Public Health Research Consortium

Project Final Report

Estimating the Costs to the NHS of Smoking in Pregnancy for Pregnant Women and Infants

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Preface: What this study adds to knowledge

This report describes the costs to the NHS in the UK related to the maternal and infant consequences of smoking in pregnancy.

Costs to the NHS related to maternal increased risk of spontaneous abortion, ectopic pregnancy, placenta previa, abruptio placenta, preterm premature rupture of membranes and decreased risk of pre-eclampsia are estimated to be between £8-64 million per year based on different costing methodologies.

Costs to the NHS related to infant (0-12 months) increased risk of preterm delivery, low birth weight, Sudden Infant Death Syndrome, perinatal mortality, asthma, otitis media, and upper and lower respiratory infections are estimated to be between £12-23.5 million per year.

Smoking cessation interventions for pregnant women have been shown to be effective in significantly increasing quitting rates. In this report, we estimate that spending between £13.60-£37.00 per pregnant smoker would yield positive cost savings for the NHS.

1. Executive summary

Background
Smoking in pregnancy is a major public health concern, posing risks to both mother and child. In the UK in 2005, around half of women who smoke quit just before or during pregnancy, but 17% of women smoke throughout pregnancy – exposing around 120,000 infants each year. Smoking in pregnancy also exhibits a strong social class gradient and contributes to health inequalities among mothers and children. Although the economic consequences of smoking in pregnancy have been studied fairly extensively in the USA, little is known about costs in the UK context.

Aims
The aim of this study was to estimate the additional costs to the NHS, during pregnancy and the year following birth, of a mother continuing to smoke during pregnancy.

Design and Methods
The study contained four phases. First, we conducted a scoping review of etiological studies and economic studies of smoking in pregnancy. Second, we conducted a review of reviews of the effects of smoking in pregnancy to establish robust estimates of relative risks. Third, we estimated actual NHS costs related to maternal and infant outcomes related to smoking in pregnancy. Fourth, we estimated the proportion of outcomes attributable to smoking in pregnancy and estimated the total NHS costs attributable to smoking.

Main Findings
The total annual cost to the NHS of smoking during pregnancy for maternal outcomes is estimated to be in the region of £8 million for top-level HRG reference costs. However this is a conservative estimate and the true costs may be as high as £64 million. The total annual cost of smoking in pregnancy for infant outcomes is estimated to be between £12 million - £23.5 million, with the majority of costs attributable to the care of low birth weight and preterm infants.

Spending on smoking cessation interventions between £13.60 - £37.00 per pregnant smoker would yield positive cost savings.

Conclusions
Smoking in pregnancy imposes a considerable economic burden on society. Our cost estimates are conservative, being limited to NHS costs during pregnancy and the first year of life. Positive economic cost savings could be generated with low-cost smoking cessation interventions.

2. Background

In the UK in 2005, 32% of women smoked cigarettes in the year before they become pregnant. [1] Studies suggest that around 80% of pregnant smokers would like to quit [2] and only around 6% have strong intentions of continuing to smoke. [3] Around half of the women who smoke in the year before pregnancy quit just before or during pregnancy, but 17% of women admit to continuing to smoke throughout pregnancy – exposing around 120,000 infants each year. [4]

Smoking in pregnancy exhibits a strong social class gradient. The rate in unskilled manual groups is estimated to be 26%, compared to 20% in skilled manual, 11% in intermediate and junior non-manual grades, and 4% among professionals. There are also inequalities by maternal age, with younger mothers having much higher rates than older mothers, and by ethnicity, with white and mixed-ethnicity mothers having higher rates of smoking than those of other ethnicities.

Between 2005-2006, the NHS Stop Smoking Services recorded 17,917 pregnant women setting a quit date; at 4 weeks post-quit date, just over half (54%) had stopped smoking, quit rates at the end of pregnancy were not recorded. [1] Meta-analysis of 48 trials suggests that smoking cessation interventions are effective for pregnant women, but the absolute effect is small (6 more women quitting per 100 smoking women assigned to interventions). [5] Relapse rates for women who quit during pregnancy are high – 67-80% of quitters are smoking again within a year. [6, 7]

Smoking in pregnancy is a major public health concern, posing risks to both mother and child. [8, 9] It is a well-known cause of many complications of pregnancy, [8] adverse foetal and infant outcomes, [9] and a suspected cause of some subtle and long-term outcomes in offspring, e.g. impaired lung growth and function, [10, 11] intellectual deficits, [12] and increased risk of disruptive behaviour disorders. [13]

Although the economic costs of smoking in pregnancy have received some attention in the USA, we are aware of only one study carried out in the UK, and this looked only at the child's hospital inpatient service utilisation and costs. [14]

3. Purpose of the study

This project originally aimed to estimate of the additional lifetime costs that accrue to society, of a mother continuing to smoke during pregnancy, compared to the alternative of her quitting. Time and resource constraints, as well as the advice of reviewers of the original proposal resulted in a modified aim, to estimate the increased costs to the NHS, during pregnancy and the year following birth, of a mother continuing to smoke through pregnancy.

4. Design and methods

The study was developed in 4 stages:

A. A **scoping review** of the economic literature, in which we: developed a full list of the maternal and infant consequences of smoking in pregnancy through the first year of the infant's life previously included in economic cost models; described the costing methodologies and economic modelling approaches used in previous economic studies

B. A **review of reviews** of the effects of smoking in pregnancy, in which we established the magnitude of the impact of smoking in pregnancy for all outcomes established by an expert review

C. **Evidence synthesis and cost estimation**, in which we estimated the actual costs of all outcomes established in stage A

D. **Attribution of cases** to smoking, in which we calculated attributable risks and **estimated the economic costs** of smoking in pregnancy for maternal and infant outcomes during pregnancy and in the year following birth

A. Scoping review of the economic literature

The first aim of the review was to identify previous studies of the **costs** of maternal smoking during pregnancy. We searched within Ovid, Pub Med, ISI web of knowledge, JSTOR, Google scholar and the British library catalogue, using the following key words:

- **Costs**- Health care costs, Economic costs, Economic implications, Cost estimates
- **Smoking**- Maternal smoking, Parental smoking, Tobacco use, Cigarette smoking
- **Pregnancy**- Pregnancy outcomes, Pregnancy implications
- **Outcomes**- Low birth weight, Premature delivery, Spontaneous abortion, Preterm, Sudden Infant Death Syndrome

Further studies were identified from searching the reference lists of relevant papers.

The search identified 49 studies, 14 were relevant to our study.

The following maternal and infant outcomes were considered in at least one of the studies of the costs of smoking in pregnancy

Maternal Outcomes	Infant Outcomes
• Ectopic pregnancy • Spontaneous abortion • Placenta praevia (PP) • Abruptio placenta (AP) • Preterm Premature Rupture of Membranes (PPROM) • Pre-eclampsia (PE)	• Preterm delivery (< 37 weeks) • Low birth weight (LBW) (< 2500g) • Sudden Infant Death Syndrome (SIDS) • Respiratory distress syndrome (RDS) • Asthma • Respiratory syncytial viral bronchitis (RSVB) • Otitis media (OM) • Upper and lower respiratory infections (URI/LRI) • Perinatal death • Foetal growth restriction

Table 1: Maternal and infant outcomes due to smoking in pregnancy

These studies were organized into a typology, which classified studies by three dimensions. These were:

(1) Outcomes studied: did the study include maternal outcomes only, infant outcomes only or both?
(2) Costing method: did the study use actual (billed) costs from health insurance claims data, or estimated costs per unit of health care, e.g, the estimated cost of an additional day spent in neonatal intensive care
(3) Analytical methodology: did the study estimate costs based on an attributable risk model in which the costs were estimated based on population risk data for smoking related disease from exposure to tobacco, or a multivariate/structural model which adjusted for other factors known to affect maternal and/or infant outcomes.

		Maternal outcomes only	Infant outcomes only	Maternal and infant outcomes
Attributable risk model	Claims data	1	1	1
	Units of health care		4	
Multivariate /structural model	Claims data		2	
	Units of health care		5	

Table 2: Number of studies identified, classified by method, source of cost data and outcomes

Almost all studies were from the United States. Most estimated costs for infant outcomes only, only 2 studies have considered costs of maternal outcomes. Some studies used indirect measures of infant outcomes, such as length of inpatient stay or admission to Neonatal Intensive Care Units (NICUs).

An early study by Manning and colleagues used parameter estimates from published sources to estimate the impact of maternal smoking during pregnancy on the risk for low birth weight infants. [15] The impacts included increased utilization of neonatal intensive care units and the average additional costs of neonatal intensive care. However, this estimate is likely to be conservative because it excludes the costs associated with complications of pregnancy other than low birth weight, and also those costs resulting from sources other than NICU usage. The results showed an

estimated $652 million in additional annual costs were incurred for the neonatal care of infants born low birth weight because of maternal smoking.

Oster et al [16] estimated expenditures on neonatal care based on relationships between maternal smoking and low birth weight. Low birth weight was the single most important predictor of neonatal morbidity and mortality and the intensity of neonatal care was significantly higher for these infants. An estimated 21-39% of low birth weight births were attributable to maternal smoking during pregnancy. These results suggested that maternal smoking during pregnancy was responsible for approximately 35,816 low-weight births in the United States in 1983, which was 14.5% of all low-weight births. Some 14,977 (6.6%) admissions to NICUs were attributable to maternal smoking, at an annual cost of $272 million (8.5% of total national NICU expenditure). The mean estimated cost of neonatal care was $288 higher for infants born to smokers when compared to non-smokers.

The long-term effects of smoking in pregnancy on childhood health and educational costs were estimated by the US Office of Technology Assessment in 1988. [17] These included costs of rehospitalisation during the first year of life at $804 (1986 prices) for a low birth weight baby and the longer term costs (to the age of 35) of early intervention programmes, special education, and other services at between $9,000 and $23,000 per low birth weight infant.

The Centers for Disease Control and Prevention (CDC) used data from the Pregnancy Risk Surveillance Survey and birth certificates to estimate the association between maternal smoking and the probability of admission to a neonatal intensive care unit (NICU). [18] Neonatal health-care costs, in 1996 dollars, were assigned on the basis of data from private health insurance claims. Results estimated smoking-attributable neonatal expenditures of $366 million in the United States in 1996, or $704 per maternal smoker (at 1996 prices), and indicated wide variations in expenditures attributable to smoking amongst US states. The considerable costs were used as evidence to support the introduction of cessation programmes aimed at pregnant smokers. In 1997, the CDC estimated that approximately 19%-27% of women smoked during their pregnancy. [19] Smoking during pregnancy was estimated to be a causal factor of 32,000-61,000 cases of low birth weight and between 14,000 and 26,000 NICU admissions. Smoking-attributable medical-care costs for chronic conditions in 1993 were approximately $50.0 billion, which was assumed to be a conservative estimate because direct medical costs of tobacco exposure for infants and children and most direct costs for pregnant women were excluded from the calculations.

