor $PM_{2.5}$ levels are strongly correlated with ETS) but not with but not self-reported ETS exposure (Jedrychowski et al 2004). A cohort study in Japan found no association between birth weight adjusted for gestation length and paternal smoking intensity (Matsubara et al 2000).
Low birth weight (not adjusted for gestation length)	Maternal exposure Sufficient	An expert group review concluded that maternal ETS exposure during early pregnancy causes small reductions in average birth weight (World Health Organization 1999). A California birth cohort study of women who did not smoke before or during pregnancy found a borderline association between low birth weight and their ETS exposure intensity at home and work (average hours per day of ETS exposure) since their last menstrual period (Windham et al 2000). A retrospective birth cohort study in the Czech Republic found an inverse dose-response relationship between birth weight and maternal ETS exposure intensity among infants of women who never smoked (the authors did not report a test of statistical significance) (Hruba and Kachlik 2000). A small retrospective cohort study of non-smoking women in Finland found no association between birth weight and maternal hair nicotine levels when both were analyzed as continuous variables; there was a borderline association between birth weight less than 3000g and maternal hair nicotine levels in segments corresponding to 3rd trimester exposure (Jaakkola et al 2001). A review of epidemiologic studies concluded that there is strong evidence for an association between low birth weight and maternal prenatal ETS exposure (Jaakkola and Jaakkola 2002). Another review concluded that the overall evidence suggests that maternal ETS exposure slightly reduces average birth weight (Lindbohm et al 2002). A retrospective cohort study in the Czech Republic found inverse associations between birth weight and maternal ETS exposure; the association occurred among both smoking and

	Paternal smoking (Inadequate)	non-smoking women but was stronger among smoking women; similarly, low birth weight was associated with maternal ETS exposure among infants of both smoking and non-smoking women and the association was stronger for infants of smoking women (Dejmek et al 2002). An expert group convened by the State of California concluded that there is sufficient evidence of a causal inverse association between birth weight and maternal prenatal ETS exposure (California Environmental Protection Agency 2004). A retrospective cohort study of non-smoking mothers in India found no association between low birth weight and maternal ETS exposure at home (Goel et al 2004). In a retrospective birth cohort study in Norway, birth weight was inversely associated with paternal smoking among infants of smoking but not non-smoking mothers (Haug et al 2000).
Birth defects	Inadequate	Two recent reviews, including one by an expert panel convened by the State of California, concluded that there is inadequate epidemiologic evidence for an association between birth defects and maternal ETS exposure (Lindbohm et al 2002, California Environmental Protection Agency 2004). The former review noted that most available studies included paternal smoking in indices of maternal ETS exposure but paternal smoking may act through paternal germ cell mutations.
Sudden infant death syndrome (SIDS)	Postnatal infant exposure Sufficient	A meta-analysis of 39 epidemiologic studies concluded that SIDS is associated with postnatal parental smoking; the pooled odds ratio for the four studies that controlled for prenatal maternal smoking was 1.9 (95% CI 1.6-2.4) (Anderson and Cook 1997, Cook and Strachan 1999). The latter reviews also noted that, among infants of non-smoking mothers, two of the three available studies found associations between SIDS and paternal smoking. An expert group review concluded that prenatal maternal active smoking is a major cause of SIDS and that there is limited evidence that postnatal ETS exposure increases the risk of SIDS (World Health Organization 1999). An expert panel review commissioned by the State of California concluded that there is sufficient evidence of a causal association between SIDS and postnatal ETS exposure, independent of prenatal maternal smoking (California Environmental Protection Agency 2004). A large European case-control study found that SIDS was associated with maternal smoking, especially if mothers shared their bed with their infant; SIDS was also associated with the number of cigarettes smoked daily in the home (Carpenter et al 2004).
Postnatal growth	Prenatal maternal or childhood ETS exposure Inadequate	A longitudinal cohort study in California found no association between height at age 5 years and prenatal ETS exposure of non-smoking mothers (confirmed by serum cotinine levels at 1st prenatal visit) (Eskenazi and Bergmann 1995). An expert panel review commissioned by the State of California concluded that there is inadequate evidence of a causal association between childhood growth in height and prenatal maternal or childhood ETS exposure and noted that this relationship has been much less studied than postnatal growth and prenatal maternal active smoking (California Environmental Protection Agency 2004).
Childhood lung function or lung function growth deficits	Prenatal maternal ETS exposure Inadequate Childhood ETS exposure Limited	A review of epidemiologic studies published up to 2000 concluded that there was inadequate evidence for an inverse association between childhood lung function indices and maternal prenatal ETS exposure (Jaakkola 2002). A meta-analysis of 22 cross-sectional and 6 cohort studies concluded that childhood FEV_1 was inversely associated with indices of childhood ETS exposure; among 19 cross-sectional studies, there was an inverse association between MMEF and childhood ETS exposure (Cook et al 1998). Most of the 10 studies comparing

		parental smoking found a stronger inverse association between FEV_1 and maternal compared to parental smoking and none found a significant association with paternal smoking alone. The authors concluded that maternal smoking is associated with small but statistically significant deficits in FEV_1 and related indices in school-aged children and that this is almost certainly a causal relationship but much of the effect may be due to prenatal maternal smoking. Cross-sectional analysis of baseline data in a large California cohort study found a borderline inverse association among non-asthmatic school-age girls but not boys between indices of bronchial obstruction (FEV_1/FVC, MMEF) and household ETS exposure; among asthmatic children, there was no association between FEV_1/FVC or MMEF and household ETS exposure (Li et al 2000). A more recent report of the California study found no associations between FEV_1/FVC or MMEF and postnatal ETS exposure among asthmatic or non-asthmatic girls or boys (Gilliland et al 2003). A cross-sectional analysis of NHANES III found inverse associations between FEV_1/FVC and MMEF and current serum cotinine levels among children whose mothers did not smoke prenatally but not among those whose mothers did smoke prenatally (Mannino et al 2001). A review of epidemiologic studies published up to 2000 concluded that there was limited evidence for inverse associations between childhood lung function and lung function growth indices and postnatal ETS (Jaakkola 2002). An expert panel review commissioned by the State of California concluded that there is limited evidence of a causal inverse association between childhood growth of lung function indices and childhood ETS exposure (California Environmental Protection Agency 2004).
Incident childhood asthma	Prenatal maternal active smoking Sufficient Postnatal ETS exposure Sufficient	A meta-analysis of studies published up to 1996 showed an association between incident asthma before age 7 years and maternal smoking (Strachan and Cook 1998c). Several recent reviews concluded that incident childhood asthma is associated with postnatal ETS exposure (World Health Organization 1999, Jaakkola and Jaakkola 2002, DiFranza et al 2004, California Environmental Protection Agency 2004). Two of these reviews stated that the association is causal (Jaakkola and Jaakkola 2002, California Environmental Protection Agency 2004). The latter review by an expert panel commissioned by the State of California stated that there is sufficient evidence of a causal association between childhood incident asthma and postnatal ETS exposure and that the evidence is particularly strong for young children and those whose mothers smoked during pregnancy (California Environmental Protection Agency 2004). A large cross-sectional study in China found no association between asthma among school-age children and household ETS exposure (Qian et al 2004). A small UK birth cohort study found associations between wheezing illness by age 3 years and postnatal maternal smoking and current plasma cotinine levels, independent of prenatal maternal smoking (Murray et al 2004). A German cross-sectional study found no association between current or past history of physician-diagnosed asthma and current urinary cotinine levels (Kramer et al 2004).
Asthma severity	Postnatal ETS exposure Sufficient	Several recent reviews concluded that the frequency and severity of symptoms among asthmatic children is associated with postnatal ETS exposure (World Health Organization 1999, Jaakkola and Jaakkola 2002, DiFranza et al 2004, California Environmental Protection Agency 2004). The two expert panel reviews concluded that this association is causal (World Health Organization 1999, California Environmental Protection Agency 2004).
Respiratory symptoms	Postnatal ETS exposure Sufficient	Several recent reviews concluded that childhood respiratory symptoms (cough, wheeze, dyspnea, sputum) are associated with postnatal ETS exposure (World Health Organization 1999, Jaakkola and Jaakkola 2002, DiFranza et al 2004, California Environmental Protection Agency 2004). Three of these reports, including the two expert panel reviews, concluded that this association is causal (World Health Organization 1999, Jaakkola and Jaakkola

		2002, California Environmental Protection Agency 2004).
Lower respiratory tract infections	Postnatal ETS exposure Sufficient	Three recent reviews concluded that postnatal ETS exposure is an important cause of lower respiratory infections during early childhood (World Health Organization 1999, Jaakkola and Jaakkola 2002, California Environmental Protection Agency 2004). A meta-analysis of 13 studies concluded that hospitalization for lower respiratory infections among young children is associated with ETS exposure with a pooled odds ratio of 1.7 (95% CI 1.3-2.2) (Li et al 1999).
Middle ear infections	Postnatal ETS exposure Sufficient	A meta-analysis of 7 studies concluded that recurrent middle ear infections are associated with either parent smoking with a pooled odds ratio of 1.5 (95% CI 1.1-2.0) (Strachan and Cook 1998a). A review of studies published up to 1998 concluded that middle ear disease was associated with parental smoking by either parent with odds ratios of 1.2-1.6; associations were generally stronger among pre-school compared to older children (Cook and Strachan 1999). Three recent reviews, including two by expert panels, concluded that postnatal ETS exposure can cause acute and chronic childhood middle ear infections (World Health Organization 1999, Jaakkola and Jaakkola 2002, California Environmental Protection Agency 2004).
All childhood cancers	Maternal smoking Inadequate	A meta-analysis of epidemiologic studies published up to 1997 found a very weak association between childhood cancers and maternal prenatal smoking (Boffetta et al (2000). An expert group convened by the State of California concluded that there is inadequate evidence of a causal association between childhood cancer and maternal smoking (California Environmental Protection Agency 2004). The California report also noted that ETS contains these known human carcinogens: benzene, 4-aminobiphenyl, 2-naphthylamine, vinyl chloride, arsenic, cadmium, chromium VI, nickel and ^{210}polonium.
	Parental smoking Limited	An expert group concluded that there is limited evidence that parental smoking may increase the risk of some childhood cancers; the relative importance of preconceptual, prenatal and postnatal exposures in explaining such associations are unknown (World Health Organization 1999).
	Paternal smoking Limited	An expert group convened by the State of California concluded that there is limited evidence of a causal association between childhood cancer and paternal smoking (California Environmental Protection Agency 2004).
Leukemia	Maternal smoking Inadequate	A meta-analysis of 12 epidemiologic studies published up to 1997 found no association between childhood leukemia and maternal prenatal smoking (Boffetta et al (2000). A large UK case-control study found no association between childhood leukemia and maternal preconceptual smoking and an *inverse* association with prenatal maternal smoking (Pang et al 2003).
	Paternal smoking Limited	A meta-analysis of 4 epidemiologic studies published up to 1997 found a weak association between childhood acute lymphatic leukemia and paternal smoking (Boffetta et al (2000). A large UK case-control study found no association between childhood leukemia and paternal preconceptual smoking (Pang et al 2003). An expert group convened by the State of California concluded that there is limited evidence of a causal association between childhood leukemia and preconceptual paternal smoking but not with prenatal or childhood ETS exposure (California Environmental Protection Agency 2004).
Lymphoma	Maternal smoking	A meta-analysis of 8 epidemiologic studies published up to 1997 found a very weak association of borderline

