

Smoking during pregnancy and child mental health and wellbeing

Evidence, policy and practice

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Abstract

Aim: The aim of this thesis was to further understand the link between maternal smoking during pregnancy and mental health outcomes among children. The thesis comprises (a) a longitudinal epidemiological analysis of smoking during pregnancy and child mental health outcomes using cohort data for UK children from before birth to 7 years of age (b) an exploration of what policy documents, official guidance and qualitative studies tell us about how the epidemiological risks of smoking in pregnancy are reflected in public policy and discourse. **Methods:** Existing epidemiological evidence was reviewed prior to the quantitative analyses. The data analysed are from the Millennium Cohort Study. Data for 13,161 mothers and children, analysed longitudinally, were used to link exposure to maternal smoking during pregnancy to child mental health outcomes (hyperactivity and aggressive behaviour) at 3, 5 and 7 years of age. Additionally a review of official and lay health guidance in two countries (United Kingdom and United States) was conducted to ascertain the extent to which the potential link between maternal smoking during pregnancy and increased risk of child mental health problems is reflected in ante-natal care policy and practice in these countries. Similarly, a review of qualitative studies was conducted to ascertain the extent to which the risk of child mental health problems is reflected in women's perceptions of the risks of smoking during pregnancy. **Results:** During the past 10 years high-quality studies (and studies of lower quality) have consistently observed an association between prenatal smoking exposure and child mental health problems, though a few well designed recent studies have provided conflicting findings, and further disentangling of exposure and potential confounding factors is needed. Prenatal smoking, socioeconomic position, genetics, family environment, parental mental health and other chemical and environmental exposures, including other endocrine disrupting chemicals, should be explored together, and in more depth, to understand the associations that have been observed between maternal smoking during pregnancy and child mental health during the past 20 years. The original and significant contribution of this thesis is a confirmation of the link between smoking in pregnancy and the development of disruptive behaviour problems in children in a large population-based sample from the United Kingdom. In terms of policy and discourse, ante-natal care packets could be modified to include information about these risks for pregnant women. **Conclusions:** Child mental health, prenatal smoking and the economic wellbeing of families are interlinked—so policies aimed at helping pregnant women to quit smoking, as well as those to help them out of disadvantage are likely to have positive effects on both the exposure (prenatal smoking) and the outcome (child mental health).

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Author's Declaration

I, Laura Vanderbloemen, confirm that the work presented in this thesis is my own. Where information has been derived from other sources I have indicated it clearly. This work has been funded by a Cancer Research UK PhD Studentship.

Thesis Aims

1. To assess and augment the epidemiological evidence of a direct, causal link between maternal smoking during pregnancy and child mental health problems over time, in particular hyperactivity and aggressive behaviour.
2. To assess whether current ante-natal policy, guidance and public discourse in two countries, the UK and USA, accurately and appropriately reflect the evidence base.
3. To assess whether women's perceptions of risk accurately reflect the evidence base, policy and guidance.

Outline

Chapter 1. Introduction and biological plausibility of prenatal exposures and child health, feasibility of detecting effects and level of certainty for predicting risks

Known and suspected risks of maternal smoking during pregnancy and low socioeconomic status on child health

Chapter 2. Existing evidence about maternal smoking during pregnancy and teratogenic effects on developing foetal brain and child mental health

Chapter 3. Methods

Chapter 4. Longitudinal analysis of intergenerational effects in the United Kingdom Millennium Cohort Study (2000-2008)

Chapter 5. Policy review: how accurately is the evidence base reflected in policy and does the evidence and guidance appear in leading popular advice literature for women?

Policy and discourse review: United Kingdom and United States

Chapter 6. Perception of risk (qualitative) review: how accurately is the link is reflected in women's perceptions of the risks of smoking during pregnancy

Systematic review of qualitative studies and nested study examining women's perceptions of risks of smoking during pregnancy, 1976-2010

Chapter 7. Conclusions and discussion

1

Prenatal exposures and child health

•Aim of this chapter

The aim of this chapter is to establish the biological plausibility of a potentially teratogenic link between maternal smoking during pregnancy and child mental health by summarising the criteria that can be used to make judgements about the quality of evidence that exists and the challenges to developing evidence of the highest ‘gold standard’ quality. This chapter also provides background information about smoking during pregnancy and what is known about the effects on child health, taking into account the detrimental effects of socio-economic and other types of stress during pregnancy.