Lightwood et al estimated the direct medical costs of low birth weight from maternal smoking, and short-term cost savings from smoking cessation programs before or during the first trimester of pregnancy above the costs for non-smokers. [20] The study used simulations of neonatal costs per live birth using population attributable risk factors, derived from the 1990 California Linked Perinatal Dataset, created by the RAND Corporation. The estimates presented by Lightwood calculated the annual number of LBW live births attributable to smoking while pregnant, the mean excess cost of a live birth to a pregnant smoker and the total annual excess cost of live births to pregnant smokers. The number of LBW live births attributable to smoking was calculated by multiplying the population attributable risk factor of LBW (calculated

from the proportion of pregnant women who smoke and the RR for LBW from smoking) by the number of live births. Total annual excess cost of a live birth was calculated by multiplying the mean excess cost of a live birth to a pregnant smoker by the annual number of births to smokers.

The mean excess direct medical costs per live birth for each pregnant smoker were $511 (1995 US dollars) and the total annual cost across the United States was $263 million. The authors estimated that a cessation programme which could generate a drop of 1% in smoking prevalence would prevent 1,300 low birth weight live births, saving $21 million in direct medical costs in the first year. Over a period of seven years the programme was estimated to potentially prevent 57,200 low birth weight infants and save $572 million in direct medical costs.

Miller and colleagues also estimated the costs attributable to smoking during pregnancy for mothers and infants in a US-based study. [21] The model estimated smoking-attributable costs for eleven different infant and maternal outcomes. The authors used a claims database of 7784 mothers who had deliveries during 1996 and calculated the total cost over the infants' first year for each mother and infant. The mean cost for smokers and non-smokers could not be computed directly because smoking status was not available from the claims data. A literature search was therefore used to identify population attributable risk percentages due to smoking for each outcome. Incremental costs associated with each smoking-related outcomes were computed using linear regression techniques.

Total costs attributable to smoking were estimated using a function of the additional cost of each adverse outcome and the population attributable risk percentage. The additional costs due to smoking were summed across all conditions and the totals in the first year after birth ranged from $1142 to $1358 per pregnant woman smoker. The authors concluded that maternal smoking during pregnancy resulted in higher health care costs both for the treatment of maternal and infant smoking related disease.

Also in the United States, Adams and Melvin used pooled odds ratios to estimate smoking-attributable cases. [22] They estimated health care costs associated with smoking-attributable cases of placenta previa, abruptio placenta, ectopic pregnancy, preterm premature rupture of the membrane (PPROM), pre-eclampsia, and spontaneous abortion. Mean cost per case for ectopic pregnancy and spontaneous abortion were applied to smoking-attributable health care costs for these conditions. Incremental costs above the costs of normal births were used to estimate smoking-attributable costs of placenta previa, abruptio placenta, PPROM, and pre-eclampsia associated with delivery. The estimates showed that smoking-attributable costs ranged from $1.3 million for PPROM to $86 million for ectopic pregnancy. Smoking during pregnancy was protective against pre-eclampsia, with a saving between $36 and $49 million. Total smoking-attributable costs ranged from $135 to $167 million (1993 prices).

Adams et al used Pregnancy Risk Assessment Monitoring System (PRAMS) data (based on samples of births from 13 states) on smoking behaviour, birth outcomes and resource utilization to estimate neonatal costs attributable to maternal smoking during pregnancy in the USA.[23] The probability of an admission to a NICU was computed

using a multivariate analysis. Neonatal costs were predicted for infants if their mother did or did not smoke. Data from the MarketScantrade mark database of the MedStattrade mark Corporation was used to attach costs to NICU and non-NICU nursery nights and data from the 1997 birth certificates to extrapolate smoking attributable fractions and consequent expenses to all states.

The study showed that maternal smoking increased the relative risk of admission to an NICU by almost 20% and for infants admitted to an NICU. Over all births, smoking increased infant length of stay by 1.1%. NICU-admitted infants cost a mean $2496 per night while in the NICU and $1796 when moved to a regular nursery compared to only $748 for non-NICU infants. Increased NICU utilisation, longer stays and higher costs resulted in a positive smoking attributable fraction (SAF) for neonatal costs. The SAF for the 13 US states in the sample was 2.2%. These results showed that amongst mothers who smoke, smoking adds in excess of $700 in neonatal costs. Smoking attributable neonatal costs in the US were approximately $367 million (1996 prices). The authors used these estimates to demonstrate how savings could be made by cessation programmes, which would prevent adverse maternal and infant outcomes even if successful only in the short term.

A greater burden was estimated by Aligne & Stoddard [24] using relative risk estimates to calculate direct medical expenditures and costs for loss of life. The estimated annual cases of childhood illness and death attributable to parental smoking included low birth weight (46,000 cases and 2800 perinatal deaths), SIDS (2000 deaths), respiratory syncytial virus bronchiolitis (22,000 hospitalizations and 1100 deaths), acute otitis media (3.4 million outpatient visits), otitis media with effusion (110,000 tympanostomies), asthma (1.8 million outpatient visits, 14 deaths), and fire-related injuries (10,000 outpatient visits, 590 hospitalizations, and 250 deaths). The overall cost of direct medical expenditures was $4.6 billion and loss of life costs of $8.2 billion.

We are aware of only one study carried out in the UK. Petrou and colleagues looked at the longer term economic impacts of smoking in pregnancy using linked birth and death data. [25] The study population comprised all infants born to women who both lived and delivered in Oxfordshire or West Berkshire during the period 1 January 1980–31 December 1989 (n = 119,028). The cost of each hospital admission, including the initial birth admission, was estimated by multiplying the length of stay by the unit cost of the respective specialty (1998–1999 prices). The effect of maternal smoking behaviour on cumulative 5-year hospital inpatient service utilisation and costs was analysed in a series of multivariate analyses, taking account of confounding clinical and socio-demographic factors. Infants born to women who reported smoking during pregnancy were hospitalised for a significantly greater number of days than infants born to women who had either never smoked or had smoked in the past. Over the first 5 years of life, the adjusted mean cost difference was estimated at £462 when infants born to women who smoked at least 20 cigarettes per day were compared to infants of non-smoking mothers, and £307 when infants born to women who smoked 10–19 cigarettes per day were compared to infants of non-smoking mothers.

Researchers in the USA have developed a software application which estimates mortality, morbidity and economic costs of smoking during pregnancy. The Maternal and Child Health Smoking Attributable Mortality, Morbidity and Economic Costs

(MCH SAMMEC) enables individual US states and other areas to estimate pregnancy related, smoking-attributable costs for their populations. [26] The MCH SAMMEC model uses a prevalence-based analysis of smoking-attributable mortality, and mean costs of infant neonatal care. The calculation of each of the impact measures is based upon an estimated smoking attributable fraction (SAF) derived from either relative risk or multivariate analysis approaches. The multivariate analysis to derive the SAF for direct health care costs is a different approach than previously adopted by the original SAMMEC model which used attributable risks. [27]

The MCH SAMMEC outcomes include infant mortality, percentage of infants with low birth weight, birth weight in grams, probability of admission to the neonatal intensive care unit (NICU), number of infant hospital days, and total neonatal health care costs (measured by the monetary cost for all health care services provided to a neonate in the hospital setting).

The AR approach applies SAFs to health care expenditures to estimate the costs attributable to smoking, but does not account for complex interactions between smoking and other factors such as age, ethnicity and gender, or isolate effects compared to other factors such as alcohol. Changing patterns of smoking during the period of pregnancy are also not incorporated due to lack of sound epidemiological evidence of their impact. Data for the MCHSAMMEC model come from PRAMS (n=25,000), and from the MedStat Corporation which enabled the estimation of the numbers of nights spent in NICUs from insurance claims data.

The published paper describing MCH SAMMEC paper does not provide any estimates of health costs; it is instead a simple introduction to the use of the software, which is available as a web based tool. The software has since been used by evaluators modelling the wider health care cost implications of trials of smoking cessation interventions amongst pregnant women. [28]

The MCH SAMMEC model has been used by Adams et al to demonstrate that if 25 percent of smokers on Medicaid were reached and between 13,500 and 18,000 pregnant women smokers quit, an estimated saving of between $10 and $13 million could be realized, in excess of national Medicaid-covered neonatal expenditure. [29] If the cost of the counseling intervention was $30, net savings of between $8 and $11 million could be generated, based on low and high estimates of programme effectiveness. The cost to the Medicaid system in the United States was estimated by CDC in 2005, using the MCH SAMMEC model. The total cost of smoking-attributable neonatal health care costs for the Medicaid system total almost $228 million, or about $738 per smoker whose delivery is paid for by state Medicaid programs. Smoking amongst pregnant women on Medicaid was on average 2.5 times that of pregnant women without Medicaid coverage in the United States. [30]

It is unclear how the MCS SAMMEC model might be applied in a UK setting. A key problem is the source of health care costs. Costs in the United States are largely estimated from insurance data, with different cost and wage schedules and different profit margins. It is therefore probable that costs in the United States differ from other countries, with the totalling up of costs into aggregate sums magnifying such discrepancies. Furthermore, it is unclear whether the attributable risk data used in

MCH SAMMEC is generalisable beyond the USA, in populations with different demographic structures.

B. Review of reviews

In our original proposal, we had planned to conduct a scoping review of the epidemiological literature to identify all relevant maternal and infant outcomes. However, just prior to the start of this project, one of us (KP) had conducted such a review (Pickett KE and Wakschlag LS. Smoking in pregnancy. In: Preece, PM, Riley, E (Eds). Drugs in Pregnancy -The Price for the Child: Exposure to Fetal Teratogens and Long Term Neurodevelopmental Outcomes. London: Mac Keith Press, forthcoming 2009). This informed our 'review of reviews'.

A systematic 'review of reviews' was used to establish the magnitude of the associations between smoking in pregnancy and all maternal and infant outcomes identified in the review of the epidemiological literature.

We searched within the following databases: Ovid Medline (1950- March, week 3, 2008), Embase (1980-2008, week 13) and the Cochrane library. CRD filters were used to identify only the systematic reviews. The search strategy is reported in Appendix I.

The search in Ovid Medline returned 260 papers on maternal outcomes and 519 on infant outcomes; EMBASE returned 39 papers on maternal outcomes and 60 on infant outcomes. No relevant results were found within the Cochrane database.