	(Inadequate)	statistical significance between childhood lymphoma and maternal prenatal smoking (Boffetta et al (2000). A large UK case-control study found no associations between childhood lymphoma and maternal preconceptual or prenatal smoking (Pang et al 2003).
	Paternal smoking Limited	A meta-analysis of 4 epidemiologic studies published up to 1997 found an association between childhood non-Hodgkin's lymphoma and paternal smoking (Boffetta et al (2000). A large UK case-control study found no association between childhood lymphoma and paternal preconceptual smoking (Pang et al 2003). An expert group convened by the State of California concluded that there is limited evidence of a causal association between childhood lymphomas and paternal smoking, possibly reflecting an association with ETS *per se* and/or with preconceptual paternal smoking (California Environmental Protection Agency 2004).
Brain cancer	Maternal smoking (Inadequate)	A meta-analysis of 4 epidemiologic studies published up to 1997 found no association between childhood brain cancer and maternal prenatal smoking (Boffetta et al (2000). A large UK case-control study found no association between childhood CNS cancers and maternal preconceptual smoking and an *inverse* association with prenatal maternal smoking (Pang et al 2003).
	Childhood ETS exposure Limited	An expert group convened by the State of California concluded that there is limited evidence of a causal association between childhood brain cancer and childhood ETS exposure; however, this association may reflect an effect of preconceptual paternal smoking (California Environmental Protection Agency 2004).
	Paternal smoking Limited	A meta-analysis of 10 epidemiologic studies published up to 1997 found a weak association between childhood brain cancer and paternal smoking (Boffetta et al (2000). A large UK case-control study found no association between childhood CNS cancers and paternal preconceptual smoking (Pang et al 2003). An expert group convened by the State of California concluded that there is limited evidence of a causal association between childhood brain cancer and childhood ETS exposure; it noted, however, that this association may reflect an effect of preconceptual paternal smoking (California Environmental Protection Agency 2004).
Hepatoblastoma	Maternal smoking (Inadequate)	A large UK case-control study found an association between hepatoblastoma and maternal preconceptual smoking (Pang et al 2003).
	Parental smoking (Inadequate)	A large UK case-control study found an association between hepatoblastoma and preconceptual smoking by both parents (Pang et al 2003).
Other childhood cancers	Maternal smoking (Inadequate)	A large UK case-control study found no association between childhood solid tumours other than brain cancer or hepatoblastoma and maternal preconceptual smoking (Pang et al 2003).
	Paternal smoking (Inadequate)	A large UK case-control study found no association between childhood solid tumours other than brain cancer or hepatoblastoma and paternal preconceptual smoking (Pang et al 2003).
Adult breast cancer	Childhood ETS exposure Sufficient	An expert group convened by the State of California concluded that there is sufficient evidence of a causal association between breast cancer and ETS exposure, particularly among premenopausal women and those exposed early in life (California Environmental Protection Agency 2004). The California report also noted that ETS contains these carcinogens known to cause breast cancer in experimental animals: benzene,

		dibenz[a,h]anthracene, 4 dibenzopyrenes, 2 nitrosamines, 8 aliphatic compounds and 3 arylamines/nitroarenes.
Fertility	Transgenerational effects of maternal smoking (Inadequate)	A Danish cohort study of non-smoking men and women found inverse associations between the likelihood of conception (after discontinuing contraception) and a history of either partner's mother smoking during pregnancy (Jensen et al 1998).
	Women exposed to ETS Limited	A review of epidemiologic studies concluded that there was inadequate evidence of an association between likelihood of conception and paternal smoking or maternal ETS exposure (Lindbohm et al 2002). A longitudinal cohort study found associations between delayed conception and ETS exposure among both women who did or did not smoke (Hull et al 2002). An expert panel review commissioned by the State of California concluded that there is limited evidence of a causal association between reduced female fertility and ETS exposure (California Environmental Protection Agency 2004). A cohort study of newly married, nonsmoking, female textile workers in China found no association between likelihood of conception and their husband's smoking intensity (Venners et al 2004).
	Men exposed to ETS Inadequate	An expert panel review commissioned by the State of California concluded that there is inadequate evidence of a causal association between reduced male fertility and ETS exposure (California Environmental Protection Agency 2004).
Cognitive function	Parental active smoking Sufficient	An expert group review concluded that childhood learning difficulties, behavioural problems and language impairment are associated with maternal and paternal active smoking (World Health Organization 1999).
	Childhood ETS exposure Limited	An expert panel review commissioned by the State of California concluded that there is limited evidence of a causal inverse association between childhood cognitive function and postnatal ETS exposure; the panel noted that this relationship has been much less studied than prenatal maternal active smoking and that smoking mothers tend to smoke both during and after pregnancy – thus associations with postnatal maternal smoking may partially reflect the impact of prenatal maternal smoking (California Environmental Protection Agency 2004).
Problem behaviours, learning difficulties	Parental active smoking Sufficient	An expert group review concluded that childhood learning difficulties, behavioural problems and language impairment are associated with maternal and paternal active smoking (World Health Organization 1999).
	Prenatal maternal ETS exposure Inadequate	The WHO concluded that there is inadequate evidence for associations between childhood learning difficulties, behavioural problems and language impairment and maternal prenatal ETS exposure (World Health Organization 1999).
	Childhood ETS exposure Limited	The WHO concluded that there is inadequate evidence for associations between childhood learning difficulties, behavioural problems and language impairment and childhood ETS exposure (World Health Organization 1999). An expert panel review commissioned by the State of California concluded that there is limited evidence of a causal association between childhood problem behaviours and childhood ETS exposure (California Environmental Protection Agency 2004).
Allergic sensitization	Maternal smoking	A literature review of studies published up to 1997 concluded that there was inadequate evidence for an

	(Inadequate) Childhood ETS exposure (Inadequate)	association between neonatal or childhood serum IgE levels and maternal smoking or between skin prick positivity and perinatal parental smoking or current ETS exposure (Strachan and Cook 1998b).
Eczema	Parental smoking Inadequate	A literature review of studies published up to 1997 concluded that there was inadequate evidence for an association between allergic rhinitis or eczema and parental smoking (Strachan and Cook 1998b). A German cross-sectional study found no association between eczema among children age 5-14 years and childhood ETS exposure (Schafer et al 1999). However, a more recent German cross-sectional study did find an association between eczema at age six years and urinary cotinine levels (Kramer et al 2004).
Sickle cell anemia severity	Childhood ETS exposure (Inadequate)	A retrospective cohort study in California found an association between hospitalization of children age 2-18 years for sickle cell anemia and ETS exposure (West et al 2003).
Dental caries	Childhood ETS exposure (Limited)	A large cross-sectional study of US children age 4-11 years found a dose-response relationship between the presence of at least one decayed deciduous tooth and serum cotinine levels (Aligne et al 2003). A cohort study of children age 4-7 years in Iowa also found an association between one or more dental caries or fillings and ETS exposure at home (Shenkin et al 2004).

2. Fetal death

Reference, location	Design	Exposure	Results	Association[b]	DR[c]	Covariates
(Ahlborg and Bodin 1991), Orebro County, Sweden	Cohort study, 4687 women recruited at 1st prenatal visit, 1980-1983, including 678 nonsmokers who reported ETS exposure; pregnancy outcomes based on hospital records, 118 early (1st trimester) and 140 late (2nd or 3rd trimester) fetal deaths	Self-reported ETS exposure at home or work during period just before conception (assumed to reflect exposure during early pregnancy also)	Early fetal death associated with maternal ETS exposure at work but not at home (relative risks, exposed vs not exposed)	work ETS 2.2 (1.2-3.8) home ETS 1.0 (0.5-1.9)		Maternal age, previous spontaneous abortion, education, planning of pregnancy, alcohol, gestation wk at recruitment
			Late fetal death not associated with maternal ETS exposure at work or home (relative risks, exposed vs not exposed)	work ETS 1.2 (0.6-2.4) home ETS 1.1 (0.6-2.1)		
(Windham et al. 1992), Santa Clara County, California	Case-control study, 626 cases early fetal death (gestation wk <20), 1300 population-based live birth controls, 1986-1987; cases identified using pathology reports from 11 hospitals	Self-reported prenatal exposures up to gestation wk 20; ETS exposure defined as 1+ hr/d in a room at home or work where someone else was smoking	Early fetal death not associated with paternal smoking after adjustment for maternal smoking (odds ratios, 1-10, 11-20 and >20 vs 0 cigs /d)	0.9 (0.6-1.3) 1.1 (0.7-1.5) 1.0 (0.6-1.5)		Maternal age, race, caffeine, alcohol, bottled water, smoking, previous fetal loss, marital status, insurance coverage, paternal age, race, education, alcohol
			Early fetal death associated with maternal ETS exposure at home or work (odds ratio by maternal smoking status, exposed vs not exposed to ETS)	all women 1.5 (1.2-1.9) nonsmokers 1.6 (1.2-2.1)		Maternal age, race, education, marital status, previous fetal loss, smoking, alcohol, caffeine, bottled water use, employment, insurance coverage, nausea, time to interview
(Chatenoud et al.	Hospital-based case-control study,	Mother-reported	Early fetal deaths not	preconceptual		Study centre, maternal

[b] Entries in this column include odds ratios, relative risks and certain other statistical measures of association as published in original epidemiologic studies; an entry of '+' means the measure of association was not an odds ratio or relative risk and was statistically significant at the 0.05 level; an entry of '(+)' means the association was almost statistically significant.

[c] 'DR' refers to a dose-response relationship in an epidemiologic study; an entry of '+' means the measure of dose-response relationship used in the citation was statistically significant at the 0.05 level; an entry of '(+)' means the association was almost statistically significant.

1998), Milano, Italy	782 cases early fetal death (gestation length ⩽12 wk), 1543 healthy infant control mothers	smoking habits of self and partner	associated with paternal preconceptual or 1st trimester smoking (odds ratios, >10 vs 0 cigs/d)	0.9 (0.7-1.1) 1st trimester 0.9 (0.7-1.1)	age, education, marital status, family and personal history of early fetal death, nausea, alcohol, coffee, 1st trimester smoking
(Windham et al. 1999), California	Prospective cohort study, 5144 women recruited at 1st prenatal visit no later than gestation wk 12, 1990-1991; pregnancy outcomes based on hospital and medical records, 499 early fetal deaths (gestational ages up to 20 wk), 32 late fetal deaths; limited analyses of ETS exposure to 4209 non-smoking women	Self-reported maternal smoking and ETS exposure; estimated avg hr/d exposed to ETS at home and work since last menstrual period	Borderline association between early fetal death and ETS exposure at home but not at work (odds ratios)	Home 1.2 (0.9-1.6) Work 0.9 (0.7-1.2)	Maternal age, previous early fetal loss, alcohol, caffeine, gestational age at interview
			Early fetal death associated with ETS exposure at home or work among women who consumed over 300 mg of caffeine/d (odds ratios)	⩽300 mg caffeine/d 0.9 (0.7-1.2) >300 mg caffeine/d 3.4 (1.7-7.0)	Maternal age, alcohol use
			Borderline association between early fetal death and ETS exposure at home or work among women who consumed over 3 alcohol drinks/wk (odds ratios)	⩽3 alcohol dr/wk 1.0 (0.8-1.2) >3 alcohol dr/wk 2.9 (0.7-12)	Maternal age, caffeine use
			Early fetal death not associated with paternal smoking intensity during 3 mos before conception (odds ratios relative to 0 cigs/d)	⩽20 cigs/d 1.0 (0.7-1.3) >20 cigs/d 1.0 (0.4-2.3)	Maternal age, previous fetal loss, alcohol, caffeine, gestational age at interview
(Lindbohm et al. 2002), Finland	Review of epidemiologic studies on developmental and reproductive		Limited evidence of an association between early		

	effects of preconceptual and prenatal ETS exposure; included 3 studies of ETS and early fetal death		fetal death and maternal ETS exposure		
(Venners et al. 2004), China	Prospective cohort study, 526 newly married, nonsmoking, female textile workers, 1996-1998; women who stopped contraception were monitored for conception and early pregnancy losses using daily urine hCG tests; pregnant women followed to detect clinical spontaneous abortions	Self-reported paternal smoking habits	Early fetal death associated with paternal smoking intensity (odds ratios relative to not current smokers)	<20 cigs/d 1.0 (0.7-1.6) ⩾20 cigs/d 1.8 (1.0-3.3)	Maternal and paternal age, education, perceived life stress, dust and noise exposure, paternal alcohol, previous smoking, exposure to toxic chemicals, maternal BMI and tea intake
			Borderline association between early fetal deaths and clinical spontaneous abortions combined and paternal smoking intensity (odds ratios relative to not current smokers)	<20 cigs/d 1.0 (0.7-1.5) ⩾20 cigs/d 1.5 (0.8-2.6)	As above
(Kharrazi et al. 2004), California	Retrospective cohort study, 2777 mother-live birth and 19 woman-fetal death pairs, enrolled in prenatal screening program during 1992, non-smokers (serum cotinine levels ≤10 ng/mL at gestation week 15-19 wk); record linkage to live birth and fetal death records	Maternal prenatal serum cotinine levels (5^{th} and 1^{st} quintile ranges were 0.236-10 and <0.026 ng/mL); self-reported tobacco smoke exposure from a subgroup	Borderline association between late fetal deaths and maternal serum cotinine levels during early pregnancy (odds ratio, 5^{th} vs 1^{st} quintile)	3.4 (0.8-14)	Maternal ethnicity, age, parity, prenatal care payment source, infant sex
			Borderline association between late fetal deaths and maternal serum cotinine levels during early pregnancy (odds ratio per unit increment of log maternal serum cotinine)	1.6 (0.8-3.2)	As above
(California Environmental Protection Agency 2004), California	Updated review of health outcomes related to environmental tobacco smoke exposure; expert group used a weight of evidence approach, considering the number and quality of epidemiologic studies and evidence of		Concluded that there is limited evidence of a causal association between early fetal death and maternal prenatal ETS exposure; noted that interpretation is		

	biologic plausibility	complicated by the role of paternal smoking

Fetal death: summary

Early fetal deaths (spontaneous abortion)

Maternal exposure A Swedish cohort study found an association between early fetal death and maternal ETS exposure at work but not at home (Ahlborg and Bodin 1991). A case-control study in California found an association between early fetal death among non-smoking women and ETS exposure before gestation week 20 at home or work (Windham et al 1992). A recent California cohort study of non-smoking women enrolled during early pregnancy found a borderline association between early fetal death and maternal ETS exposure at home but not at work; there were relatively strong associations with ETS exposure at home or work among subgroups of women with relatively high intakes of caffeine or alcohol (Windham et al 1999). A literature review concluded that the three available epidemiologic studies provided limited evidence of an association between early fetal death and maternal ETS exposure (Lindbohm et al 2002). An expert panel review concluded that there is limited evidence of a causal association between early fetal death and maternal prenatal ETS exposure but there is uncertainty concerning mechanisms of paternal smoking (e.g., preconceptual germ cell mutations among active male smokers) (California Environmental Protection Agency 2004).

Paternal exposure A case-control study in California found no association between early fetal death and paternal smoking after adjustment for maternal smoking (Windham et al 1992). A large hospital-based case-control study in Italy found no association between early fetal death and paternal preconceptual or 1st trimester smoking (Chatenoud et al 1998). A recent California cohort study of non-smoking women enrolled during early pregnancy found no association between early fetal death and paternal smoking intensity during the 3 months before conception (Windham et al 1999). A cohort study of nonsmoking women in China found an association between early fetal death and paternal smoking of 20 or more cigarettes daily; this study monitored women for conception using daily urine hCG tests (Venners et al 2004).

Late fetal deaths (stillbirths)

Maternal exposure A Swedish cohort study found no association between late fetal death and maternal ETS exposure at work or at home (Ahlborg and Bodin 1991). A retrospective cohort study in California found a statistically non-significant association between late fetal deaths and maternal serum cotinine levels during early pregnancy (Kharrazi et al 2004).

3. Preterm birth, birth weight deficits

Reference, location	Design	Exposure	Results	Association[d]	DR[e]	Covariates
(World Health Organization 1999), Geneva	Expert group review of the effects of ETS on child health		Maternal ETS exposure during early pregnancy causes small reductions in avg birth weight			
(Windham et al. 2000), California	Birth cohort study, 4103 singleton live births to women recruited at 1st prenatal visit no later than gestation wk 12, 1990-1991; pregnancy outcomes based on hospital and medical records	Self-reported maternal smoking and ETS exposure; estimated avg hr/d exposed to ETS at home and work since last menstrual period; based analyses of ETS exposure women who did not smoke before or during pregnancy	Birth weight not associated with ETS exposure (avg difference, 1-6 and ⩾7 vs 0 hr/d ETS exposure)	1-6 hr/d +0.7 g (-47, 48) ⩾7 hr/d +8.2 g (-86, 103)		Maternal age, race, BMI, pregnancy history, education, marital status, life events, caffeine, alcohol
			Borderline association between low birth weight (<2500 g) and maternal ETS exposure (odds ratio, ⩾7 vs 0 hr/d ETS exposure)	1.8 (0.8-4.1)		Race, BMI, pregnancy history, education, life events
			SGA not associated with maternal ETS exposure (odds ratio, ⩾7 vs 0 hr/d ETS exposure)	0.6 (0.3-1.5)		As above
			Borderline or significant associations between preterm and very preterm birth and maternal ETS exposure (odds ratios, ⩾7 vs 0 hr/d ETS exposure)	<37 wk 1.6 (0.9-2.9) <35 wk 2.4 (1.0-5.3)		As above
			Associations between preterm and very preterm birth and	age <30 yr 1.1 (0.5-2.6)		As above

[d] Entries in this column include odds ratios, relative risks and certain other statistical measures of association as published in original epidemiologic studies; an entry of '+' means the measure of association was not an odds ratio or relative risk and was statistically significant at the 0.05 level; an entry of '(+)' means the association was almost statistically significant.

[e] 'DR' refers to a dose-response relationship in an epidemiologic study; an entry of '+' means the measure of dose-response relationship used in the citation was statistically significant at the 0.05 level; an entry of '(+)' means the association was almost statistically significant.

			maternal ETS exposure among older but not younger mothers (odds ratios for preterm birth shown, ⩾7 vs 0 hr/d ETS exposure)	age ⩾30 yr 2.8 (1.2-6.6)	
(Matsubara et al. 2000), Nagoya, Japan	Population-based birth cohort study, 7411 mother-singleton infant pairs, recruited during prenatal visits during 1989-1991; assessment of ETS and birth weight limited to non-smoking women	Self-reported maternal smoking and ETS exposure including husband's smoking status and maternal hr/wk ETS exposure at work, home or elsewhere	Borderline inverse association between gestation length and paternal smoking intensity during pregnancy (avg gestation length, 0, 1-10, 11-20 and 21+ cigs/day)	39.0, 39.1, 39.0, 38.8 wk (p-trend=0.07)	Maternal age, height, BMI, education, working status, alcohol intake, parity, infant sex
			Gestation length not associated with maternal ETS exposure intensity (avg gestation length, 0, <2 and 2+ hr/wk)	39.0, 39.1, 39.0 wk (p-trend=0.99)	As above
			Birth weight adjusted for gestation length not associated with paternal smoking intensity (avg birth weight, 0, 1-10, 11-20 and 21+ cigs/day)	3104, 3098, 3098, 3082 g (p-trend=0.21)	As above plus gestation length
			Birth weight adjusted for gestation length not associated with maternal ETS exposure intensity (avg gestation length, 0, <2 and 2+ hr/wk)	3108, 3082, 3101 g (p-trend=0.38)	As above
(Haug et al. 2000), Norway	Retrospective cohort study, 22883 live births with birth weight ≥2500g and no birth defects, 1970-1991;	Self-reported parental smoking during pregnancy	Among infants of non-smoking women, birth weight not associated with paternal smoking (avg difference in birth weight)	-1g (-17, 15)	Maternal age
			Among infants of smoking women, birth weight inversely associated with paternal smoking (avg difference in birth weight)	-48g p<0.01)	Maternal age
(Hruba and	Retrospective cohort study,	Self-reported smoking and	Birth weight reduced among	-88 g	

Kachlik 2000), Czech Republic	1147 mothers recruited after delivery, 727 never-smokers, 320 former smokers, 50 current smokers; limited statistical analysis	ETS exposure; ever-smokers were 3-fold more likely (52%) to report ETS exposure compared to never-smokers (17%)	ETS-exposed never-smokers (avg birth wt difference, exposure at home or work vs no ETS exposure)			
			Greater birth weight deficit among never-smoker women exposed to ETS both at home and work (avg birth weight difference, exposure at home and work vs no ETS exposure)	-189 g		
			Term low birth weight not associated with maternal ETS exposure (relative risk, exposed vs not exposed; calculated from data in paper)	1.4 (0.6-3.2)		
(Jaakkola et al. 2001), Finland	Retrospective cohort study, 389 non-smoking women; self-reported exposure information	Measured nicotine levels in maternal hair segment (collected after delivery) corresponding to 3rd trimester exposure; mean hair nicotine levels for ETS-unexposed women and those exposed at home, work or both, respectively, were 0.9, 2.9, 2.1 and 4.3 µg/g	Birth weight not associated with maternal hair nicotine when analyzed as continuous variables; change in birth weight (g) per µg/g hair nicotine	-0.9g (CI -20, 18)		Sex, birth order, maternal age, BMI before pregnancy, marital status, parental education, prenatal alcohol, prenatal employment
			Birth weight <3000g not associated with maternal hair nicotine categories; odds ratios for 0.75-3.99 and ⩾4.0 vs <0.75 µg/g	1.3 (0.6-2.6) 1.6 (0.6-4.4)		As above
			Borderline association between birth weight <3000g and maternal hair nicotine analyzed as a continuous variable; odds ratio per µg/g	1.1 (1.0- 1.2)	(+)	As above
			IUGR not associated with maternal hair nicotine categories; odds ratios for 0.75-	1.1 (0.4-2.5) 1.2 (0.3-4.2)		As above

		3.99 and ⩾4.0 vs <0.75 µg/g			
		No association between IUGR and maternal hair nicotine analyzed as a continuous variable; odds ratio per µg/g	1.0 (0.9-1.2)		As above
		Dose-response relationship between preterm delivery and maternal hair nicotine levels (odds ratios for 0.75-3.99 and ⩾4.0 vs <0.75 µg/g)	1.3 (0.3-5.6) 6.1 (1.3-29)		As above
		Preterm delivery associated with maternal hair nicotine when analyzed as a continuous variable; odds ratio per µg/g	1.2 (1.1-1.4)	+	As above
		Inverse nonlinear dose-response relationship between birth weight at term (⩾37 wk) and 3rd trimester urinary cotinine level with a steeper slope at lower smoking intensities; percent of variance attributable to cigarettes/day	4.0%		As above
(Jaakkola and Jaakkola 2002), Finland	Review of literature on effects of ETS on the respiratory health of children, included reports published during 1966 to October 2000	The authors concluded that there is strong evidence for an association between low birth weight and maternal prenatal ETS exposure			
		The authors concluded that there is strong evidence for an association between preterm birth and maternal prenatal ETS exposure			
(Lindbohm et al. 2002), Finland	Review of epidemiologic studies on developmental and reproductive effects of	Limited evidence of an association between preterm birth and maternal ETS			

	preconceptual and prenatal ETS exposure; included 6 studies of ETS and preterm birth and 2 meta-analyses and subsequent reports representing about 30 studies of ETS and birth weight		exposure Noted that meta-analyses by Windham et al (1999) and Peacock et al (1998) found avg birth weight decrements of 25-30g among infants of ETS-exposed women; concluded that overall evidence suggests that maternal ETS exposure slightly reduces average birth weight Limited evidence of associations between low birth weight and small for gestational age and maternal ETS exposure		
(Ha et al. 2002), Beijing, China	Retrospective cohort study, 1,222 non-smoking female employees of a large petrochemical industry who had a singleton live birth infant with no major birth defects during 1996-1998; assessed birth weight	Self-reported maternal ETS exposure	Non-significant inverse association between birth weight and maternal ETS exposure (birth weight deficit, exposed vs unexposed mothers)	-37g (-83, 8) p=0.11	Gestation length, infant sex, maternal prepregnancy BMI, age, paternal height, education
(Dejmek et al. 2002), Czech Republic	Retrospective cohort study, 6866 singleton live births, 1994-1999; assessed birth weight	Self-reported smoking and ETS exposure	Birth weight inversely associated with cigs/day; birth weight decrements for 1-10 and >10 cigs/day in 3rd trimester compared to non-smokers	-130g (-95, -166) -239g (-154, -323)	Maternal age, ethnicity, height, education, parity, prepregnancy weight, alcohol, paternal education, infant sex, district, season
			Birth weight inversely associated with ETS exposure among non-smokers and smokers; birth weight	non-smokers -53g (-24, -82) smokers	As above

			decrements, ETS vs no ETS exposure	-119g (-48, -190)	
			Birth weight <2500g associated with ETS exposure; odds ratios, exposed vs unexposed	non-smokers 1.4 (1.0-2.0) smokers, 1-10 cigs/day 2.4 (1.8-3.7) smokers, >10 cigs/day 2.6 (1.4-4.8)	As above
			IUGR associated with ETS exposure; odds ratios, exposed vs unexposed	non-smokers 1.2 (1.0-1.5) smokers, 1-10 cigs/day 2.1 (1.7-2.7) smokers, >10 cigs/day 3.4 (2.2-5.4)	As above
(Dejin-Karlsson and Ostergren 2003), Malmo, Sweden	Prospective cohort study, 747 nulliparous women recruited at 1st prenatal visit, 1991-1992; 2 prenatal ultrasound examinations, pregnancy outcomes identified in perinatal database	Self-reported maternal smoking and ETS exposure at home or work	Small for gestational age associated with maternal ETS exposure (odds ratio, exposed vs unexposed, exposure status confirmed at two visits)	4.8 (1.5-16)	Maternal age, height, country of birth, education, smoking
			Small for gestational age associated with maternal ETS exposure during early but not late pregnancy (odds ratios, exposed vs unexposed, adjusted for exposure during other pregnancy time period)	exposed in early preg 2.6 (1.0-6.9) exposed in late preg 1.3 (0.6-2.5)	As above plus ETS exposure during early or late pregnancy
(Hong et al. 2003), Korea	Retrospective cohort study, 266 non-smokers; self-reported ETS and other	Measured cotinine in urine samples collected at delivery; ETS exposure defined as	Birth weight at term not associated with ETS exposure as binary variable; mean birth	2993 vs 3069 g (p=0.38)	Maternal dietary habits, alcohol, occupation, residential area, infant

	exposures; used PCR to analyze glutathione-*S*-transferase (GST) polymorphisms – GSTM1, GSTT1 (involved in metabolism of tobacco smoke toxicants)	urinary cotinine ⩾120 µg/g creatinine	weights in exposed vs unexposed as defined by urinary cotinine at delivery		sex, gestational age
			Birth weight at term reduced among subgroup of women with GSTT1 null genotype; mean birth weights in exposed vs unexposed as defined by urinary cotinine at delivery	2864 vs 3100g (p=0.04)	As above
			Non-significant deficit in birth weight at term among subgroup of women with GSTM1 null genotype; mean birth weights in exposed vs unexposed as defined by urinary cotinine at delivery	2966 vs 3124g (p=0.16)	As above
(Pichini et al. 2003), Spain	Retrospective cohort study, 150 mother-infant pairs; birth weight and other information from birth records, self-reported smoking habits, ETS exposure	Measured nicotine in maternal and neonatal hair segments	Birth weight inversely associated with nicotine levels in maternal hair segments corresponding to the gestation period; avg decrements in moderate or high compared to low exposure categories	-75g (NS) -247g (p<0.05)	Gestation length
			Head circumference at birth inversely associated with nicotine levels in maternal hair segments corresponding to the gestation period; avg decrements in moderate or high compared to low exposure groups	-0.2 cm (NS) -0.8 cm (p<0.05)	Sex, gestation length
(California Environmental Protection Agency 2004),	Updated review of health outcomes related to environmental tobacco smoke exposure; expert group used a		Concluded that there is sufficient evidence of a causal inverse association between birth weight and maternal		