	Total Papers	Relevant papers
Maternal outcomes	299	15
Infant outcomes	579	20

Table 3: Numbers of reviews identified as relevant

Some papers were duplicated across databases, and were eliminated. We also excluded papers published in languages other than English. Two independent raters also examined a random 10% of retrieved papers to validate relevance. The search resulted in 15 relevant reviews of maternal outcomes and 20 reviews of infant outcomes (some reviews covered more than one outcome).

A template was designed for data extraction (Appendix II) and estimates were sought for the effect of any smoking during pregnancy at any time, as well as more detailed information on the effect of quitting, of dose, and to timing of smoking. Tables summarizing these reviews are included in Appendix II. Results are summarized here.

Maternal outcomes

Two reviews were found for ectopic pregnancy, with relative risk estimates for any smoking ranging from 1.77-2.0. [8, 31] One review reported a dose-response effect, with odds ratios of 1.6 for women who smoked 1-5 cigarettes per day and 3.5 for

women who smoked >20. [31] Recurrence of ectopic pregnancy also increased with smoking. Four reviews of spontaneous abortion were found and relative risk estimates were between 0.83-2.0. [9, 32-34] The PAR was estimated at 3%-7.5% in the USA in one of the reviews. [32] A dose-response effect was reported in two reviews with relative risk increasing with the number of cigarettes smoked per day. [9, 33] Five reviews were identified for placenta previa, with the relative risk of any smoking between 1.28-4.4 [8, 35-38]. Two of the reviews reported a dose response effect, with relative risks of 1.4 for women who smoked less than 10 cigarettes per day and up to 2.0 for women who smoked at least 10 cigarettes per day. [35, 37] In six reviews of abruptio placenta, estimates of relative risk for any smoking were between 1.23 to 4.0. [8, 34, 35, 37-39] The estimated PAR was 15% to 25% and one review reported a significantly stronger association in non-USA than in USA studies. [37, 39] Four reviews reported a dose- response effect, with a relative risk of 1.2 to 2.1 for women who smoked at most 20 cigarettes per day and from 1.7 to 2.9 for women who smoked more than 20 cigarettes per day. One review also reported an increase in the relative risk with increased number of years of smoking.[35] Five reviews of preterm premature rupture of membranes had estimates of relative risk of any smoking from 1.6-3.0. [8, 37, 38, 40, 41] Four reviews identified a protective effects of snoking for pre-eclampsia, with risk of pre-eclampsia is approximately halved among smokers compared to non-smokers. [8, 38, 42, 43]. A dose- response relationship was reported in two reviews. [42, 43] One review reported a relative risk of 0.77 to 0.87 for women who smoked less than 10 cigarettes per day and from 0.61 to 0.67 for women who smoked at least 10 cigarettes per day. [42]

Infant outcomes

Seven reviews reported the impact of smoking on preterm delivery, with relative risks between 1.1-1.7. [34, 37, 38, 44-47] Two of the reviews reported a dose- response effect with a relative risk of 1.2 to 1.4 for light smokers and 1.31 to 1.7 for heavy smokers. [37, 45] PAR of 12% - 15% were reported for the UK. [46] Seven reviews of the effect of smoking on low birth weight were obtained and they reported relative risks from 1.4 to 3.0. %.[9, 32, 37, 44, 46-48] A reduction of mean birth weight of 70 to 250g due to smoking during pregnancy was reported. [9, 37, 46, 48] A dose-response effect was also reported in two reviews, and one of them reported an increase in the relative risk by a factor of 1.51 for every 10 cigarettes smoked. [9, 37] A PAR of 29% - 39% was reported for the UK. [46] Fifteen reviews of maternal smoking and SIDS reported a relative risk between 1.4 and 8.4. [32, 34, 37, 38, 47, 49-58] As most mothers smoking during pregnancy continued smoking after pregnancy, it was difficult in these reviews to separate prenatal and post natal exposure. It is also difficult to separate the contribution of other environmental tobacco exposure. The age at death of infant varied within as well as between the reviews. One review reported a greater relative risk in premature neonates when compared to neonates and infants born at full term.[34] Six of the reviews reported a dose- response effect with a relative risk of 2.2 to 6.6 for light to moderate smokers and 4.8 to 7.2 for heavy smokers [32, 34, 49, 52-54] A PAR of 40% was reported for New Zealand.[58]

The relative risk of asthma was between 1.3 to 2.0 in the 3 reviews obtained. [46, 50, 51] The reviews did not separate prenatal from post-natal exposure. The reviews also

included studies in children beyond the age of infancy. Four reviews of otitis media were obtained. [50-52, 59]. The reported relative risks of otitis media ranged from 1.0 to 3.0. The reviews did not separate maternal smoking during pregnancy from other forms of tobacco smoke exposure to infants. The reviews also varied on the age of children considered. One review looked at early childhood whilst one looked at children during their first 3 years of life. Four reviews were identified that examined smoking in pregnancy in relation to upper and lower respiratory tract infections and relative risk estimates were between 1.6-2.8. [46, 50-52] Three of the reviews reported a dose-response effect. [46, 50, 52] The reviews did not separate maternal smoking during pregnancy from other forms of tobacco smoke exposure to infants. The age range considered in the reviews also varied, with one of the reviews considering children up to 3 years. We identified 4 reviews covering smoking and perinatal and infant mortality other than SIDS. [9, 32, 37, 38] Relative risks ranged from 1.2-1.6. . PAR of 3.4% to 10.5% were reported for the USA. [32, 37] One review reported a dose- response effect whilst one review reported no clear dose-response effect. [9, 37] Six reviews on maternal smoking during pregnancy and fetal growth restrictions were identified. The relative risks ranged from 2.3 to 2.8.[32, 37, 38, 46-48] A PAR of 18% was reported. [48] Three of the reviews reported a dose-response effect with a relative risk of 2.4 to 2.68 for light to moderate smokers and 2.88 for heavy smokers. .[32, 37, 46]

We found no reviews of the effect of smoking on RDS or RSVB

C. Evidence synthesis and cost estimation

Maternal and infant outcomes

Estimation of the costs of smoking amongst pregnant women fall into two major categories: costs associated with outcomes amongst pregnant women themselves, and costs associated outcomes amongst infants as a consequence of their mothers' smoking.

The estimation of NHS costs first requires strict specification of the outcomes using ICD-10 definitions. ICD-10 codes were matched to the maternal and infant outcomes identified in the literature reviews. These ICD codes were then used to identify the total number of episodes for 2005/6. The relevant ICD-10 codes are listed in Table 4.

Table 4: ICD-10 codes and HRGs for maternal and infant outcomes

Maternal Outcomes	HRG	ICD-10
• Ectopic pregnancy	M15	O00.0 Abdominal pregnancy O00.1 Tubal pregnancy Fallopian pregnancy Rupture of (fallopian) tube due to pregnancy Tubal abortion O00.2 Ovarian pregnancy O00.8 Other ectopic pregnancy Pregnancy: • cervical • cornual • intraligamentous • mural O00.9 Ectopic pregnancy, unspecified

• Spontaneous abortion	M09	O03
• Placenta previa (PP)	N12	O44 O44.0 Placenta praevia specified as without haemorrhage Low implantation of placenta specified as without haemorrhage O44.1 Placenta praevia with haemorrhage Low implantation of placenta, NOS or with haemorrhage Placenta praevia:
• Abruption placenta (AP)	N12	O45 O45.0 Premature separation of placenta with coagulation defect Abruptio placentae with (excessive) haemorrhage associated with: · afibrinogenaemia · disseminated intravascular coagulation · hyperfibrinolysis · hypofibrinogenaemia O45.8 Other premature separation of placenta O45.9 Premature separation of placenta, unspecified Abruptio placentae NOS
• Preterm Premature Rupture of Membranes (PPROM)	N12	O42 O42.0 Premature rupture of membranes, onset of labour within 24 hours O42.1 Premature rupture of membranes, onset of labour after 24 hours O42.2 Premature rupture of membranes, labour delayed by therapy O42.9 Premature rupture of membranes, unspecified
• Pre-eclampsia (PE)	N12	O140, O141, O142 O14 O14.0 Moderate pre-eclampsia O14.1 Severe pre-eclampsia O14.9 Pre-eclampsia, unspecified
Infant Outcomes		
• Preterm delivery < 3 weeks	N01-N05	O60 Onset (spontaneous) of labour before 37 completed weeks of gestation O60.0 Preterm labour without delivery O60.1 Preterm labour with preterm delivery Preterm labour with delivery NOS O60.2 Preterm labour with term delivery
• Low birth weight (LBW) (< 2500g)	N05	P07 P07.0 Extremely low birth weight

		Birth weight 999 g or less. P07.1 Other low birth weight Birth weight 1000-2499 g.
• Sudden Infant Death Syndrome (SIDS)	E28	R96 R96.0 Instantaneous death R96.1 Death occurring less than 24 hours from onset of symptoms, not otherwise explained Death known not to be violent or instantaneous for which no cause can be discovered Death without sign of disease
• Respiratory distress syndrome (RDS)	P04	P22 P22.0 Respiratory distress syndrome of newborn Hyaline membrane disease P22.1 Transient tachypnoea of newborn P22.8 Other respiratory distress of newborn P22.9 Respiratory distress of newborn, unspecified
• Asthma	P01	J45-J46.X
• Respiratory syncytial viral bronchitis (RSVB)	P04	J12.1 Respiratory syncytial virus pneumonia
• Otitis media (OM)	P03	H66.9 Otitis media, unspecified H67* Otitis media in diseases classified elsewhere H67.0* Otitis media in bacterial diseases classified elsewhere H67.1* Otitis media in viral diseases classified elsewhere H67.8* Otitis media in other diseases classified elsewhere
• Upper and lower respiratory infections (URI/LRI)	P03/P04	J00.X – J06.9 J22.8-J39.8
• Perinatal death		P95 Fetal death of unspecified cause Deadborn fetus NOS Stillbirth NOS
• Foetal growth restriction		

ICD-10 codes were then matched to HRGs to identify relevant unit costs. However, unit costs are only available at the top-level for the HRG, so each HRG will include a significant number of different ICD-10 groups. It is not possible to disaggregate cost data to a more accurate level, and therefore the unit costs are an approximation and may be an underestimate of the actual NHS cost.

Costs were taken from the NHS Reference Cost schedules for 2005/6. The mean costs for elective and non-elective care were calculated, weighted by the number of cases. The following table summarises the unit costs of the maternal and infant outcomes used in this study.