California	weight of evidence approach, considering the number and quality of epidemiologic studies and evidence of biologic plausibility		prenatal ETS exposure Concluded that there is sufficient evidence of a causal association between low birth weight and maternal prenatal ETS exposure Concluded that there is limited evidence of a causal association between intrauterine growth retardation and maternal prenatal ETS exposure Concluded that there is limited evidence of a causal association between preterm birth and maternal prenatal ETS exposure			
(DiFranza et al. 2004), USA	Review of literature on child health and prenatal and postnatal ETS exposure		There is an inverse dose-response between birth weight and prenatal maternal smoking, independent of gestation length Head circumference at birth is inversely associated with maternal smoking; association not observed among women who quit smoking before gestation wk 32			
(Hanke et al. 2004), Poland	Birth cohort study, 183 mother-infant pairs; ultrasound measurements of head and abdominal circumference and femur length at gestation wk 20-24 and at birth	Measured maternal serum cotinine at gestation wk 20-24; serum cotinine levels <10 ng/ml are associated with ETS exposure and higher levels with active smoking; 66% were active smokers, 24% passive smokers and	Inverse dose-response relationships between birth weight (g) and head circumference at gestation wk 20-24 and the log of maternal serum cotinine (ng/ml) at gestation wk 20-24; coefficients from multiple	birth weight -70±24g (p=0.004) head circumference -0.50±0.18cm (p=0.005)	+ +	Gestation length, sex, maternal pre-pregnancy weight

		10% were not exposed to tobacco smoke	variable linear regression analysis			
			Borderline inverse dose-response relationships between birth weight (g) and head circumference at gestation wk 20-24 and the log of maternal serum cotinine (ng/ml) at gestation wk 20-24 among the 139 women with serum cotinine levels below 10 ng/ml; coefficients from multiple variable linear regression analysis	birth weight -100±60g (p=0.09) head circumference -0.17±0.09cm (p=0.06)	(+) (+)	As above
(Perera et al. 2004), New York	Birth cohort study, 214 mother-infant pairs, Dominican and African American women, non-smokers	Personal air monitoring during 3rd trimester; maternal and cord plasma samples at delivery analyzed for cotinine (detected in about 50% of maternal and cord blood samples) and benzo[a]pyrene DNA adducts (detected in about 40% of maternal and cord blood samples)	Birth weight not associated with household ETS exposure, maternal or cord plasma cotinine, or cord blood BaP-DNA adduct levels; respective multiple linear regression coefficients for log transformed birth outcomes	ETS β=-0.02, p=0.28 plasma cotinine β=-0.02, p=0.42 BaP-DNA β=-0.01, p=0.52		Ethnicity, sex, maternal BMI, dietary PAH (frequency of eating fried, broiled, or barbequed foods during previous 2 wk), gestational age; also included cesarean section for analyses of head circumference
			Head circumference at birth inversely associated with household ETS exposure but not with maternal or cord plasma cotinine or cord blood BaP-DNA adduct levels; respective multiple linear regression coefficients for log transformed birth outcomes	ETS β=-0.01, p=0.04 plasma cotinine β=-0.001, p=0.85 BaP-DNA β=-0.006, p=0.39	+	As above
			Birth weight and head	birth weight	+	As above

			circumference at birth inversely associated with interaction between BaP-DNA adducts and household ETS exposure; respective multiple linear regression coefficients for log transformed birth outcomes Authors concluded that the effect of ETS on intrauterine growth is mediated by non-PAH components and that BaP DNA adducts may reflect individual susceptibility and PAH exposure from non-ETS sources	-0.088, p=0.05 head circumference -0.032, p=0.01	+ +	
(Goel et al. 2004), India	Retrospective cohort study, 576 non-smoking mothers with singleton live births	Self-reported ETS exposure at home; prevalence was 24%	Preterm birth (<37 wk) not associated with self-reported ETS exposure among non-smoking women; odds ratio	1.2 (0.7-1.9)		Maternal age, education, occupation, birth order, parity, anemia
			Birth weight <2500g not associated with self-reported ETS exposure among non-smoking women; odds ratio	1.0 (0.7-1.7)		As above
			IUGR associated with self-reported ETS exposure among non-smoking women; odds ratio	2.1 (1.3-3.5)		As above
(Kharrazi et al. 2004), California	Retrospective cohort study, 2777 mother-live birth and 19 woman-fetal death pairs, enrolled in prenatal screening program during 1992, non-smokers (serum cotinine levels ≤10 ng/mL at gestation week 15-19 wk); record linkage to live birth and fetal death records	Maternal prenatal serum cotinine levels (5^{th} and 1^{st} quintile ranges were 0.236-10 and <0.026 ng/mL); self-reported tobacco smoke exposure from a subgroup	Preterm delivery associated with maternal serum cotinine levels during early pregnancy (odds ratio, 5^{th} vs 1^{st} quintile)	1.8 (1.0-3.1)		Maternal ethnicity, age, parity, prenatal care payment source, infant sex
			Borderline association between	1.8 (0.7-4.8)		As above

			term low birth weight and maternal serum cotinine levels during early pregnancy (odds ratio, 5th vs 1st quintile)		
			Borderline inverse association between birth weight (adjusted for gestation length) and maternal serum cotinine levels during early pregnancy (difference, 1st minus 5th quintile)	-40g (-96, 16)	As above plus gestation length
			Inverse association between birth weight (adjusted for gestation length) and maternal serum cotinine levels during early pregnancy when analyzed as continuous variables (β-coefficient)	β=-27g (-54, -0.6) R^2=0.29	As above
(Jedrychowski et al. 2004), New York City, USA and Krakow, Poland	Cohort study, 362 nonsmoking women who gave birth at gestation wk 34-43 during 2001-2003;	Self-reported maternal prenatal ETS exposure and personal $PM_{2.5}$ levels during 2nd trimester; note: indoor $PM_{2.5}$ levels strongly correlated with ETS	Birth weight associated with maternal prenatal $PM_{2.5}$ but not ETS exposure (β-coefficients)	$PM_{2.5}$ -201g (-386, -16) ETS 32g (-92, 156)	Maternal education, gravidity, height, prepregnancy wt, gestation length, infant sex, season, log $PM_{2.5}$
			Birth length not associated with maternal prenatal $PM_{2.5}$ but not ETS exposure (β-coefficients)	$PM_{2.5}$ -1.4cm (-2.6, -0.3) ETS -0.2cm (-1.0, 0.5)	As above
			Head circumference not associated with maternal prenatal $PM_{2.5}$ but not ETS exposure (β-coefficients)	$PM_{2.5}$ -0.7cm (-1.3, -0.1) ETS 0.2cm (-0.3, 0.6)	As above

Preterm birth, birth weight deficits: summary

Gestation length

Maternal exposure A California birth cohort study of women who did not smoke before or during pregnancy found an association between very preterm birth (gestation length < 35 weeks) and average ETS exposure of 7 hours or more per day at home and work since their last menstrual period; the associations between preterm (gestation length < 37 weeks) and very preterm births occurred mainly among women age 30 years or older (Windham et al 2000). A cohort study in Japan found no association between gestation length and maternal ETS exposure at home and work (hours per week) during pregnancy (Matsubara et al 2000). A small retrospective cohort study of non-smoking women in Finland found a dose-response relationship between preterm birth and maternal hair nicotine levels in segments corresponding to 3rd trimester exposure (Jaakkola et al 2001). A review of epidemiologic studies concluded that there is strong evidence for an association between preterm birth and maternal prenatal ETS exposure (Jaakkola and Jaakkola 2002). Another review concluded that there is limited evidence of an association between preterm birth and maternal ETS exposure (Lindbohm et al 2002). An expert group convened by the State of California concluded that there is limited evidence for an association between preterm birth and maternal prenatal ETS exposure (California Environmental Protection Agency 2004). A retrospective cohort study of non-smoking mothers in India found no association between preterm birth and maternal ETS exposure at home (Goel et al 2004). However, a large retrospective cohort study of non-smoking mothers in California (confirmed by low serum cotinine levels at gestation week 15-19) found an association between preterm birth and 2nd trimester maternal serum cotinine levels (Goel et al 2004).

Paternal smoking A cohort study in Japan found a borderline inverse association between gestation length and paternal smoking intensity during pregnancy (Matsubara et al 2000).

Birth weight low for gestational age

Maternal exposure A California birth cohort study of women who did not smoke before or during pregnancy found no association between birth weight low for gestational age and average ETS exposure of 7 hours or more per day at home and work since their last menstrual period (Windham et al 2000). A cohort study in Japan found no association between birth weight adjusted for gestation length and maternal ETS exposure at home and work (hours per week) during pregnancy (Matsubara et al 2000). A retrospective birth cohort study in the Czech Republic found no association between term low birth weight and maternal ETS exposure (Hruba and Kachlik 2000). A small retrospective cohort study of non-smoking women in Finland found no association between IUGR and maternal hair nicotine levels in segments corresponding to 3rd trimester exposure (Jaakkola et al 2001). A literature review concluded that there is limited evidence of an association between birth weight low for gestational age and maternal ETS exposure (Lindbohm et al 2002). A retrospective cohort study in China found a borderline inverse association between birth weight and maternal ETS exposure among infants of non-smoking women (Ha et al 2002). A retrospective cohort study in the Czech Republic found associations between IUGR and maternal ETS exposure among infants of both smoking and non-smoking women; the association was stronger among infants of smoking women (Dejmek et al 2002). A prospective cohort study in Sweden found a strong association between birth weight low for gestational age and maternal ETS exposure at home or work; the association occurred among infants of women exposed during early pregnancy but not among those exposed during late pregnancy (after adjustment for exposure during the other time period) (Dejin-Karlsson and Ostergren 2003). A small retrospective cohort study of non-smoking women in Korea found an inverse association between birth weight at term and maternal urinary cotinine levels at delivery among infants of women with the GSTT1 null genotype but not among the whole cohort (Hong et al 2003). A small retrospective cohort study in Spain found inverse associations between birth weight and head circumference (adjusted for gestation length) and maternal hair nicotine levels in segments corresponding to the gestation period (Pichini et al 2003). An expert group convened by the State of California concluded that there is sufficient evidence of causal associations between maternal prenatal ETS exposure and reduced birth weight, including birth weights below 2500g; they found limited evidence for an association between IUGR and maternal prenatal ETS exposure (California Environmental Protection Agency 2004). A literature review concluded that there is an inverse dose-response between birth weight and prenatal maternal smoking, independent of gestation length (DiFranza et al 2004). A small cohort study in Poland found a borderline inverse association between birth weight adjusted for gestation length and maternal serum cotinine levels at gestation week 20-24 among infants of non-smoking mothers (Hanke et al 2004). A small cohort study of non-smoking Dominican and African American women in New York City found no association between birth weight and self-reported household ETS exposure, maternal or cord plasma cotinine or cord blood BaP-DNA adduct levels; there was an inverse association between head circumference at birth and self-reported household ETS exposure but not with maternal or cord plasma cotinine or cord blood BaP-DNA adduct levels (Perera et al 2004). A retrospective cohort study of non-smoking mothers in India found an association between IUGR and maternal ETS exposure at home (Goel et al

2004). A large retrospective cohort study of non-smoking mothers in California (confirmed by low serum cotinine levels at gestation week 15-19) found borderline associations between term low birth weight and birth weight adjusted for gestation length and maternal 2nd trimester serum cotinine levels; the inverse association between birth weight and maternal serum cotinine levels was statistically significant when they were analyzed as continuous variables (Goel et al 2004). A small cohort study of non-smoking women in New York City and Krakow (Poland) found an inverse association between birth weight adjusted for gestation length and maternal 2nd trimester personal $PM_{2.5}$ levels (note: indoor $PM_{2.5}$ levels are strongly correlated with ETS) but not with but not self-reported ETS exposure (Jedrychowski et al 2004).

Paternal smoking A cohort study in Japan found no association between birth weight adjusted for gestation length and paternal smoking intensity (Matsubara et al 2000).

Low birth weight (not adjusted for gestation length)

Maternal exposure An expert group review concluded that maternal ETS exposure during early pregnancy causes small reductions in average birth weight (World Health Organization 1999). A California birth cohort study of women who did not smoke before or during pregnancy found a borderline association between low birth weight and their ETS exposure intensity at home and work (average hours per day of ETS exposure) since their last menstrual period (Windham et al 2000). A retrospective birth cohort study in the Czech Republic found an inverse dose-response relationship between birth weight and maternal ETS exposure intensity among infants of women who never smoked (the authors did not report a test of statistical significance) (Hruba and Kachlik 2000). A small retrospective cohort study of non-smoking women in Finland found no association between birth weight and maternal hair nicotine levels when both were analyzed as continuous variables; there was a borderline association between birth weight less than 3000g and maternal hair nicotine levels in segments corresponding to 3rd trimester exposure (Jaakkola et al 2001). A review of epidemiologic studies concluded that there is strong evidence for an association between low birth weight and maternal prenatal ETS exposure (Jaakkola and Jaakkola 2002). Another review concluded that the overall evidence suggests that maternal ETS exposure slightly reduces average birth weight (Lindbohm et al 2002). A retrospective cohort study in the Czech Republic found inverse associations between birth weight and maternal ETS exposure; the association occurred among both smoking and non-smoking women but was stronger among smoking women; similarly, low birth weight was associated with maternal ETS exposure among infants of both smoking and non-smoking women and the association was stronger for infants of smoking women (Dejmek et al 2002). An expert group convened by the State of California concluded that there is sufficient evidence of a causal inverse association between birth weight and maternal prenatal ETS exposure (California Environmental Protection Agency 2004). A retrospective cohort study of non-smoking mothers in India found no association between low birth weight and maternal ETS exposure at home (Goel et al 2004).