Reference costs weighted by elective and non-elective activity		
HRG Code	**HRG Label**	**National Average Unit Cost**
E28	SIDS	£1,173*
M09	Threatened or Spontaneous Abortion	£492*
M15	Non-Surgical Treatment of Ovary, Tube, or Pelvis Disorders	£876*
N01	Neonates - Died <2 days old	£639*
N02	Neonates with Multiple Minor Diagnoses	£982*
N03	Neonates with one Minor Diagnosis	£727*
N04	Neonates with Multiple Major Diagnoses	£3,280*
N05	Neonates with one Major Diagnosis	£1,486*
N12	Antenatal Admissions not Related to Delivery Event	£588*
P01	Asthma or Wheezing	£699*
P03	Upper Respiratory Tract Disorders	£619*
P04	Lower Respiratory Tract Disorders without Acute Bronchiolitis	£1,166*
P05	Major Infections (including Immune Disorders)	£2,422*
P06	Minor Infections (including Immune Disorders)	£815*

Source: *Department of Health (2007) ** RAND (1998)

Table 5: Unit costs of maternal and infant outcomes

Costs of caring for low birth weight and premature babies are extremely variable. It is unclear which measure is the most appropriate to use when estimating the cost attributable to smoking in pregnancy. The greatest costs are attributable to the <1000g category or the under 27 weeks gestation delivery as length of stay and therefore costs are inversely correlated with birth weight and weeks preterm. Several US studies have estimated the cost of low birth weight. [60, 61] Lightwood et al estimated the cost of very low birth weight babies in the US as $56,599 (1995 prices), whilst moderately low birth weight babies cost $6,179. [20] The current UK equivalent costs are £54,967 and £6,002 respectively. [Costs are converted from 1995 US dollars at the exchange rate (0.64) at the time of the study and inflated using the HCHS index. The index (based on 1988/9 index year = 100) was 166.0 for 1995/6 and 251.9 for 2006/7.]

A more recent study published in 2007 by Russell et al divided costs into extreme immaturity (ICD-9-CM codes 765.00-765.09) which lists babies born with a birth

weight of under 1000 grams, and other preterm births with a birth weight of <2500 grams. [62] The costs in 2001 US dollars were $36,800 and $7,500 respectively. The equivalent costs in UK 2006/7 prices are £30,077 and £6,130 respectively. [Converted using exchange rate 0.67, and uprated using HCHS index 2001/2=206.5, 2006/7=251.9]

The costs used in the current study were estimated using a separate analysis of data from the Oxford Record Linkage Study, kindly supplied by Dr. Stavros Petrou of the Health Economics Research Centre, University of Oxford.

The following tables present the cost of the initial hospitalisation of the baby based on weeks of gestation and birth weight. The data show that the initial hospitalisation costs fall as the length of gestation increases, with the exception of the 20-23 week group, which can be explained by the low survival rate. Based on birth weight, as expected, initial hospitalisation costs are lower as birth weight increases.

Table 6: Cost of initial hospitalisation by birth weight

Gestation	Mean	Std Deviation	N
20-23 weeks	£1,261	£2790	15
24-27 weeks	£7,362	£9692	222
28-31 weeks	£6,920	£4909	589
32-36 weeks	£1,917	£1586	4,841
37 weeks and more	£824	£940	90,234

Table 7: Cost of initial hospitalisation by birth weight

Birth weight	Mean	Std Deviation	N
< 1000g	£6,430	£9,642	264
1000-1499g	£5,779	£5,310	523
1500-1999g	£3,234	£3,119	1,341
2000-2499g	£1,606	£1,256	4,853
> 2500g	£835	£978	107,850

References:

Separate analyses of Oxford Record Linkage Study data. Data supplied by Dr. Stavros Petrou. [63]

As the published NHS reference costs are only available for top level HRG groups, which cover a wide range of different procedures, and can only be used as a very rough approximation of the actual cost of the outcomes identified, an additional literature search was conducted to identify studies which had undertaken analyses using more specific outcomes. This was only necessary for the maternal outcomes, as the reference costs and Oxford Record Linkage Study data were specific enough for the infant outcomes.

The table below shows the unit costs for maternal outcomes as derived from the search of published studies. It was not possible to identify current UK costs for all outcomes, so where necessary US based costs have been converted from dollars to UK pounds sterling using the exchange rate that prevailed at the time of the study using the FX Converter (http://www.oanda.com/convert/classic), and then inflated to current UK prices using the HCHS inflation index.

These cost estimates provide a higher cost estimate of the cost of maternal outcomes, but this estimate is likely to be more reflective of the true cost since it is based on a more narrow definition of the outcome.

Outcome	Cost (2006/7 prices)	Source
Medical Termination of Pregnancy	£6,480	Department of Health (2008)
Preeclampsia	£9,000	Meads et al (2008)
Miscarriage	£756	De Sutter et al (2002)
Spontaneous Abortion	£1,190	Petrou et al (2006)
Ectopic pregnancy	£1,791	Alexander (1996)
PPROM	£4,103	Grable (2002)
Placenta previa	£10,404	Adams (1998)
Abruptio placenta	£7,859	Adams (1998)

Table 8: Unit costs for maternal outcomes

D. Attributing episodes to smoking

The results of the 'review of reviews' were used to estimate the cost of smoking in pregnancy, based on maternal and infant outcomes.

Attributable Risks

Pregnancy costs attributable to smoking were calculated using the population attributable risk percentage as outlined below.

$$\frac{E * (RR - 1)}{E * (RR - 1) + 1}$$

Where E = prevalence of exposure and RR = relative risk. The mid-range estimate from the 'review of reviews' was chosen for each outcome.

The percentage of pregnant women smoking throughout their pregnancy was estimated to be 17% in 2005. [1] This figure is taken as a conservative estimate and excludes mothers who smoked for only part of their pregnancy.

For example, if the prevalence of smoking is 17%, the relative risk is 1.89 and there are 9,719 cases of ectopic pregnancy in the population we can estimate that:-

$$= \frac{0.17 * (1.89 - 1)}{0.17 * (1.89 - 1) + 1}$$

$$= \frac{0.17 * (1.89 - 1)}{(0.17 * (0.89)) + 1}$$

$$= \frac{0.1513}{1.1513}$$

$$= 0.1314$$

This suggests that 13.14% of all cases of ectopic pregnancy are attributable to smoking. Therefore, for an endpoint with 9,719 cases per annum, we attribute 1,277 to smoking.

Therefore, based on a unit cost of £876, we estimate the cost of the outcome attributable to smoking to be approximately £1,115,314.

The table below shows the number of cases attributable to smoking for maternal and infant outcomes, using the attributable risk methodology outlined above. In all cases the relative risk is greater for smokers when compared to non-smokers, with the exception of pre-eclampsia for which smoking reduces risk.

Table 9: Cases due to smoking

Pregnancy outcomes

	Relative risk	Total Cases	Population attributable risk percentage	Cases due to Smoking
Ectopic Pregnancy	1.89	9,719	0.1314	1,277
Pre-eclampsia	0.59	13,101	-0.0749	-982
Spontaneous Abortion	1.42	46,200	0.0659	3,045
Placenta Previa	2.84	4,731	0.2383	1,127
Abruption placenta	2.62	1,541	0.2159	333
PPROM	2.30	49,673	0.1810	8,991

Infant outcomes

	Relative risk	Total Cases	Population attributable risk percentage	Cases due to Smoking
LBW <1000	2.20	2,400	0.1694	407
LBW 1000-1499	2.20	3,100	0.1694	525
LBW 1500-1999	2.20	6,600	0.1694	1,118
LBW 2000-2499	2.20	23,800	0.1694	4,033
Asthma	1.65	1,574	0.0995	157
URI/LRI	2.20	8,461	0.1694	1,434
SIDS	4.90	4	0.3987	2
Otitis media	2.00	2,036	0.1453	296

5. Main findings

Table 10 presents the estimated economic cost of smoking in pregnancy for maternal and infant outcomes during pregnancy and for the year following birth. These costs are based on an NHS perspective, and so represent a conservative estimate of the true economic cost.

It should be noted that the total societal cost of smoking in pregnancy extends beyond the first year, and potentially includes higher educational costs, costs to the judicial system, and costs of health care beyond the first year for mothers and children.

Table 10 presents the costs using top level HRG costs from the NHS Reference Costs. [64] These costs provide a lower bound estimate, being based on top level HRG codes. Table 11 presents the maternal cost estimates calculated using literature based unit costs.

The total annual cost of smoking during pregnancy is estimated to be approximately £8.1 million for maternal outcomes when using top level HRG reference costs. However, when more specific literature based costs are substituted the total cost rises to almost £64 million. The total cost of infant outcomes is an estimated £23.5 million, with the majority of the cost (£22 million) being attributable to the care of low birth weight babies. However, using an alternative methodology using pre-term births as the endpoint the total cost falls to £12 million (Table 12), due to the lower relative risk for preterm delivery.

Table 10

Disease costs: Smoking in Pregnancy (NHS Reference costs)

Pregnancy outcomes	Unit cost	Relative risk	Cases	Population attributable risk percentage	Cases due to Smoking	Cost/smoking
Ectopic Pregnancy	£876	1.89	9,719	0.1314	1277	£1,118,342
Pre-eclampsia	£588	0.59	13,101	-0.0749	-982	-£577,049
Spontaneous Abortion	£492	1.42	46,200	0.0659	3045	£1,497,113
Placenta Previa	£588	2.84	4,731	0.2383	1127	£662,704
Abruption placenta	£588	2.62	1,541	0.2159	333	£195,622
PPROM	£588	2.30	49,673	0.1810	8991	£5,285,613
						£8,182,346

Infant outcomes	Unit cost	Relative risk	Cases	Population attributable risk percentage	Cases due to Smoking	Cost/smoking
LBW <1000	£8,978*	2.20	2,400	0.1694	407	£3,650,895
LBW 1000-1499	£8,069*	2.20	3,100	0.1694	525	£4,238,278
LBW 1500-1999	£4,516*	2.20	6,600	0.1694	1118	£5,049,578
LBW 2000-2499	£2,243*	2.20	23,800	0.1694	4033	£9,044,124
Asthma	£699	1.65	1,574	0.0995	157	£109,444
URI/LRI	£892	2.20	8,461	0.1694	1434	£1,279,216
SIDS	£1,173	4.90	4	0.3987	2	£1,870
Otitis media	£619	2.00	2,036	0.1453	296	£182,977
						£23,556,380

* Separate analyses of Oxford Record Linkage Study data. Data supplied by Dr. Stavros Petrou. [63]

Table 11

Disease costs (Literature based costs)

Pregnancy outcomes	Unit cost	Relative risk	Cases	Population attributable risk percentage	Cases due to Smoking	Cost/smoking
Ectopic Pregnancy	£1,791	1.89	9,719	0.1314	1277	£2,287,534
Pre-eclampsia	£9,000	0.59	13,101	-0.0749	-982	-£8,833,986
Spontaneous Abortion	£6,480	1.42	46,200	0.0659	3045	£19,729,090
Placenta Previa	£10,404	2.84	4,731	0.2383	1127	£11,727,933
Abruption placenta	£7,859	2.62	1,541	0.2159	333	£2,615,095
PPROM	£4,103	2.30	49,673	0.1810	8991	£36,889,139
						£64,414,804

Table 12

Costs of pre-term births attributable to smoking

	Unit cost	Relative risk	Cases	Population attributable risk percentage	Cases due to Smoking	Cost/smoking
Pre-term birth (20-23 weeks)	£1,760	1.40	550	0.0637	35	£61,641
Pre-term birth (24-27 weeks)	£10,280	1.40	2,600	0.0637	166	£1,701,744
Pre-term birth (28-31 weeks)	£9,663	1.40	4,900	0.0637	312	£3,014,795
Pre-term birth (32-36 weeks)	£2,677	1.40	34,700	0.0637	2209	£5,914,611
						£10,692,791

Smoking Cessation for pregnant women

The economic burden attributable to smoking during pregnancy is considerable. Here we present some simple calculations which indicate the potential returns from a low-cost smoking cessation intervention directed at pregnant women.