Paternal smoking In a retrospective birth cohort study in Norway, birth weight was inversely associated with paternal smoking among infants of smoking but not non-smoking mothers (Haug et al 2000).

4. Birth defects

Reference, location	Design	Exposure	Results	Association[f]	DR[g]	Covariates
(Lindbohm et al. 2002), Finland	Review of epidemiologic studies on developmental and reproductive effects of preconceptual and prenatal ETS exposure; included 6 studies of ETS and preterm birth		Inadequate evidence of an association between birth defects and maternal ETS exposure; most studies assessed paternal smoking as index of maternal ETS exposure but paternal smoking may act through paternal germ cell mutations			
(California Environmental Protection Agency 2004), California	Updated review of health outcomes related to environmental tobacco smoke exposure; expert group used a weight of evidence approach, considering the number and quality of epidemiologic studies and evidence of biologic plausibility		Concluded that there is inadequate evidence of a causal association between birth defects and maternal prenatal ETS exposure			

Birth defects: summary

Two recent reviews, including one by an expert panel convened by the State of California, concluded that there is inadequate epidemiologic evidence for an association between birth defects and maternal ETS exposure (Lindbohm et al 2002, California Environmental Protection Agency 2004). The former review noted that most available studies included paternal smoking in indices of maternal ETS exposure but paternal smoking may act through paternal germ cell mutations.

[f] Entries in this column include odds ratios, relative risks and certain other statistical measures of association as published in original epidemiologic studies; an entry of '+' means the measure of association was not an odds ratio or relative risk and was statistically significant at the 0.05 level; an entry of '(+)' means the association was almost statistically significant.

[g] 'DR' refers to a dose-response relationship in an epidemiologic study; an entry of '+' means the measure of dose-response relationship used in the citation was statistically significant at the 0.05 level; an entry of '(+)' means the association was almost statistically significant.

5. SIDS

Reference, location	Design	Exposure	Results	Association[h]	DR[i]	Covariates
(Anderson and Cook 1997), UK	Meta-analysis, 39 epidemiologic studies of SIDS and parental smoking published up to April 1997		SIDS associated with postnatal maternal smoking (pooled odds ratio, 4 studies that controlled for prenatal maternal smoking)	1.9 (1.6-2.4)		Prenatal maternal smoking
			Among infants of non-smoking mothers, 2 of 3 studies found an association between SIDS and paternal smoking (odds ratios by study)	Nicholl 1992 1.6 (1.1-2.4) Mitchell 1993 1.0 (0.6-1.6) Blair 1996 3.4 (2.0-5.9)		
(Cook and Strachan 1999), UK	Review of literature on effects of parental smoking on the respiratory health of children; included reports published up to June 1998		Included corrected pooled odds ratios for association between SIDS and prenatal parental smoking and postnatal ETS exposure	prenatal smoking 2.1 (1.9-2.4) postnatal smoking 1.9 (1.6-2.4)		
(World Health Organization 1999), Geneva	Expert group review of the effects of ETS on child health		Maternal smoking is a major causes of SIDS; there is limited evidence that postnatal ETS exposure increases the risk of SIDS			
(California Environmental Protection Agency	Updated review of health outcomes related to environmental tobacco smoke exposure; expert group used a		Concluded that there is sufficient evidence of a causal association between			

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[i] 'DR' refers to a dose-response relationship in an epidemiologic study; an entry of '+' means the measure of dose-response relationship used in the citation was statistically significant at the 0.05 level; an entry of '(+)' means the association was almost statistically significant.

2004), California	weight of evidence approach, considering the number and quality of epidemiologic studies and evidence of biologic plausibility	SIDS and postnatal ETS exposure (independent of prenatal maternal smoking)		
(Carpenter et al. 2004), Europe (20 regions)	Case-control study, 745 SIDS cases, 2411 live birth controls, 1992-1996	SIDS associated with maternal smoking especially among mothers who shared their bed with infant (odds ratio, smoked and shared bed vs neither risk factor)	18 (10-30)	Infant sleeping position, other household smokers, history of apparent life-threatening events, infant sex, birth weight, neonatal intensive care, multiple birth, maternal age, urinary tract infection, parity, marital status, partner employment status
		SIDS associated with number of cigarettes smoked daily in home (odds ratios relative to 0/day)	1-9 cigs/d 1.1 (0.7-1.6) 10-19 cigs/d 1.5 (1.1-2.1) 20-29 cigs/d 1.7 (1.2-2.5) 30+ cigs/d 3.3 (1.8-6.0)	As above except adjusted for maternal smoking instead of number of cigarettes smoked daily in home

SIDS: summary

Postnatal infant exposure A meta-analysis of 39 epidemiologic studies concluded that SIDS is associated with postnatal parental smoking; the pooled odds ratio for the four studies that controlled for prenatal maternal smoking was 1.9 (95% CI 1.6-2.4) (Anderson and Cook 1997, Cook and Strachan 1999). The latter reviews also noted that, among infants of non-smoking mothers, two of the three available studies found associations between SIDS and paternal smoking. An expert group review concluded that prenatal maternal active smoking is a major cause of SIDS and that there is limited evidence that postnatal ETS exposure increases the risk of SIDS (World Health Organization 1999). An expert panel review commissioned by the State of California concluded that there is sufficient evidence of a causal association between SIDS and postnatal ETS exposure, independent of prenatal maternal smoking (California Environmental Protection Agency 2004). A large European case-control study found that SIDS was associated with maternal smoking, especially if mothers shared their bed with their infant; SIDS was also associated with the number of cigarettes smoked daily in the home (Carpenter et al 2004).

6. Postnatal growth

Reference, location	Design	Exposure	Results	Association[j]	DR[k]	Covariates
(Eskenazi and Bergmann 1995), California	Cohort study, 2622 women-child pairs enrolled at prenatal visit, 1964-1967, and child followed to age 5 yr; measured child height	Self-reported maternal smoking habits and serum cotinine; ETS exposure defined as non-smokers with serum cotinine 2-10 ng/ml	Child height at age five years not associated with prenatal ETS exposure among infants of non-smoking mothers (avg height at age 5 yr, children of exposed vs unexposed mothers)	110.3 vs 109.9 cm		
(California Environmental Protection Agency 2004), California	Updated review of health outcomes related to environmental tobacco smoke exposure; expert group used a weight of evidence approach, considering the number and quality of epidemiologic studies and evidence of biologic plausibility		Concluded that there is inadequate evidence of a causal association between childhood growth in height and prenatal and/or postnatal ETS exposure (much less studied than prenatal maternal active smoking)			

Postnatal growth: summary

A longitudinal cohort study in California found no association between height at age 5 years and prenatal ETS exposure of non-smoking mothers (confirmed by serum cotinine levels at 1st prenatal visit) (Eskenazi and Bergmann 1995). An expert panel review commissioned by the State of California concluded that there is sufficient evidence of a causal association between SIDS and postnatal ETS exposure, independent of prenatal maternal smoking (California Environmental Protection Agency 2004).

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7. Lung function

Reference, location	Design	Exposure	Results	Association[l]	DR[m]	Covariates
(Cook et al. 1998), UK	Review of epidemiologic studies of lung function in children and parental smoking published during 1979 to April 1997; conducted meta-analyses based on 22 cross-sectional and 6 cohort studies (including 1 cohort included in the cross-sectional analysis)	Exposure variably defined as maternal/not, either parent/neither, both parents/neither, high vs low cotinine levels	Among 21 cross-sectional studies of FEV_1, 18 found lower FEV_1 among ETS-exposed children (avg difference, exposed vs unexposed)	-1.4% (-1.9, -1.0)		
			Among 10 studies comparing maternal and paternal smoking, most showed stronger inverse association between FEV_1 and maternal smoking and none found a significant association with paternal smoking alone			
			Among 19 cross-sectional studies of MMEF, there was an inverse association with ETS exposure (avg difference, exposed vs unexposed)	-5.0% (-6.6, -3.3)		
(Li et al. 2000), Children's Health Study, California	Cross-sectional study, 5263 children age 7-18 yr in 12 southern California communities, recruited during 1993 and 1996; parent-reported information on medical history, annual child-reported information and lung function testing; this report	Parent-reported information on household characteristics including maternal prenatal smoking (19%) and postnatal ETS exposure at home (past 11%, current 22%)	Lung function indices not associated with current ETS exposure among non-asthmatic boys (avg % difference, exposed vs unexposed boys)	FEV_1/FVC 0.3% (-0.7, 1.2) MMEF -0.6% (-3.9, 2.8)		Community, age, race, log height, school grade, spirometer, technician, barometric pressure

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	analyzed baseline cross-sectional data				
			Borderline inverse association between lung function indices and current ETS exposure among non-asthmatic girls (avg % difference, exposed vs unexposed girls)	FEV_1/FVC -0.7% (-1.6, 0.2) MMEF -2.4% (-5.7, 1.0)	As above
			Lung function indices not associated with current ETS exposure among asthmatic boys (avg % difference, exposed vs unexposed boys)	FEV_1/FVC -1.7% (-4.6, 1.4) MMEF -2.9% (-13, 8.6)	As above
			Lung function indices not associated with current ETS exposure among asthmatic girls (avg % difference, exposed vs unexposed girls)	FEV_1/FVC 0.9% (-2.2, 4.1) MMEF 10% (-0.9, 23)	As above
(Mannino et al. 2001), NHANES III, USA	Nationally representative cross-sectional study, 5400 children, age 4-16 yr, enrolled 1988-1994; conducted pulmonary function tests for children age 8-16 yr, excluded smokers and those with serum cotinine >113.6 nmol/L; parent-reported respiratory symptoms and physician-diagnosed asthma	Self-reported prenatal maternal smoking reported for children age 4-11 yr, child serum cotinine	Lung function inversely associated with serum cotinine among children age 8-11 yr whose mothers did not smoke during pregnancy (avg % change in lung function per serum cotinine tertile)	FEV_1/FVC -1.3% (-2.3, -0.3) MMEF -7.4% (-11, -3.4)	Age, race/ethnicity, SES, parental asthma, family size, sex, sitting height
			Lung function not associated with serum cotinine among children age 8-11 yr whose mothers smoked during pregnancy (avg % change in lung function per serum cotinine tertile)	FEV_1/FVC -0.8% (-2.6, 1.0) MMEF 1.8% (-7.0, 9.7)	As above

(Jaakkola and Jaakkola 2002), Finland	Review of literature on effects of ETS on the respiratory health of children, included reports published during 1966 to October 2000		Inadequate evidence for an association between reduced lung function during childhood and maternal prenatal ETS exposure Limited evidence for an association between reduced lung function among school-age children and postnatal ETS exposure Limited evidence for an association between reduced lung function growth rates during childhood and postnatal ETS exposure		
(Gilliland et al. 2003), Children's Health Study, California	Cohort study, 5933 children age 7-18 yr in 12 southern California communities, recruited during 1993 and 1996, followed to 2001; parent-reported information on medical history, annual child-reported information and lung function testing (see Gilliland et al 2000 above)	Parent-reported information on household characteristics including maternal prenatal smoking (19%) and postnatal ETS exposure at home (past 11%, current 22%)	Lung function indices not associated with ever-exposure to ETS among non-asthmatic boys (avg % difference, exposed vs unexposed children)	FEV_1/FVC -0.2% (-1.0, 0.5) FEF_{25-75}/ FVC -0.6% (-3.0, 1.9)	Age, log height, race, community, spirometer, technician, barometric pressure, temperature, respiratory illness, family history of atopy and asthma
			Lung function indices not associated with ever-exposure to ETS among non-asthmatic girls (avg % difference, exposed vs unexposed children)	FEV_1/FVC -0.4% (-1.0, 0.3) FEF_{25-75}/ FVC -1.4% (-3.6, 0.9)	As above
			Lung function indices not associated with ever-exposure to ETS among boys with early-onset	FEV_1/FVC 0.2% (NS) FEF_{25-75}/	As above

		asthma (avg % difference, exposed vs unexposed children)	FVC 0.8% (NS)	
		Lung function indices not associated with ever-exposure to ETS among girls with early-onset asthma (avg % difference, exposed vs unexposed children)	FEV_1/FVC 1.7% (NS) FEF_{25-75}/ FVC 5.1% (NS)	As above
(California Environmental Protection Agency 2004), California	Updated review of health outcomes related to environmental tobacco smoke exposure; expert group used a weight of evidence approach, considering the number and quality of epidemiologic studies and evidence of biologic plausibility	Concluded that there is limited evidence of a causal inverse association between childhood growth of lung function indices and childhood ETS exposure		

Lung function: summary

Prenatal maternal ETS exposure A review of epidemiologic studies published up to 2000 concluded that there was inadequate evidence for an inverse association between childhood lung function indices and maternal prenatal ETS exposure (Jaakkola 2002).

Childhood ETS exposure A meta-analysis of 22 cross-sectional and 6 cohort studies concluded that childhood FEV_1 was inversely associated with indices of childhood ETS exposure; among 19 cross-sectional studies, there was an inverse association between MMEF and childhood ETS exposure (Cook et al 1998). Most of the 10 studies comparing parental smoking found a stronger inverse association between FEV_1 and maternal compared to parental smoking and none found a significant association with paternal smoking alone. The authors concluded that maternal smoking is associated with small but statistically significant deficits in FEV_1 and related indices in school-aged children and that this is almost certainly a causal relationship but much of the effect may be due to prenatal maternal smoking. Cross-sectional analysis of baseline data in a large California cohort study found a borderline inverse association among non-asthmatic school-age girls but not boys between indices of bronchial obstruction (FEV_1/FVC, MMEF) and household ETS exposure; among asthmatic children, there was no association between FEV_1/FVC or MMEF and household ETS exposure (Li et al 2000). A more recent report of the California study found no associations between FEV_1/FVC or MMEF and postnatal ETS exposure among asthmatic or non-asthmatic girls or boys (Gilliland et al 2003). A cross-sectional analysis of NHANES III found inverse associations between FEV_1/FVC and MMEF and current serum cotinine levels among children whose mothers did not smoke prenatally but not among those whose mothers did smoke prenatally (Mannino et al 2001). A review of epidemiologic studies published up to 2000 concluded that there was limited evidence for inverse associations between childhood lung function and lung function growth indices and postnatal ETS (Jaakkola 2002). An expert panel review commissioned by the State of California concluded that there is limited evidence of a causal inverse association between childhood growth of lung function indices and childhood ETS exposure (California Environmental Protection Agency 2004).

8. Incident asthma

Reference, location	Design	Exposure	Results	Association[n]	DR[o]	Covariates
(Cook and Strachan 1998), UK	Review of epidemiologic studies of childhood bronchial hyperreactivity and ETS exposure; based on studies published during 1983-1996 including 1 study of neonates, 19 population-based studies of school-age children and 3 test chamber studies of acute ETS exposure		Bronchial hyperreactivity among children associated with maternal smoking (pooled odds ratio, 10 studies); authors concluded that there is limited evidence for this association	1.3 (1.1-1.5)		
			No consistent association between bronchial hyperreactivity and paternal smoking in the 4 relevant studies			
			2 small experimental studies of acute ETS exposure provided inadequate data to assess the relationship between BHR and acute ETS exposure			
(Strachan and Cook 1998c), UK	Review of epidemiologic studies of childhood asthma and parental smoking; based on studies published during 1974-1996		New-onset asthma before age 7 yr associated with maternal smoking (pooled odds ratio based on 4 cohort studies)	1.3 (1.2-1.4)		
			Prevalent asthma among children up to age 18 yr associated with maternal but not paternal smoking (pooled odds ratios based on 14 case-control studies)	maternal smk 1.6 (1.3-2.0) paternal smk 0.9 (0.8-1.1)		
(World Health Organization 1999), Geneva	Expert group review of the effects of ETS on child health		Postnatal ETS exposure increases the risk of childhood asthma			

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(Jaakkola and Jaakkola 2002), Finland	Review of literature on effects of ETS on the respiratory health of children, included reports published during 1966 to October 2000		Limited evidence for an association between childhood asthma and maternal prenatal ETS exposure Strong and consistent evidence that postnatal ETS exposure induces childhood asthma		
(DiFranza et al. 2004), USA	Review of literature on child health and prenatal and postnatal ETS exposure		Incident asthma among young children associated with residential ETS exposure, independent of many potential confounders		
(California Environmental Protection Agency 2004), California	Updated review of health outcomes related to environmental tobacco smoke exposure; expert group used a weight of evidence approach, considering the number and quality of epidemiologic studies and evidence of biologic plausibility		Concluded that there is sufficient evidence of a causal association between childhood incident asthma and postnatal ETS exposure; the evidence is particularly strong for young children and those whose mothers smoked during pregnancy		
(Qian et al. 2004), China	Cross-sectional study, 7058 children in primary schools in 4 cities with a range of outdoor air pollution levels, recruited during 1993-1996; parent-reported physician-diagnosed asthma	ETS defined as paternal household smokers other than mother	Childhood asthma not associated with ETS (odds ratio)	1.0 (0.7-1.5)	Age, sex, study district, coal smoke (heating, cooking), SES, ventilation, parental asthma
(Murray et al. 2004), UK	Birth cohort study, 369 mother-infant pairs, mothers recruited during gestation wk 8-10; both parents had history of allergic disease; parent-completed diaries of symptoms and physician – diagnosed illnesses and treatments up to age 3 yr; skin prick and house dust testing at ages 1 and 3 yr	Parent-reported smoking habits, measured cotinine in cord plasma and peripheral plasma at age 1 yr	Wheeze by age 3 yr associated with history of postnatal maternal smoking and with detectable plasma cotinine at age 1 yr	postnatal maternal smoking 1.8 (1.1-3.1) detectable plasma cotinine at age 1 yr 1.8 (1.0-3.3)	Exposure to dust mite antigen, pet ownership, maternal asthma, child's sex, prenatal maternal smoking
Kramer et al 2004 Germany	Cross-sectional study, 1669 children, avg age 6.5 yr, 1996; dermatological examination by physicians, skin prick tests, serum IgE levels, history of physician-diagnosed asthma	Parent-reported cigarettes smoked daily in home; urinary cotinine	Current or past history of physician-diagnosed asthma at age 6 yr not associated with urinary cotinine levels (odds ratio per increment of 100 ng cotinine per	1.0 (0.5-2.3)	Nationality, sex, parental atopy

mg of creatinine)

Incident asthma: summary

Prenatal maternal active smoking A review of studies published up to 1996 concluded that there is limited evidence of an association between childhood bronchial hyperactivity and maternal smoking (Cook and Strachan 1998). A meta-analysis of studies published up to 1996 showed an association between incident asthma before age 7 years and maternal smoking (Strachan and Cook 1998c).

Postnatal ETS exposure

Several recent reviews concluded that incident childhood asthma is associated with postnatal ETS exposure (World Health Organization 1999, Jaakkola and Jaakkola 2002, DiFranza et al 2004, California Environmental Protection Agency 2004). Two of these reviews stated that the association is causal (Jaakkola and Jaakkola 2002, California Environmental Protection Agency 2004). The latter review by an expert panel commissioned by the State of California stated that there is sufficient evidence of a causal association between childhood incident asthma and postnatal ETS exposure and that the evidence is particularly strong for young children and those whose mothers smoked during pregnancy (California Environmental Protection Agency 2004). A large cross-sectional study in China found no association between asthma among school-age children and household ETS exposure (Qian et al 2004). A small UK birth cohort study found associations between wheezing illness by age 3 years and postnatal maternal smoking and current plasma cotinine levels, independent of prenatal maternal smoking (Murray et al 2004). A German cross-sectional study found no association between current or past history of physician-diagnosed asthma and current urinary cotinine levels (Kramer et al 2004).

9. Asthma severity

Reference, location	Design	Exposure	Results	Association[p]	DR[q]	Covariates
(World Health Organization 1999), Geneva	Expert group review of the effects of ETS on child health		Postnatal ETS exposure increases the severity and frequency of symptoms among asthmatic children			
(Jaakkola and Jaakkola 2002), Finland	Review of literature on effects of ETS on the respiratory health of children, included reports published during 1966 to October 2000		Limited evidence for an association between poor control of childhood asthma and childhood ETS exposure			
(DiFranza et al. 2004), USA	Review of literature on child health and prenatal and postnatal ETS exposure		Asthma severity among young children associated with residential ETS exposure			
(California Environmental Protection Agency 2004), California	Updated review of health outcomes related to environmental tobacco smoke exposure; expert group used a weight of evidence approach, considering the number and quality of epidemiologic studies and evidence of biologic plausibility		Concluded that there is sufficient evidence of a causal association between childhood asthma exacerbation and ETS exposure			

Asthma severity: summary

Several recent reviews concluded that the frequency and severity of symptoms among asthmatic children is associated with postnatal ETS exposure (World Health Organization 1999, Jaakkola and Jaakkola 2002, DiFranza et al 2004, California Environmental Protection Agency 2004). The two expert panel reviews concluded that this association is causal (World Health Organization 1999, California Environmental Protection Agency 2004).

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10. Respiratory symptoms

Reference, location	Design	Exposure	Results	Association[r]	DR[s]	Covariates
(World Health Organization 1999), Geneva	Expert group review of the effects of ETS on child health		Postnatal ETS exposure causes chronic lower respiratory tract symptoms (cough, wheeze, dyspnea, sputum) among school-age children			
(Jaakkola and Jaakkola 2002), Finland	Review of literature on effects of ETS on the respiratory health of children, included reports published during 1966 to October 2000		Authors concluded that there is strong and consistent evidence that postnatal ETS exposure causes chronic respiratory symptoms (e.g., cough, sputum, wheezing) in school-age children			
(DiFranza et al. 2004), USA	Review of literature on child health and prenatal and postnatal ETS exposure		Incident cough and wheeze among young children associated with residential ETS exposure			
(California Environmental Protection Agency 2004), California	Updated review of health outcomes related to environmental tobacco smoke exposure; expert group used a weight of evidence approach, considering the number and quality of epidemiologic studies and evidence of biologic plausibility		Concluded that there is sufficient evidence of a causal association between childhood respiratory symptoms and ETS exposure			

Respiratory symptoms: summary

Several recent reviews concluded that childhood respiratory symptoms (cough, wheeze, dyspnea, sputum) are associated with postnatal ETS exposure (World Health Organization 1999, Jaakkola and Jaakkola 2002, DiFranza et al 2004, California Environmental Protection Agency 2004). Three of these reports, including the two expert panel reviews, concluded that this association is causal (World Health Organization 1999, Jaakkola and Jaakkola 2002, California Environmental Protection Agency 2004).

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11 Respiratory and middle ear infections

Reference, location	Design	Exposure	Results	Association[t]	DR[u]	Covariates
(Strachan and Cook 1997), UK	Meta-analysis of epidemiologic studies of lower respiratory illness during early childhood and parental smoking; 21 studies (14 cohort, 2 controlled trials, 2 case-control, 3 cross-sectional) published during 1974-1996		9 of 12 cohort studies found dose-response relationships between lower respiratory tract illnesses and number of smokers or amount smoked in the household or by the mother (pooled odds ratio, 11 studies, both vs neither parent smoking)	1.7 (1.4-2.1)		
			Lower respiratory tract illnesses associated with postnatal ETS exposure from paternal smoking (pooled odds ratio, 14 studies)	1.3 (1.2-1.4)		
(Strachan and Cook 1998a), UK	Meta-analysis of 7 epidemiologic studies of recurrent childhood middle ear infections and parental smoking; published during 1985-1995		Recurrent middle ear infections associated with either parent smoking (pooled odds ratio)	1.5 (1.1-2.0)		
(Li et al. 1999), Australia	Meta-analysis of epidemiologic studies of serious lower respiratory tract infections during early childhood and ETS exposure; based on 13 studies (3 cohort, 2 case-control, 8 cross-sectional) published during 1974-1994	ETS exposure based on parental and/or other household smokers	Hospitalization for lower respiratory infections (bronchitis/bronchiolitis, pneumonia) among young children associated with ETS exposure (pooled odds ratios, 7 studies of children age 0-2 yr, 2 studies of children age 3-6 yr)	age 0-2 yr 1.7 (1.3-2.2) age 3-6 yr 1.3 (0.9-1.8)		
(Cook and Strachan 1999), UK	Review of literature on effects of parental smoking on the respiratory health of children; included reports published up to June 1998		Reviewed studies were consistent in showing associations between respiratory illnesses and symptoms and middle ear disease and smoking by either parent with odds ratios of 1.2-1.6; associations were generally stronger among pre-school compared to older children.			
(World Health Organization 1999),	Expert group review of the effects of ETS on child health		Postnatal ETS exposure is an important cause of lower respiratory tract illnesses including croup,			

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Geneva		bronchitis/bronchiolitis and pneumonia during early childhood Postnatal ETS exposure causes increased risk of acute and chronic middle ear disease
(Jaakkola and Jaakkola 2002), Finland	Review of literature on effects of ETS on the respiratory health of children, included reports published during 1966 to October 2000	Authors concluded that there is sufficient evidence that postnatal ETS exposure causes acute and recurrent middle ear infections among young children Authors concluded that there is sufficient evidence that postnatal ETS exposure causes lower respiratory illnesses among infants age 0-2 yr
(DiFranza et al. 2004), USA	Review of literature on child health and prenatal and postnatal ETS exposure	Bronchiolitis, bronchitis, pneumonia and middle ear infections among young children associated with residential ETS exposure
(California Environmental Protection Agency 2004), California	Updated review of health outcomes related to environmental tobacco smoke exposure; expert group used a weight of evidence approach, considering the number and quality of epidemiologic studies and evidence of biologic plausibility	Concluded that there is sufficient evidence of a causal association between childhood lower respiratory illnesses (including bronchitis/bronchiolitis and pneumonia) and ETS exposure Concluded that there is sufficient evidence of a causal association between childhood middle ear infections and ETS exposure

Respiratory and middle ear infections: summary

Lower respiratory tract infections

Three recent reviews concluded that postnatal ETS exposure is an important cause of lower respiratory infections during early childhood (World Health Organization 1999, Jaakkola and Jaakkola 2002, California Environmental Protection Agency 2004). A meta-analysis of 13 studies concluded that hospitalization for lower respiratory infections among young children is associated with ETS exposure with a pooled odds ratio of 1.7 (95% CI 1.3-2.2) (Li et al 1999).