The range of estimates for the effectiveness of smoking cessation interventions in pregnancy is considerable.

The evidence base for cessation services for pregnant smokers is very limited, although studies have demonstrated that the costs of these interventions can be very low. Consequently, effectiveness rates do not have to be high in order for these programmes to pay for themselves, whereby the costs of service provision more than outweigh the savings from the reduced rates of adverse outcomes as a result of smoking during pregnancy. Hajek et al evaluated a programme of midwife advice, written material and mutual support, where women were paired with other women for assistance in quitting. [6] The intervention was very low cost, approximately £4 per patient, and at six months following the birth of their child 2.9% of the intervention group were abstinent compared to 2.5% of the control.

Lee et al conducted a survey of NHS smoking cessation services. [65] Three key services were identified and the results were used to create some simple simulations with respect to potential cost savings to the NHS. However, the absence of controls in these studies makes it very difficult to reliably attribute quitting to the programme.

Service	Resources	Coverage	Total cost (annual)	Quitters
1	Full time midwife Registered nurse Administrator	864 pregnant smokers, of which 267 set a quit date.	£46,459 (£53.77/smoker and £174/smoker setting quit date)	99 (11.46% for all smokers, 37.08% of smokers setting quit date)
2	Clinician (home visits and telephone calls)	1,512 pregnant smokers, of which 120 set a quit date	£21,118 (£13.97/smoker and £175.98/smoker setting quit date)	61 (4.03%, 50.83%)
3	Two clinicians 1.7 midwives Administrator	864 pregnant smokers, 215 setting quit date	£86,584 (£100.21/smoker and £402.72/smoker setting quit date)	105 (12.15%, 48.84%)

Source: Adapted from Lee M, et al. (2006)

The estimates we use in this report are based upon the Cochrane review by Lumley et al. [5] The review was based on randomised and quasi-randomised trials of smoking cessation programs implemented during pregnancy, which included 64 trials. Fifty-one RCTs covering 20,931 women and six cluster-randomised trials covering 7,500

women provided data on smoking cessation and/or perinatal outcomes. The studies included in the review were varied in the intensity of the intervention and the extent of reminders and reinforcement through the pregnancy

The pooled results from 48 trials demonstrated a significant reduction in smoking in the intervention groups. The relative risk was 0.94 with a 95% confidence interval ranging from 0.93 to 0.95. This suggests a 6% reduction in the number of women smoking during their pregnancy. A total of 36 trials also included biochemical validation of smoking status, and in these trials smoking cessation interventions had the same impact with a relative risk of 0.94 and a slightly wider 95% confidence interval from 0.92 to 0.95.

Smoking cessation interventions were shown to reduce the occurrence of low birth weight with a relative risk of 0.81 with a 95% confidence interval from 0.70 to 0.94). The impact upon preterm births was a relative risk of 0.84 (95% confidence interval from 0.72 to 0.98).

Cessation studies reporting birth outcomes also demonstrated a 33 gram increase in mean birth weight (95% confidence interval from 11 g to 55 g). Changes in stillbirths, perinatal and neonatal mortality were not statistically significant due to the limited power of the studies. Notably, two trials were identified which demonstrated that a programme of rewards plus social support could reduce smoking rates much more successfully than other strategies, with a relative risk of 0.77 (95% confidence interval ranging from 0.72 to 0.82.

Taking an effectiveness rate of 6%, and assuming that all pregnant smokers receive the intervention, the intervention will yield positive economic cost savings up to an outlay of £13.60 per smoker, based on the NHS reference cost scenario. This would represent approximately half an hour of practice nurse time (£23.00 per hour [66]) plus £2.10 worth of materials, which could cover various printed self-help materials and booklets. However, it should be noted that when literature based costs are used in these calculations, net economic savings are experienced up to a programme cost of £37 per smoker, up to which point we would experience dominance in the presence of any positive health benefits (positive cost savings and positive health outcomes).

A range of different scenarios can be constructed using different cessation rates and NHS Reference Costs. Assuming 50% of smokers are given half, positive economic benefits would be generated provided the effectiveness rate was at least 5.6%.

It should be noted that these estimates are made purely from an economic perspective and do not include health benefits. Therefore, under such circumstances, if we assume positive health benefits to either mother or baby or, as is the most likely scenario both mother and baby, the intervention would be beneficial. It should also be noted that these benefits are confined solely to just one year after birth. Therefore health care cost savings beyond the first year, and also additional societal costs are excluded from these calculations.

6. Contribution to Consortium themes

This study contributes to four of the Consortium themes: it increases our understanding of the **risks to health** of **smoking** in pregnancy for mothers and children in the first year of life and, through an estimation of the economic costs of smoking in pregnancy, provides direct evidence for policy **incentives and regulation** related to smoking cessation interventions for pregnant women. As smoking in pregnancy is strongly determined by socioeconomic status, this study indirectly addresses an important source of **health inequalities** for mothers and children.

7. Conclusions/Considerations

This project estimates, for the first time, the costs to the NHS in the UK of maternal and infant consequences of smoking in pregnancy.

Costs related to maternal outcomes (including increased risk of spontaneous abortion, ectopic pregnancy, placenta previa, abruptio placenta, preterm premature rupture of membranes and decreased risk of pre-eclampsia) are estimated to cost the NHS between £8 million and £64 million per year.

Costs related to infant outcomes (including increased risk of preterm delivery, low birth weight, Sudden Infant Death Syndrome, perinatal mortality, asthma, otitis media, and upper and lower respiratory infections) are estimated to cost the NHS between £12 million and £23.5 million per year.

These estimates are conservative. As well as being confined to NHS costs, without consideration of costs related to health and health-related quality of life or years of potential life lost, our estimates are restricted to the first year of life. As smoking in pregnancy has long-term effects on health, and may also have long-term effects on cognition and behaviour, with consequential costs to education, social work and judicial systems, the real costs to society are clearly much higher. In fact, smoking in pregnancy is likely to have intergenerational effects on health and well-being, the costs of which can only be guessed at.

We found no evidence that the entrenched socioeconomic inequalities in smoking in pregnancy are associated with differential impacts of smoking, or indeed of differential effectiveness of smoking cessation interventions.

Smoking cessation interventions for pregnant women have been shown to be effective in significantly increasing quitting rates. We estimate that spending between £13.60 - £37 per pregnant smoker would yield one-year positive cost savings for the NHS in purely financial terms, not taking into account the positive health benefits for mother and baby. Further research is needed to estimate the non-NHS and long-term costs of smoking in pregnancy, and the enhanced investment in smoking cessation interventions which would be cost effective within such an extended cost framework.

8. Dissemination/Outputs

We plan to submit abstracts for presentation at relevant academic conferences.

We also plan to submit a research paper to the peer-reviewed journal Tobacco Control.

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Appendices

Appendix I

Database: Ovid MEDLINE(R) <1950 to March Week 2 2008>
Search Strategy: Maternal Outcomes
---

1 Smoking/ (87387)
2 exp Pregnancy/ (608875)
3 pregnan$.mp. [mp=title, original title, abstract, name of substance word, subject heading word] (628564)
4 2 or 3 (652834)
5 1 and 4 (6905)
6 exp Pregnancy, Ectopic/ (11463)
7 exp Abortion, Spontaneous/ (24616)
8 exp Placenta Previa/ (1946)
9 exp Abruptio Placentae/ (1533)
10 exp Fetal Membranes, Premature Rupture/ (4354)
11 PPROM.mp. [mp=title, original title, abstract, name of substance word, subject heading word] (283)
12 exp Pre-Eclampsia/ (18576)
13 ecclampsia$.mp. [mp=title, original title, abstract, name of substance word, subject heading word] (5)
14 or/6-13 (59811)
15 5 and 14 (533)
16 limit 15 to humans (525)
17 limit 16 to "reviews (sensitivity)" (260)
18 from 17 keep 1-260 (260)

Search Strategy: Infant Outcomes
---

1 exp Smoking/ (88359)
2 exp Pregnancy/ (608559)
3 pregnan$.mp. [mp=title, original title, abstract, name of substance word, subject heading word] (628239)
4 2 or 3 (652485)
5 1 and 4 (6950)
6 exp Obstetric Labor, Premature/ (12061)
7 exp Premature Birth/ (1411)
8 exp Infant, Premature/ (31548)
9 exp Infant, Low Birth Weight/ (19251)
10 exp Sudden Infant Death/ (6134)
11 SIDS.mp. [mp=title, original title, abstract, name of substance word, subject heading word] (2642)
12 exp Respiratory Distress Syndrome, Newborn/ (12053)
13 exp Perinatal Mortality/ (29)
14 (perinatal adj1 death).mp. [mp=title, original title, abstract, name of

substance word, subject heading word] (1443)
15 or/6-14 (71918)
16 exp Asthma/ (83778)
17 exp Respiratory Syncytial Virus Infections/ (3008)
18 exp Otitis Media/ (18995)
19 exp Respiratory Tract Infections/ (231382)
20 or/16-19 (324571)
21 limit 20 to "all infant (birth to 23 months)" (38952)
22 5 and 15 (1017)
23 5 and 21 (94)
24 22 or 23 (1090)
25 limit 24 to humans (1080)
26 limit 25 to "reviews (sensitivity)" (518)
27 from 26 keep 1-518 (518)

Appendix II: Evidence Tables for 'Review of Reviews' of Maternal Outcomes

Ectopic Pregnancy

Reference	**Period Covered**	**Number of studies included for review**	**Is it a Meta-analysis**	**Pooled Odds Ratio/ Relative Risk (95% CI)**	**Odds Ratio/ Relative Risk Range**	**Dose-response effect**	**Comments**
Castles et al[8]	1966 to May 1995	9	Yes	1.77 (1.31, 2.22)	N/A	-	
Nusbaum et al[31]	Not specified	5	No	N/A	2.0	Yes.	