Middle ear infections

A meta-analysis of 7 studies concluded that recurrent middle ear infections are associated with either parent smoking with a pooled odds ratio of 1.5 (95% CI 1.1-2.0) (Strachan and Cook 1998a). A review of studies published up to 1998 concluded that middle ear disease was associated with parental smoking by either parent with odds ratios of 1.2-1.6; associations were generally stronger among pre-school compared to older children (Cook and Strachan 1999). Three recent reviews, including two by expert panels, concluded that postnatal ETS exposure can cause acute and chronic childhood middle ear infections (World Health Organization 1999, Jaakkola and Jaakkola 2002, California Environmental Protection Agency 2004).

12. Cancer

Reference, location	Design	Exposure	Results	Association[v]	DR[w]	Covariates
(World Health Organization 1999), Geneva	Expert group review of the effects of ETS on child health		There is limited evidence that parental smoking may increase the risk of some childhood cancers; the potential roles of preconceptual, prenatal and postnatal exposures are unknown			
(Boffetta et al. 2000), Lyon, France	Meta-analysis of epidemiologic studies of childhood cancer and postnatal ETS exposure	Self-reported parental smoking	Weak association between total childhood cancers and maternal smoking during pregnancy (pooled odds ratio from 4 cohort and 8 case-control studies published during 1971-1997)	1.1 (1.0-1.2)		
			Childhood leukemia not associated with maternal smoking during pregnancy (pooled odds ratio from 8 studies published during 1985-1997)	1.1 (0.8-1.3)		
			Borderline weak association between childhood lymphoma and maternal smoking during pregnancy (pooled odds ratio from 6 studies published during 1985-1997)	1.1 (0.9-1.5)		
			Childhood brain cancer not associated with maternal smoking during pregnancy (pooled odds ratio from 12 studies published during 1982-1997)	1.0 (0.9-1.2)		
			Childhood acute lymphatic leukemia weakly associated with paternal smoking (pooled odds ratio from 4 studies published during 1982-1997)	1.2 (1.0-1.4)		
			Childhood non-Hodgkin's lymphoma	2.1 (1.1-4.0)		

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			associated with paternal smoking (pooled odds ratio from 4 studies published during 1982-1997)		
			Childhood brain cancer weakly associated with paternal smoking (pooled odds ratio from 10 studies published during 1982-1997)	1.2 (1.1-1.4)	
(Lindbohm et al. 2002), Finland	Review of epidemiologic studies on developmental and reproductive effects of preconceptual and prenatal ETS exposure; included 1 review (Sasco and Vainio 1999) and 1 meta-analysis (Boffetta et al 2000) of childhood cancer and ETS exposure		Limited evidence of an association between childhood cancer and maternal ETS exposure during pregnancy		
			Limited evidence of an association between childhood brain cancer and lymphomas and paternal smoking; association appears to be related to maternal prenatal exposure to father's smoking rather than preconceptual paternal smoking		
(Pang et al. 2003), United Kingdom Childhood Cancer Study	Case-control study, 3838 childhood cancer cases, 7629 healthy control children, age <15 yr, 1991-1994	Self-reported parental smoking	Childhood leukemia not associated with paternal preconceptual smoking (odds ratios, 1-19 and 20 vs 0 cigs/d)	1.1 (1.0-1.3) 1.0 (0.9-1.2) p-trend=0.74	Matched for sex, DOB, region; adjusted for SES, parental age at child's birth
			Childhood lymphoma not associated with paternal preconceptual smoking (odds ratios, 1-19 and 20 vs 0 cigs/d)	1.3 (0.9-1.7) 1.1 (0.8-1.5) p-trend=0.42	As above
			Childhood CNS cancer not associated with paternal preconceptual smoking (odds ratios, 1-19 and 20 vs 0 cigs/d)	1.1 (0.9-1.4) 1.0 (0.8-1.3) p-trend=0.71	As above
			Other solid tumours of children not associated with paternal preconceptual smoking (odds ratios, 1-19 and 20 vs 0 cigs/d)	1.1 (0.9-1.3) 1.0 (0.8-1.2) p-trend=0.91	As above

		Childhood cancers not associated with maternal preconceptual smoking (results similar to paternal preconceptual smoking)		
		Childhood leukemia *inversely* associated with maternal smoking during pregnancy (odds ratios, 1-19 and 20 vs 0 cigs/d)	0.9 (0.8-1.1) 0.8 (0.6-1.0) p-trend=0.03	Parental age, SES
		Childhood lymphoma not associated with maternal smoking during pregnancy (odds ratios, 1-19 and 20 vs 0 cigs/d)	0.9 (0.7-1.3) 0.7 (0.4-1.2) p-trend=0.21	As above
		Childhood CNS cancer *inversely* associated with maternal smoking during pregnancy (odds ratios, 1-19 and 20 vs 0 cigs/d)	0.9 (0.7-1.1) 0.6 (0.4-0.9) p-trend=0.01	As above
		Other solid tumours of children *inversely* associated with maternal smoking during pregnancy (odds ratios, 1-19 and 20 vs 0 cigs/d)and 20 vs 0 cigs/d)	0.9 (0.8-1.1) 0.7 (0.5-0.9) p-trend=0.03	As above
		Childhood hepatoblastoma associated with both parents smoking preconceptually (mother only, father only and both parents vs neither parent)	2.0 (0.4-10) 1.9 (0.5-7.6) 4.7 (1.7-13) p-trend=0.06	As above
		Childhood hepatoblastoma associated with maternal preconceptual smoking (odds ratios, 1-19 and 20 vs 0 cigs/d)and 20 vs 0 cigs/d)	3.0 (1.2-7.8) 2.2 (0.7-7.2) p-trend=0.06	As above
(California Environmental Protection Agency 2004), California	Updated review of health outcomes related to environmental tobacco smoke exposure; expert group used a weight of evidence approach, considering the number and quality of epidemiologic studies and evidence of biologic	Concluded that there is limited evidence of a causal association between childhood cancer and paternal smoking and inadequate evidence of a causal association between childhood cancer and maternal smoking		

plausibility		
		Concluded that there is limited evidence of a causal association between childhood brain cancer and childhood ETS exposure, or possibly paternal preconceptual smoking
		Concluded that there is limited evidence of a causal association between childhood leukemia and preconceptual paternal smoking but not with prenatal or postnatal ETS exposure
		Concluded that there is limited evidence of a causal association between childhood lymphomas and paternal smoking (these may reflect associations with ETS *per se* and/or with preconceptual paternal smoking)
		Concluded that there is sufficient evidence of a causal association between breast cancer and ETS exposure, particularly among premenopausal women and those exposed early in life
		ETS contains these known human carcinogens: benzene, 4-aminobiphenyl, 2-naphthylamine, vinyl chloride, arsenic, cadmium, chromium VI, nickel and ^{210}polonium
		ETS contains these carcinogens known to cause breast cancer in experimental animals: benzene, dibenz[a,h]anthracene, 4 types of dibenzopyrene, 2 nitrosamines, 8 aliphatic compounds and 3 arylamines/nitroarenes

Childhood cancer: summary

All childhood cancers

Maternal smoking A meta-analysis of epidemiologic studies published up to 1997 found a very weak association between childhood cancers and maternal prenatal smoking (Boffetta et al (2000). An expert group convened by the State of California concluded that there is inadequate evidence of a causal association between childhood cancer and maternal smoking (California Environmental Protection Agency 2004). The California report also noted that ETS contains these known human carcinogens: benzene, 4-aminobiphenyl, 2-naphthylamine, vinyl chloride, arsenic, cadmium, chromium VI, nickel and ^{210}polonium.

Parental smoking An expert group concluded that there is limited evidence that parental smoking may increase the risk of some childhood cancers; the relative importance of preconceptual, prenatal and postnatal exposures in explaining such associations are unknown (World Health Organization 1999).

Paternal smoking An expert group convened by the State of California concluded that there is limited evidence of a causal association between childhood cancer and paternal smoking (California Environmental Protection Agency 2004).

Leukemia

Maternal smoking A meta-analysis of 12 epidemiologic studies published up to 1997 found no association between childhood leukemia and maternal prenatal smoking (Boffetta et al (2000). A large UK case-control study found no association between childhood leukemia and maternal preconceptual smoking and an *inverse* association with prenatal maternal smoking (Pang et al 2003).

Paternal smoking A meta-analysis of 4 epidemiologic studies published up to 1997 found a weak association between childhood acute lymphatic leukemia and paternal smoking (Boffetta et al (2000). A large UK case-control study found no association between childhood leukemia and paternal preconceptual smoking (Pang et al 2003). An expert group convened by the State of California concluded that there is limited evidence of a causal association between childhood leukemia and preconceptual paternal smoking but not with prenatal or childhood ETS exposure (California Environmental Protection Agency 2004).

Lymphoma

Maternal smoking A meta-analysis of 8 epidemiologic studies published up to 1997 found a very weak association of borderline statistical significance between childhood lymphoma and maternal prenatal smoking (Boffetta et al (2000). A large UK case-control study found no associations between childhood lymphoma and maternal preconceptual or prenatal smoking (Pang et al 2003).

Paternal smoking A meta-analysis of 4 epidemiologic studies published up to 1997 found an association between childhood non-Hodgkin's lymphoma and paternal smoking (Boffetta et al (2000). A large UK case-control study found no association between childhood lymphoma and paternal preconceptual smoking (Pang et al 2003). An expert group convened by the State of California concluded that there is limited evidence of a causal association between childhood lymphomas and paternal smoking, possibly reflecting an association with ETS *per se* and/or with preconceptual paternal smoking (California Environmental Protection Agency 2004).

Brain cancer

Maternal smoking A meta-analysis of 4 epidemiologic studies published up to 1997 found no association between childhood brain cancer and maternal prenatal smoking (Boffetta et al (2000). A large UK case-control study found no association between childhood CNS cancers and maternal preconceptual smoking and an *inverse* association with prenatal maternal smoking (Pang et al 2003).

Childhood ETS exposure An expert group convened by the State of California concluded that there is limited evidence of a causal association between childhood brain cancer and childhood ETS exposure; this association may reflect an effect of preconceptual paternal smoking (California Environmental Protection Agency 2004).

Paternal smoking A meta-analysis of 10 epidemiologic studies published up to 1997 found a weak association between childhood brain cancer and paternal smoking (Boffetta et al (2000). A large UK case-control study found no association between childhood CNS cancers and paternal preconceptual smoking (Pang et al 2003). An expert group convened by the State of California concluded that there is limited evidence of a causal association between childhood brain cancer and childhood ETS exposure; this association may reflect an effect of preconceptual paternal smoking (California Environmental Protection Agency 2004).

Hepatoblastoma

Maternal smoking A large UK case-control study found an association between hepatoblastoma and maternal preconceptual smoking (Pang et al 2003).

Parental smoking A large UK case-control study found an association between hepatoblastoma and preconceptual smoking by both parents (Pang et al 2003).

Other childhood cancers

Maternal smoking A large UK case-control study found no association between childhood solid tumours other than brain cancer or hepatoblastoma and maternal preconceptual smoking (Pang et al 2003).

Paternal smoking A large UK case-control study found no association between childhood solid tumours other than brain cancer or hepatoblastoma and paternal preconceptual smoking (Pang et al 2003).

Adult breast cancer

Childhood ETS exposure An expert group convened by the State of California concluded that there is sufficient evidence of a causal association between breast cancer and ETS exposure, particularly among premenopausal women and those exposed early in life (California Environmental Protection Agency 2004). The California report also noted that ETS contains these carcinogens known to cause breast cancer in experimental animals: benzene, dibenz[a,h]anthracene, 4 dibenzopyrenes, 2 nitrosamines, 8 aliphatic compounds and 3 arylamines/nitroarenes.