Spontaneous Abortion

Reference	**Period Covered**	**Number of Studies included in the review**	**Is it a Meta-analysis**	**Pooled Odds Ratio/ Relative Risk (95% CI)**	**Odds Ratio/ Relative Risk Range**	**Dose-response effect**	**Comments**
Walsh[9]	Not specified	5	No	N/A	1.34 to 1.68	Yes	
DiFranza and Lew[32]	All published articles regardless of year of publication	13	Yes	*1.24 (1.19,1.30) † 1.32 (1.18,1.48)	N/A	-	PAR 3% to 7.5% in the USA. 7 cohort studies. 6 case control studies.
Hughes and Brennan[33]	1966 to 1996	7	No	N/A	0.83 to 2.02.	Yes	Significant clinical heterogeneity among studies.
Haustein[44]	Not Specified	1	No	N/A	1.7	-	

* Pooled Relative Risk from cohort studies.
† Pooled Odds Ratio from case control studies.

Placenta Previa

Reference	Period Covered	Number of Studies included in the review	Is it a Meta-analysis	Pooled Odds Ratio/ Relative Risk (95% CI)	Odds Ratio/ Relative Risk Range	Dose-response effect	Comments
Castles et al[8]	1966 to May 1995	6	Yes	1.58 (1.04, 2.12)	N/A	-	
Andres[34]	Not specified	6	No	N/A	1.9 to 3.0	Yes	Only 1 study did not report a dose- response effect.
Fiaz and Ananth[35]	1966 to March 2000	9	Yes	1.6 (1.4, 1.8)	N/A	-	PAR 26% 8 studies from the USA.
Andres and Day[54]	Not specified	5	No	N/A	1.28 to 4.4	Yes	
Salihu and Wilson[63]	Not specified	4	No	N/A	1.36 to 2.6	Inconclusive	Some studies demonstrated a dose- response effect but others did not.

Abruptio Placenta

Reference	Period Covered	Number of Studies included in the review	Is it a Meta-analysis	Pooled Odds Ratio/ Relative Risk (95% CI)	Odds Ratio/ Relative Risk Range	Dose-response effect	Comments
Castles et al[8]	1966 to May 1995	8	Yes	1.62 (1.46, 1.77)	N/A	-	
Haustein[44]	Not specified	4	No	N/A	1.39	-	
Andres[34]	Not specified	4	No	N/A	1.86 to 2.5	Yes	
Ananth et al[37]	1966 to 1997	13	Yes	1.9 (1.8, 2.0)	N/A	Yes	Pooled PAR 15 to 20%.
Andres and Day[54]	Not specified	3	No	N/A	1.23 to 1.9	Yes	PAR 15% to 25% for the USA.
Salihu and Wilson[63]	Not specified	4	No	N/A	1.4 to 4.0	Yes	

Preterm Premature Rupture of Membranes (PPROM).

Reference	**Period Covered**	**Number of Studies included in the review**	**Is it a Meta-analysis**	**Pooled Odds Ratio/ Relative Risk (95% CI)**	**Odds Ratio/ Relative Risk Range**	**Dose-response effect**	**Comments**
Castles et al[8]	1966 to May 1995	6	Yes	1.70 (1.18, 2.25)	N/A	-	
French and McGregor[38]	Not specified	6	No	N/A	1.6 to 2.2	Yes	
Shubert et al[39]	Not specified	6	No	N/A	2.1 to 3.0	Yes	
Andres and Day[54]	Not specified	4	No	N/A	2.8 to 3.0	Yes	
Salihu and Wilson[63]	Not specified	1	No	N/A	1.70 to 2.25	-	

Pre-eclampsia

Reference	Period Covered	Number of Studies included in the review	Is it a Meta-analysis	Pooled Odds Ratio/ Relative Risk (95% CI)	Odds Ratio/ Relative Risk Range	Dose-response effect	Comments
Castles et al[8]	1966 to May 1995	5	Yes	0.51 (0.38, 0.64)	N/A	-	
Conde-Agudelo et al[41]	1966 to 1998	35	Yes	*0.68 (0.67, 0.69) †0.68 (0.57, 0.81	N/A	Yes	28 cohort studies. 7 case control studies.
England and Zhang[42]	1959 to March 2006	11	No	N/A	-	Yes	Up to 50% risk reduction. No reduction in pre-eclampsia risk among smokers for 2 of the studies.
Salihu and Wilson[63]	Not specified	2	No	N/A	-	-	Protective effect reported but OR/RR not quoted.

* Pooled Relative Risk from cohort studies.
† Pooled Odds Ratio from case control studies.

Review of Reviews for Infant Outcomes

Preterm Delivery

Reference	Period Covered	Number of studies included for review	Is it a Meta-analysis	Pooled Odds Ratio/ Relative Risk (95% CI	Odds Ratio/ Relative Risk Range	Dose-response effect	Comments
Haustein[44]	Literature published up to the review period.	1	No	N/A	-	-	Increased risk reported
Kaltreider and Kohl[45]	1970 to 1976	2	No	N/A	-	-	Increased risk reported
Shah and Bracken[48]	1966 to 1997	20	Yes	1.27 (1.21–1.33)	N/A	Yes	
Delpisheh et al.[49]	Not specified	7	No	N/A	-	-	PAR 12 to 15% in the UK. Increased risk reported
Triche and Hossain[51]	Not specified		No	N/A	-	-	Increased risk reported
Andres and Day[54]	Not specified	5	No	N/A	1.2 to 1.7	Yes	PAR 15% in the USA.

Reference	Period Covered	Number of studies included for review	Is it a Meta-analysis	Pooled Odds Ratio/ Relative Risk (95% CI	Odds Ratio/ Relative Risk Range	Dose-response effect	Comments
Salihu and Wilson[63]	Not Specified	2	No	N/A	1.15 to 1.69	-	

Low Birth Weight

Reference	Period Covered	Number of studies included for review	Is it a Meta-analysis	Pooled Odds Ratio/ Relative Risk (95% CI	Odds Ratio/ Relative Risk Range	Dose-response effect	Comments
Walsh[9]	Not specified	16	No	N/A	1.4 to 3.0	Yes	Suggested an increase in the relative risk by a factor of 1.51 for every 10 cigarettes smoked.
DiFranza and Lew[32]	Literature published up to the review period.	23	Yes	1.82 (1.67, 1.97)	-	-	PAR 11%-21% in the USA. 2 studies limited analysis to premature infants and 1 limited analysis to term infants.
Kaltreider and Kohl[45]	1970 to 1976	2	No	N/A	-	-	Increased risk reported
Delpisheh et al.[49]	Not specified	16	No	N/A	-	-	Reduction in mean birth weight of 174g

Reference	Period Covered	Number of studies included for review	Is it a Meta-analysis	Pooled Odds Ratio/ Relative Risk (95% CI	Odds Ratio/ Relative Risk Range	Dose-response effect	Comments
							PAR 29% - 39% in the UK.
Triche and Hossain[51]	Not specified		No	N/A	-	-	Increased risk reported
Valero De Bernabe[52]	Not specified	7	No	N/A	-	-	Reduction in mean birth weight of 150-250g
Andres and Day[54]	Not specified	7	No	N/A	1.64 to 2.21	Yes	Reduction in mean birth weight of 70 – 242g PAR 20%-30% in the USA.

SIDS

Reference	Period Covered	Number of studies included for review	Is it a Meta-analysis	Pooled Odds Ratio/ Relative Risk (95% CI	Odds Ratio/ Relative Risk Range	Dose-response effect	Comments
DiFranza and Lew[32]	Literature published up to the review period	11	Yes	2.98 (2.51, 3.54)	N/A	-	PAR 21.7%-40.7% in the USA No separation of utero exposure and exposure after birth for all the studies except one.
Haustein[44]	Literature published up to the review period	13	No	N/A	2.2 to 8.4	Yes	Risk is greater in premature neonates (relative risk up to 8.4)
Triche and Hossain[51]	Not specified		No	N/A	-	-	Increased risk reported
Anderson and Cook[53]	Literature published up to the review period	34	Yes	2.08 (1.82, 2.38)	N/A	Yes	Pooled adjusted OD reported for 16 studies only. Age of infants for most Studies was

Reference	Period Covered	Number of studies included for review	Is it a Meta-analysis	Pooled Odds Ratio/ Relative Risk (95% CI	Odds Ratio/ Relative Risk Range	Dose-response effect	Comments
							from 7 days up to 1 year; Some studies started at 1 month and other included up to 2 years.
Andres and Day[54]	Not specified	2	No	N/A	2.08 to 4	-	
Cook and Strachan[56]	April 1997 to June 1998	18	Yes	2.13 (1.86 to 2.43)	-	-	Reported the pooled OR of the thorax series. No distinction between maternal smoking during pregnancy and parental smoking after pregnancy. Focus of the paper is actually on ETS i.e. the infant's exposure to TS after birth. Figures given for

Reference	Period Covered	Number of studies included for review	Is it a Meta-analysis	Pooled Odds Ratio/ Relative Risk (95% CI	Odds Ratio/ Relative Risk Range	Dose-response effect	Comments
							the pooled OR are for mother smoking.
DiFranza et al[57]	Not specified	10	No	N/A	3.3 to 6.0	Yes	No separation of prenatal and post natal exposure.
Dybing and Sanner[58]	Not specified	4	No	N/A	2.08	Yes	No separation of prenatal and post natal exposure.
Fleming and Blair[59]	Not specified	7	No	N/A	2 to 3	Yes	Most mothers smoking during pregnancy continued smoking after pregnancy therefore difficult to separate prenatal and post natal exposure.
Golding[60]	Not specified	18	No	N/A	1.4 to 4.8	Yes	Difficult to separate prenatal

Reference	Period Covered	Number of studies included for review	Is it a Meta-analysis	Pooled Odds Ratio/ Relative Risk (95% CI	Odds Ratio/ Relative Risk Range	Dose-response effect	Comments
							and post natal exposure.
Malloy et al.[61]	Not specified	3	No	N/A	1.98 to 3.24	No clear dose-response effect.	Excluded deaths at less than 7 days old
Mitchell and Milerad[62]	Not specified	69	Yes	**2.86 (2.77, 2.95) ††3.93 (3.78, 4.08	N/A	-	
Salihu and Wilson[63]	Not specified	2	No	N/A	2.3 – 6.43	-	
Spiers[64]	Not specified	4	No	N/A	1.8 to 3.0	-	
Taylor[65]	Not specified	1	No	N/A	2.45 (1.32, 4.55)	-	PAR 40% for New Zealand. (Results from only one study)

** Before the prone sleeping position intervention program (52 studies)
††After the prone sleeping position intervention program (52 studies)

Asthma

Reference	Period Covered	Number of studies included for review	Is it a Meta-analysis	Pooled Odds Ratio/ Relative Risk (95% CI	Odds Ratio/ Relative Risk Range	Dose-response effect	Comments
Delpisheh et al.[49]	Not specified	2	No	N/A	1.3 to 2.0	-	Considered infants and children up to the age of 7 years. Maternal smoking during pregnancy.
Cook and Strachan[56]	April 1997 to June 1998	4	Yes	1.31 (1.22, 1.41)	N/A	-	Considered infants and children up to the age of 6 years. No distinction between prenatal and postnatal tobacco smoke exposure. Mother smoking considered.
DiFranza et al[57]	Not specified	11	No	N/A	1.37	-	No separation of prenatal and post natal exposure

Otitis Media

Reference	Period Covered	Number of studies included for review	Is it a Meta-analysis	Pooled Odds Ratio/ Relative Risk (95% CI	Odds Ratio/ Relative Risk Range	Dose-response effect	Comments
Cook and Strachan[56]	April 1997 to June 1998	8	No	N/A	1.0 to 1.6	-	Looked at infancy and early childhood. No age limit indicated. No separation of prenatal and post natal exposure. The results actually for either parents smoking.
DiFranza et al[57]	Not specified	8	No	N/A	1.0 to 1.6	-	No separation of prenatal and post natal exposure
Dybing and Sanner[58]	Not specified	3	No	N/A	3	-	During the first 3 years of life No separation of prenatal and post natal exposure

Reference	Period Covered	Number of studies included for review	Is it a Meta-analysis	Pooled Odds Ratio/ Relative Risk (95% CI	Odds Ratio/ Relative Risk Range	Dose-response effect	Comments
Thornton and Lee[67]	1979 to 1998	5	No	N/A	1.06 to 1.47		No association reported in 2 studies. Only one study tried to separate the effects of maternal smoking after and during pregnancy. Age limits for children not specified.

Upper and Lower Respiratory Tract Infections

Reference	Period Covered	Number of studies included for review	Is it a Meta-analysis	Pooled Odds Ratio/ Relative Risk (95% CI	Odds Ratio/ Relative Risk Range	Dose-response effect	Comments
Delpisheh et al.[49]	Not specified	1	No	N/A	2.8	Yes	For mothers who smoked at least 1 pack of cigarettes per day. Study in infants
Cook and Strachan[56]	April 1997 to June 1998	5	Yes	1.57 (1.33, 1.86)	N/A	Yes	Considered children from age 0 to 2 years. No separation of prenatal and post natal exposure. The results for maternal smoking.
DiFranza et al[57]	Not specified.	6	No	N/A	-	-	No separation of prenatal and post natal exposure
Dybing and Sanner[58]	Not specified	7	No	N/A	1.72	Yes	Children up to 3 years. No separation of prenatal and post

Reference	Period Covered	Number of studies included for review	Is it a Meta-analysis	Pooled Odds Ratio/ Relative Risk (95% CI	Odds Ratio/ Relative Risk Range	Dose-response effect	Comments
							natal exposure

Perinatal and infant mortality other than SIDS

Reference	**Period Covered**	**Number of studies included for review**	**Is it a Meta-analysis**	**Pooled Odds Ratio/ Relative Risk (95% CI**	**Odds Ratio/ Relative Risk Range**	**Dose-response effect**	**Comments**
Walsh[9]	Not specified	11	No	N/A	1.33	No clear dose-response effect.	Considered, late fetal deaths and deaths from birth to the 28th day of life.
DiFranza and Lew[32]	Literature published up to the review period	25	Yes	*1.26 (1.19, 1.34) †1.23 (1.12-1.41)	N/A	-	23 cohort studies 2 case control studies Definitions of perinatal death vary among studies. PAR 3.4%-8.4% in the USA.
Andres and Day[54]	Not specified	4	No	N/A	1.08 to 1.62	Yes	PAR 10.5% in the USA.
Salihu and Wilson[63]	Not specified	9	No	N/A	1.2 to 1.4	-	

* Pooled Relative Risk from cohort studies.
† Pooled Odds Ratio from case control studies.

Fetal Growth Restrictions

Reference	Period Covered	Number of studies included for review	Is it a Meta-analysis	Pooled Odds Ratio/ Relative Risk (95% CI	Odds Ratio/ Relative Risk Range	Dose-response effect	Comments
Delpisheh et al.[49]	Not Specified	3	No	N/A	-	Yes	Increased risk reported. Effect greatest with smoking during the third trimester.
Triche and Hossain[51]	Not specified	-	No	N/A	-	-	Increased risk reported.
Valero De Bernabe[52]	Not specified	1	No	N/A	-	-	PAR of 18%
Andres and Day[54]	Not specified	2	No	N/A	2.4 to 2.8	Yes	
DiFranza et al[57]	Not specified	11	No	N/A	-	Yes	Increased risk reported.
Salihu and Wilson[63]	Not specified	8	No	N/A	2.3	-	

OUTCOME: _____

	1st trimester Weeks 1-12	2nd trimester Weeks 13-27	3rd trimester Weeks 28-40	**Overall pregnancy**
Never smoked	Ref	Ref	Ref	Ref
Quit				
Continuous light smoker 1-9				
Continuous moderate smoker 10-19				
Continuous heavy smoker 20+				
Any smoking				

Notes:

If figures in table are NOT relative risks, relative rates or odds ratios, indicate what kind of measure, e.g. AR, AR% etc

How many reviews? _____

How many studies? _____

Any other info_____
_____

Appendix III

Glossary

Ectopic Pregnancy	An ectopic pregnancy is a complication of pregnancy in which the fertilized ovum is implanted in any tissue other than the uterine wall.
Spontaneous abortion	Any pregnancy that is not viable or in which the foetus is born before the 20th week of pregnancy is a spontaneous abortion. Spontaneous abortion occurs in at least 15-20% of all recognized pregnancies and usually takes place before the13th week of pregnancy.
Placenta praevia (PP)	Placenta previa is a complication of pregnancy when the placenta is abnormally placed, and partially or totally covers the cervix.
Abruptio placenta (AP)	A complication of pregnancy, wherein the placental lining has separated prematurely from the uterus of the mother. Abruption is a potentially serious problem both for the mother and baby.
Preterm Premature Rupture of Membranes (PPROM)	Preterm premature rupture of the membranes is the rupture of membranes prior to the onset of labour in a patient who is at less than 37 weeks gestation.
Pre-eclampsia (PE)	A condition in pregnancy characterized by abrupt hypertension, albuminuria (leakage of protein albumin into the urine) and oedema (swelling) of the hands, feet, and face.
Preterm delivery	The birth of an infant after the period of viability, that is before 37 weeks, but before full term.
Low birth weight (LBW)	An infant born weighing less than 5.5 pounds (2500 grams) regardless of gestational age
Sudden Infant Death Syndrome (SIDS)	Sudden infant death syndrome (SIDS) is the unexplained death of an apparently healthy infant, usually during sleep. The condition is also known as crib death.
Respiratory distress syndrome (RDS)	Respiratory distress syndrome of

	newborn", is a syndrome caused in premature infants by developmental insufficiency of surfactant production and structural immaturity in the lungs.
Asthma	Asthma is a chronic inflammatory pulmonary disorder that is characterized by reversible obstruction of the airways.
Otitis media (OM)	Inflammation of the middle ear characterized by the accumulation of fluid in the middle ear, bulging of the eardrum, pain in the ear and, if eardrum is perforated, drainage of purulent material (pus) into the ear canal.
Perinatal death	Refers to the death of a foetus or neonate during the perinatal period. The perinatal period commences at 22 completed weeks (154 days) of gestation and ends seven completed days after birth.
Foetal growth restriction	Intrauterine or Foetal growth restriction (IUGR) is a syndrome characterized by a severe deficiency of foetal growth compared to the normal standards for the gestational age.
Respiratory syncytial viral bronchitis (RSVB)	
Upper and lower respiratory infections (URI/LRI)	

Appendix IV: Unit costs of maternal and infant outcomes

	National Schedule of Reference Costs - NHS Trusts Non Elective In Patient HRG Data							
HRG		No. of	National	Interquartile Range of Unit Costs [2]		No. of	Average	No. of Data
Code	HRG Label	FCEs	Average Unit Cost	Lower Quartile	Upper Quartile	Bed Days	Length of	Submissions
			£	£	£		Stay [Days]	
E28	Cardiac Arrest	2,070	1,150	549	1,608	8,378	4	507
M09	Threatened or Spontaneous Abortion	68,870	492	398	740	77,533	1	518
M15	Non-Surgical Treatment of Ovary, Tube, or Pelvis Disorders	12,047	869	602	1,134	26,184	2	719
N01	Neonates - Died <2 days old	1,033	639	382	715	1,143	1	109
N02	Neonates with Multiple Minor Diagnoses	14,514	981	772	1,415	37,834	3	235
N03	Neonates with one Minor Diagnosis	29,115	724	577	1,102	53,534	2	357
N04	Neonates with Multiple Major Diagnoses	4,213	3,277	1,102	5,468	45,759	11	165
N05	Neonates with one Major Diagnosis	8,919	1,481	991	2,551	40,710	5	230
N12	Antenatal Admissions not Related to Delivery Event	618,564	587	446	815	736,816	1	952
P01	Asthma or Wheezing	38,345	696	442	810	51,382	1	462
P03	Upper Respiratory Tract Disorders	79,288	615	426	863	95,356	1	699
P04	Lower Respiratory Tract Disorders without Acute Bronchiolitis	32,599	1,149	613	1,476	73,561	2	666
P05	Major Infections (including Immune Disorders)	4,124	2,416	1,030	2,853	20,498	5	495
P06	Minor Infections (including Immune Disorders)	55,984	808	521	1,104	90,075	2	1,267