13. Reproductive effects

Reference, location	Design	Exposure	Results	Association[x]	DR[y]	Covariates
(Jensen et al. 1998), Denmark	Cohort study, 430 couples recruited from trade union members, age 20-35 yr, enrolled during 1992-1995; followed after discontinuing contraception for 6 menstrual cycles or until clinically recognized pregnancy	Self-reported information from both partners on smoking and other factors at enrollment and each month of follow-up; prenatal smoking status of their mothers	Among non-smoking men and women, likelihood of conception inversely associated with history of subject's mother smoking during pregnancy (odds ratios, exposed vs unexposed)	females 0.7 (0.5-1.0) males 0.7 (0.5-1.0)		Female BMI, smoking and alcohol, male and female reproductive organ diseases, menstrual cycle duration
(Lindbohm et al. 2002), Finland	Review of epidemiologic studies on developmental and reproductive effects of preconceptual and prenatal ETS exposure; 8 studies of time to pregnancy and paternal smoking and maternal ETS exposure; found no studies of semen quality and ETS exposure		Inadequate evidence of an association between likelihood of conception and paternal smoking or maternal ETS exposure			
(Hull et al. 2002), Avon Longitudinal Study of Pregnancy and Childhood Study, UK	Retrospective cohort study, women recruited during pregnancy up to gestation wk 18 during 1991-1992; self-reported information on time taken to conception	Self-reported parental smoking habits and maternal ETS exposure at home and work	Time to conception ⩾6 mos associated with maternal ETS exposure (odds ratios, by active and ETS exposure status)	ETS only 1.2 (1.0-1.4) Maternal smoking only 1.2 (1.0-1.5) Maternal smoking + ETS 1.5 (1.3-1.8)		Parental age, education and alcohol intake, duration oral contraceptive use, own/rent home, housing type, overcrowding
			Time to conception ⩾12 mos associated with maternal ETS exposure	ETS only 1.1 (0.9-1.4)		As above

[x] Entries in this column include odds ratios, relative risks and certain other statistical measures of association as published in original epidemiologic studies; an entry of '+' means the measure of association was not an odds ratio or relative risk and was statistically significant at the 0.05 level; an entry of '(+)' means the association was almost statistically significant.

[y] 'DR' refers to a dose-response relationship in an epidemiologic study; an entry of '+' means the measure of dose-response relationship used in the citation was statistically significant at the 0.05 level; an entry of '(+)' means the association was almost statistically significant.

			(odds ratios, by active and ETS exposure status)	Maternal smoking only 1.5 (1.2-2.0) Maternal smoking + ETS 1.6 (1.3-2.0)	
(California Environmental Protection Agency 2004), California	Updated review of health outcomes related to environmental tobacco smoke exposure; expert group used a weight of evidence approach, considering the number and quality of epidemiologic studies and evidence of biologic plausibility		Concluded that there is limited evidence of a causal association between reduced female fertility and ETS exposure; inadequate evidence of a causal association between reduced male fertility and ETS exposure		
(Venners et al. 2004), China	Prospective cohort study, 526 newly married, nonsmoking, female textile workers, 1996-1998; women who stopped contraception were monitored for conception and early pregnancy losses using daily urine hCG tests; pregnant women followed to detect clinical spontaneous abortions	Self-reported paternal smoking habits	Likelihood of conception not associated with paternal smoking intensity (odds ratios relative to not current smokers)	<20 cigs/d 0.9 (0.7-1.2) ⩾20 cigs/d 1.0 (0.7-1.4)	Maternal and paternal age, education, perceived life stress, dust and noise exposure, paternal alcohol, previous smoking, exposure to toxic chemicals, maternal BMI and tea intake

Reproductive effects

Fertility

Transgenerational effects of maternal smoking A Danish cohort study of non-smoking men and women found inverse associations between the likelihood of conception (after discontinuing contraception) and a history of either partner's mother smoking during pregnancy (Jensen et al 1998). An expert panel review commissioned by the State of California concluded that there is limited evidence of a causal association between reduced female fertility and ETS exposure (California Environmental Protection Agency 2004).

Women exposed to ETS A review of epidemiologic studies concluded that there was inadequate evidence of an association between likelihood of conception and paternal smoking or maternal ETS exposure (Lindbohm et al 2002). A longitudinal cohort study found associations between delayed conception and ETS exposure among both women who did or did not smoke (Hull et al 2002). An expert panel review commissioned by the State of California concluded that there is inadequate evidence of a causal association between reduced male fertility and ETS exposure (California Environmental Protection Agency 2004). A cohort study of newly married, nonsmoking, female textile workers in China found no association between likelihood of conception and their husband's smoking intensity (Venners et al 2004).

14. Cognitive function and behaviour

Reference, location	Design	Exposure	Results	Association[z]	DR[aa]	Covariates
(World Health Organization 1999), Geneva	Expert group review of the effects of ETS on child health		Childhood learning difficulties, behavioural problems and language impairment are associated with maternal and paternal active smoking There is inadequate evidence that learning difficulties, behavioural problems or language impairment are associated with maternal prenatal ETS exposure or childhood ETS exposure			
(DiFranza et al. 2004), USA	Review of literature on child health and prenatal and postnatal ETS exposure		Hyperactivity, attention deficit and other behaviour problems from infancy to adolescence associated with prenatal maternal smoking, independent of many potential confounders Cognitive function inversely associated with prenatal maternal smoking Academic performance inversely associated with prenatal maternal smoking			
(California Environmental Protection Agency 2004), California	Updated review of health outcomes related to environmental tobacco smoke exposure; expert group used a weight of evidence approach, considering the number and quality of epidemiologic studies and evidence of biologic plausibility		Concluded that there is limited evidence of a causal inverse association between childhood cognitive function and postnatal ETS exposure; noted that this relationship has been much less studied than prenatal maternal active smoking and that smoking mothers tend to smoke both during and after pregnancy – thus associations with postnatal maternal smoking may partially reflect the impact of prenatal maternal smoking Concluded that there is limited evidence of a causal association between childhood problem behaviours and postnatal ETS exposure			

[z] Entries in this column include odds ratios, relative risks and certain other statistical measures of association as published in original epidemiologic studies; an entry of '+' means the measure of association was not an odds ratio or relative risk and was statistically significant at the 0.05 level; an entry of '(+)' means the association was almost statistically significant.

[aa] 'DR' refers to a dose-response relationship in an epidemiologic study; an entry of '+' means the measure of dose-response relationship used in the citation was statistically significant at the 0.05 level; an entry of '(+)' means the association was almost statistically significant.

Cognitive function and behaviour: summary

Cognitive function

Parental active smoking An expert group review concluded that childhood learning difficulties, behavioural problems and language impairment are associated with maternal and paternal active smoking (World Health Organization 1999).

Childhood ETS exposure An expert panel review commissioned by the State of California concluded that there is limited evidence of a causal inverse association between childhood cognitive function and postnatal ETS exposure; the panel noted that this relationship has been much less studied than prenatal maternal active smoking and that smoking mothers tend to smoke both during and after pregnancy – thus associations with postnatal maternal smoking may partially reflect the impact of prenatal maternal smoking (California Environmental Protection Agency 2004).

Problem behaviours, learning difficulties

Parental active smoking An expert group review concluded that childhood learning difficulties, behavioural problems and language impairment are associated with maternal and paternal active smoking (World Health Organization 1999).

Prenatal maternal ETS exposure The WHO concluded that there is inadequate evidence for associations between childhood learning difficulties, behavioural problems and language impairment and maternal prenatal ETS exposure (World Health Organization 1999).

Childhood ETS exposure The WHO concluded that there is inadequate evidence for associations between childhood learning difficulties, behavioural problems and language impairment and childhood ETS exposure (World Health Organization 1999). An expert panel review commissioned by the State of California concluded that there is limited evidence of a causal association between childhood problem behaviours and childhood ETS exposure (California Environmental Protection Agency 2004).

15. Other health effects

Reference, location	Design	Exposure	Results	Association[bb]	DR[cc]	Covariates
(Strachan and Cook 1998b), UK	Review of literature on parental smoking and allergic sensitization in children including IgE levels, skin prick positivity, and allergic rhinitis or eczema; review based on 36 reports published up to April 1997; among these, there were 9 studies of IgE in neonates, 8 studies of IgE in older children, 12 studies of skin prick tests, and 10 studies describing symptoms of allergic disease other than asthma or wheezing		Several large studies failed to confirm previous reports of an association between neonatal or childhood serum IgE levels and maternal smoking			
			Reviewed studies were generally consistent in finding no association between skin prick positivity and perinatal parental smoking or current ETS exposure (pooled odds ratios); note – there was much greater heterogeneity of odds ratios relating skin prick positivity to current parental smoking	perinatal parental smoking 0.9 (0.6-1.2) current ETS 1.2 (0.7-2.0)		
			No consistent evidence of an association between allergic rhinitis or eczema and parental smoking			Few studies adjusted for potential confounding variables
West et a; 2003 California	Retrospective cohort study, 52 cases of sickle cell anemia, age 2-18 yr; hospital admissions and clinic and emergency room visits during 2 years (1998-2000) before study based on review of medical records	Self (age 8+ yr) or parent (age< 8 yr) reported household smoking	Sickle cell anemia severity among children age 2-18 yrs associated with ETS exposure (odds ratios)	Hospitalization for sickle cell crisis 1.9 (1.3-2.7)		Age, history of asthma, homozygous sickle cell disease

[bb] Entries in this column include odds ratios, relative risks and certain other statistical measures of association as published in original epidemiologic studies; an entry of '+' means the measure of association was not an odds ratio or relative risk and was statistically significant at the 0.05 level; an entry of '(+)' means the association was almost statistically significant.

[cc] 'DR' refers to a dose-response relationship in an epidemiologic study; an entry of '+' means the measure of dose-response relationship used in the citation was statistically significant at the 0.05 level; an entry of '(+)' means the association was almost statistically significant.

Schafer et al 1999 Germany	Cross-sectional study, 2200 children age 5-14 yr, 1992-1993; 55 cases of eczema based on skin examination by dermatologist	Parent-reported household smoking	Eczema among children age 5-14 yr not associated with childhood ETS exposure (odds ratios)	Current ETS 1.1 (0.6-1.9) ETS before age 1 yr 1.0 (0.5-1.8)	
Kramer et al 2004 Germany	Cross-sectional study, 1669 children, avg age 6.5 yr, 1996; dermatological examination by physicians, skin prick tests, serum IgE levels	Parent-reported cigarettes smoked daily in home; urinary cotinine	Atopic eczema at age 6 yr associated with urinary cotinine levels (odds ratio per increment of 100 ng cotinine per mg of creatinine)	2.0 (1.2-3.2)	Nationality, sex, parental atopy
Kramer et al 2004 Germany	Cross-sectional study, 1669 children, avg age 6.5 yr, 1996; dermatological examination by physicians, skin prick tests, serum IgE levels, history of physician-diagnosed asthma	Parent-reported cigarettes smoked daily in home; urinary cotinine	Current or past history of physician-diagnosed asthma at age 6 yr not associated with urinary cotinine levels (odds ratio per increment of 100 ng cotinine per mg of creatinine)	1.0 (0.5-2.3)	Nationality, sex, parental atopy
Aligne et al 2003 NHANES III, USA	Cross-sectional study, nationally representative sample of 3531 children age 4-11 yr; dental examination	ETS exposure defined as serum cotinine level of 0.2 to <10 ng/mL	At least one decayed tooth among children age 4-11 yr associated with ETS exposure based on serum cotinine levels (odds ratios, serum cotinine of 0.2-9.9 vs <0.2 ng/dL)	deciduous teeth 1.8 (1.2-2.7) permanent teeth 1.2 (0.8-1.9)	Age, race/ethnicity, SES, region, education of household head, blood lead, time since last dental visit
			Dose-response relationship between at least one decayed deciduous tooth among children age 4-11 yr and serum cotinine levels (odds ratios, serum cotinine of 0.05-<0.2, 0.2-1.0 and >1.0-<10 vs <0.05 ng/dL)	1.3 (0.8-2.3) 2.2 (1.3-3.6) 2.3 (1.4-3.9)	As above
Shenkin et al 2004 Iowa	Cohort study, 637 children recruited at birth during 1992-1995; dental examination at age 4-7 yr	Parent-reported household smoking	One or more dental caries or fillings at age 4-7 yr associated with ETS exposure at home (odds ratio, exposed vs unexposed)	3.4 (1.7-6.8)	Age, brushing frequency/d, cumulative fluoride intake from water, beverages, foods, dentifrices and

	supplements from age 16-60 mos, cumulative intake of powdered drinks and soda pop from ages 16-60 mos

Other health effects: summary

Allergic sensitization

A literature review of studies published up to 1997 concluded that there was inadequate evidence for an association between neonatal or childhood serum IgE levels and maternal smoking or between skin prick positivity and perinatal parental smoking or current ETS exposure (Strachan and Cook 1998b).

Eczema

A literature review of studies published up to 1997 concluded that there was inadequate evidence for an association between allergic rhinitis or eczema and parental smoking (Strachan and Cook 1998b). A German cross-sectional study found no association between eczema among children age 5-14 years and childhood ETS exposure (Schafer et al 1999). However, a more recent German cross-sectional study did find an association between eczema at age six years and urinary cotinine levels (Kramer et al 2004).

Sickle cell anemia severity

A retrospective cohort study in California found an association between hospitalization of children age 2-18 years for sickle cell anemia and ETS exposure (West et al 2003).

Dental caries

A large cross-sectional study of US children age 4-11 years found a dose-response relationship between the presence of at least one decayed deciduous tooth and serum cotinine levels (Aligne et al 2003). A cohort study of children age 4-7 years in Iowa also found an association between one or more dental caries or fillings and ETS exposure at home (Shenkin et al 2004).

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