	National Schedule of Reference Costs - NHS Trusts Elective In Patient HRG Data							
HRG Code	HRG Label	No. of FCEs	National Average Unit Cost	Interquartile Range of Unit Costs [2] Lower Quartile	Upper Quartile	No. of Bed Days	Average Length of Stay [Days]	No. of Data Submissions
			£	£	£			
E28	Cardiac Arrest	54	£2,024	697	2,011	296	5	45
M09	Threatened or Spontaneous Abortion	1,916	£488	368	743	2,105	1	134
M15	Non-Surgical Treatment of Ovary, Tube, or Pelvis Disorders	406	£1,062	560	1,425	952	2	162
N01	Neonates - Died <2 days old	3	£791	695	952	4	1	3
N02	Neonates with Multiple Minor Diagnoses	74	£1,064	598	1,343	167	2	41
N03	Neonates with one Minor Diagnosis	448	£886	482	1,117	684	2	112
N04	Neonates with Multiple Major Diagnoses	67	£3,526	705	4,001	1,254	19	24
N05	Neonates with one Major Diagnosis	156	£1,788	684	1,744	847	5	54
N12	Antenatal Admissions not Related to Delivery Event	2,953	£780	473	999	4,382	1	219
P01	Asthma or Wheezing	264	£1,055	520	1,286	416	2	84
P03	Upper Respiratory Tract Disorders	1,150	£882	479	1,245	1,528	1	233
P04	Lower Respiratory Tract Disorders without Acute Bronchiolitis	714	£1,936	880	2,541	2,160	3	199
P05	Major Infections (including Immune Disorders)	161	£2,577	877	3,710	778	5	93
P06	Minor Infections (including Immune Disorders)	1,311	£1,092	528	1,470	2,212	2	255
	National Schedule of Reference Costs - NHS Trusts Elective and Non-Elective In Patient HRG Data							

WEIGHTED AVERAGE COSTS								
HRG Code	**HRG Label**	**No. of FCEs**	**National Average Unit Cost**					
			£					
E28	Cardiac Arrest	2,124	£1,173					
M09	Threatened or Spontaneous Abortion	70,786	£492					
M15	Non-Surgical Treatment of Ovary, Tube, or Pelvis Disorders	12,453	£876					
N01	Neonates - Died <2 days old	1,036	£639					
N02	Neonates with Multiple Minor Diagnoses	14,588	£982					
N03	Neonates with one Minor Diagnosis	29,563	£727					
N04	Neonates with Multiple Major Diagnoses	4,280	£3,280					
N05	Neonates with one Major Diagnosis	9,075	£1,486					
N12	Antenatal Admissions not Related to Delivery Event	621,517	£588					
P01	Asthma or Wheezing	38,609	£699					
P03	Upper Respiratory Tract Disorders	80,438	£619					
P04	Lower Respiratory Tract Disorders without Acute Bronchiolitis	33,313	£1,166					
P05	Major Infections (including Immune Disorders)	4,285	£2,422					
P06	Minor Infections (including Immune Disorders)	57,295	£815					

APPENDIX V: FCEs for maternal and infant outcomes

PRIMARY DIAGNOSIS: 4 CHARACTER	FCES
MATERNAL OUTCOMES	
ECTOPIC PREGNANCY	
O00.0 Abdominal pregnancy	34
O00.1 Tubal pregnancy	6,859
O00.2 Ovarian pregnancy	102
O00.8 Other ectopic pregnancy	319
O00.9 Ectopic pregnancy, unspecified	2,405
	9,719
SPONTANEOUS ABORTION	
O03.0 Incomplete spont abort comp by genital tract & pelvic infec	90
O03.1 Incomplete spont abort comp by delay/excess haemor'ge	1,232
O03.2 Incomplete spont abort, complicated by embolism	10
O03.3 Incomplete spont abort with other and unspec complication	260
O03.4 Incomplete spont abort, without complication	22,219
O03.5 Complete or unsp spont abort comp by gen tract & pelvic infn	67
O03.6 Complete or unsp spont abort comp by delay/excess haemor'ge	467
O03.7 Complete or unsp spont abort comp complicated by embolism	1
O03.8 Complete or unsp spont abort comp with other & unsp comp	149
O03.9 Complete or unsp spont abort comp without complication	21,705
	46,200
PLACENTA PREVIA	
O44.0 Placenta praevia specified as without haemorrhage	1,410
O44.1 Placenta praevia with haemorrhage	3,321
	4,731
ABRUPTION PLACENTA	
O45.0 Premature separation of placenta with coagulation defect	118
O45.8 Other premature separation of placenta	53
O45.9 Premature separation of placenta, unspecified	1,370
	1,541
PRETERM RUPTURE	
O42.0 Prem rupture of membranes onset of labour within 24 hours	16,468
O42.1 Prem rupture of membranes onset of labour after 24 hours	10,175
O42.2 Premature rupture of membranes, labour delayed by therapy	695
O42.9 Premature rupture of membranes, unspecified	22,335
	49,673
PRE-ECLAMPSIA	
O14.0 Moderate pre-eclampsia	1,955
O14.1 Severe pre-eclampsia	1,965
O14.9 Pre-eclampsia, unspecified	9,181
	13,101

INFANT OUTCOMES	
PRETERM DELIVERY	
O60.X Preterm delivery	10,901
	10,901
LOW BIRTH WEIGHT	
P07.0 Extremely low birth weight	3,354
P07.1 Other low birth weight	26,925
P07.2 Extreme immaturity	1,235
P07.3 Other preterm infants	15,810
	47,324
RDS	
P22.0 Respiratory distress syndrome of newborn	3,043
P22.1 Transient tachypnoea of newborn	3,206
P22.8 Other respiratory distress of newborn	834
P22.9 Respiratory distress of newborn, unspecified	2,720
	9,803
RSVB	
J12.1 Respiratory syncytial virus pneumonia	96
	96
Aged under 1 only	5
OTITIS MEDIA	
H65.0 Acute serous otitis media	321
H65.1 Other acute nonsuppurative otitis media	261
H65.2 Chronic serous otitis media	710
H65.3 Chronic mucoid otitis media	22,366
H65.4 Other chronic nonsuppurative otitis media	1,440
H65.9 Nonsuppurative otitis media, unspecified	3,957
H66.0 Acute suppurative otitis media	321
H66.1 Chronic tubotympanic suppurative otitis media	127
H66.2 Chronic atticoantral suppurative otitis media	45
H66.3 Other chronic suppurative otitis media	1,575
H66.4 Suppurative otitis media, unspecified	343
H66.9 Otitis media, unspecified	8,136
	39,602
Aged under 1 only	2,036
PERINATAL DEATH	
P95.X Fetal death of unspecified cause	2,557
	2,557
UPPER RESPIRATORY	
J00.X Acute nasopharyngitis [common cold]	1,131
J01.0 Acute maxillary sinusitis	156
J01.1 Acute frontal sinusitis	86
J01.2 Acute ethmoidal sinusitis	58
J01.3 Acute sphenoidal sinusitis	15

J01.4 Acute pansinusitis	41
J01.8 Other acute sinusitis	80
J01.9 Acute sinusitis, unspecified	700
J02.0 Streptococcal pharyngitis	342
J02.8 Acute pharyngitis due to other specified organisms	371
J02.9 Acute pharyngitis, unspecified	4,562
J03.0 Streptococcal tonsillitis	501
J03.8 Acute tonsillitis due to other specified organisms	281
J03.9 Acute tonsillitis, unspecified	35,627
J04.0 Acute laryngitis	716
J04.1 Acute tracheitis	337
J04.2 Acute laryngotracheitis	127
J05.0 Acute obstructive laryngitis [croup]	13,061
J05.1 Acute epiglottitis	529
J06.0 Acute laryngopharyngitis	51
J06.8 Other acute upper respiratory infections of multiple sites	323
J06.9 Acute upper respiratory infection, unspecified	48,580
	107,675
Aged under 1 only	5,336
LOWER RESPIRATORY	
J22.X Unspecified acute lower respiratory infection	122,093
J30.0 Vasomotor rhinitis	85
J30.1 Allergic rhinitis due to pollen	977
J30.2 Other seasonal allergic rhinitis	65
J30.3 Other allergic rhinitis	348
J30.4 Allergic rhinitis, unspecified	287
J31.0 Chronic rhinitis	1,230
J31.1 Chronic nasopharyngitis	37
J31.2 Chronic pharyngitis	435
J32.0 Chronic maxillary sinusitis	1,113
J32.1 Chronic frontal sinusitis	183
J32.2 Chronic ethmoidal sinusitis	200
J32.3 Chronic sphenoidal sinusitis	54
J32.4 Chronic pansinusitis	229
J32.8 Other chronic sinusitis	311
J32.9 Chronic sinusitis, unspecified	3,490
J33.0 Polyp of nasal cavity	3,835
J33.1 Polypoid sinus degeneration	31
J33.8 Other polyp of sinus	1,630
J33.9 Nasal polyp, unspecified	6,120
J34.0 Abscess, furuncle and carbuncle of nose	523
J34.1 Cyst and mucocele of nose and nasal sinus	356
J34.2 Deviated nasal septum	22,047
J34.3 Hypertrophy of nasal turbinates	3,286
J34.8 Other specified disorders of nose and nasal sinuses	9,114
J35.0 Chronic tonsillitis	28,688
J35.1 Hypertrophy of tonsils	4,701
J35.2 Hypertrophy of adenoids	4,477
J35.3 Hypertrophy of tonsils with hypertrophy of adenoids	4,411
J35.8 Other chronic diseases of tonsils and adenoids	1,038
J35.9 Chronic disease of tonsils and adenoids, unspecified	1,162
J36.X Peritonsillar abscess	6,849

J37.0 Chronic laryngitis	280
J37.1 Chronic laryngotracheitis	6
J38.0 Paralysis of vocal cords and larynx	1,119
J38.1 Polyp of vocal cord and larynx	1,366
J38.2 Nodules of vocal cords	753
J38.3 Other diseases of vocal cords	3,391
J38.4 Oedema of larynx	711
J38.5 Laryngeal spasm	365
J38.6 Stenosis of larynx	403
J38.7 Other diseases of larynx	2,236
J39.0 Retropharyngeal and parapharyngeal abscess	174
J39.1 Other abscess of pharynx	107
J39.2 Other diseases of pharynx	1,763
J39.3 Upper resp tract hypersensitivity reaction, site unspec	33
J39.8 Other specified diseases of upper respiratory tract	937
	243,049
Aged under 1 only	3125
STILL BIRTH	
Still birth	3100
ASTHMA	
J45.0 Predominantly allergic asthma	5,700
J45.1 Nonallergic asthma	90
J45.8 Mixed asthma	18
J45.9 Asthma, unspecified	68,445
J46.X Status asthmaticus	9,534
	83,787
Aged under 1 only	1574

Source: The NHS Information Centre (England), Hospital Episode Statistics - 2005-06. Ungrossed data. Please see Explanatory notes file from HES online for more details.