1.1 Exposure definitions

1.2 Outcome definitions

1.3 Cause and effect in intergenerational health

1.4 Chapter conclusions

Background

Smoking during pregnancy is an important cause of health problems for both mothers and children. It is the best known modifiable risk factor for ill health during pregnancy and for infant and child health (British Medical Association, 2004). Beyond this, there are three good reasons to care about maternal smoking during pregnancy. First is the issue of fairness and the fact that many existing behavioural health interventions tend to benefit the already better-off (Lorenc et al. 2013) who are able to modify their own environments--for example to take time off work to attend smoking cessation counselling, leaving more disadvantaged and stressed groups behind.

Second is the issue of the societal costs of maternal smoking during pregnancy (Godfrey et al. 2011) perpetuating a potentially disability-generating exposure for which accumulating evidence suggests not only short-term harm for infants and children but also possible long-term harm across generations.

The third is that smoking throughout pregnancy is not inevitable. Well designed, comprehensive, nurturing and age-relevant ante-natal care could focus more attention on improving smoking cessation and reduction and many other aspects of intergenerational health simultaneously, at a significant moment in the life-course of families. This would require a rethinking of the purpose of ante-natal care and how to engage women and families comprehensively to ensure a long-term commitment to healthy lives, both by individuals, community and the whole society.

1.1 Exposure definitions: who smokes during pregnancy?

In the UK, about 25% of mothers smoked in the 12 months before or during pregnancy in 2010. Of these, about half (54%) quit smoking before the birth. 12% of mothers continued to smoke throughout pregnancy. The proportion of women who smoke throughout pregnancy has decreased in the decade since the Millennium Cohort Study mothers were pregnant: in 2000 the proportion was 19%, in 2005 it was 17% and most recently 12% in 2010 (The NHS Information Centre 2011). Adolescent mothers are more likely to smoke during pregnancy than older mothers, and both the UK and USA have very high adolescent birth rates compared to other rich, market democracies (UNICEF 2001).

Figure 1.1 Flow chart: One hundred pregnant women and smoking during pregnancy

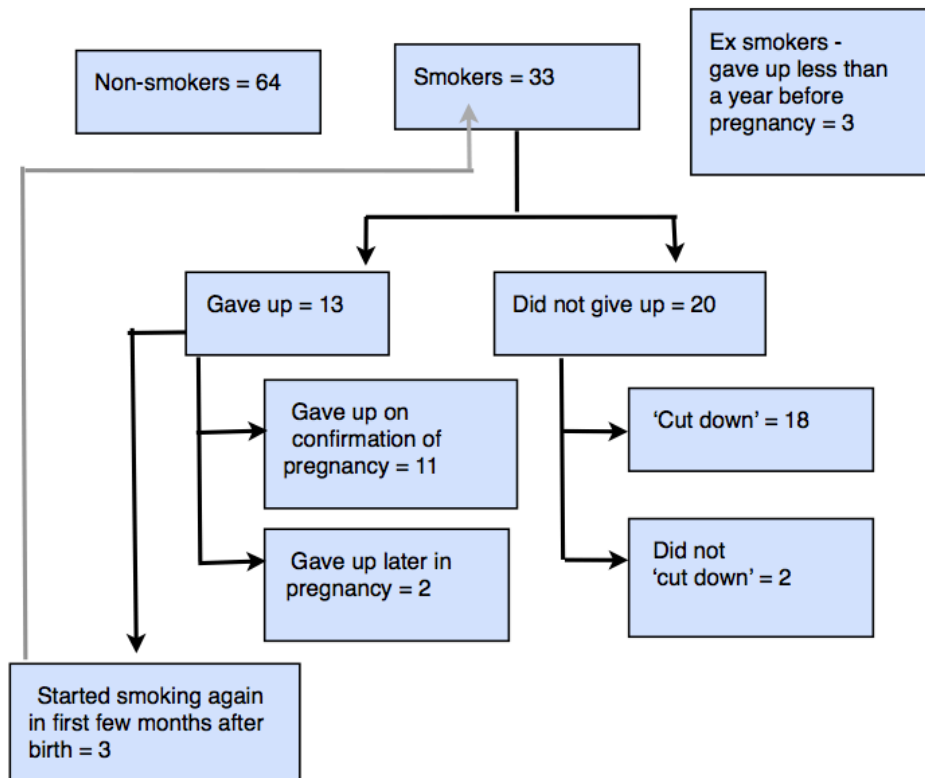


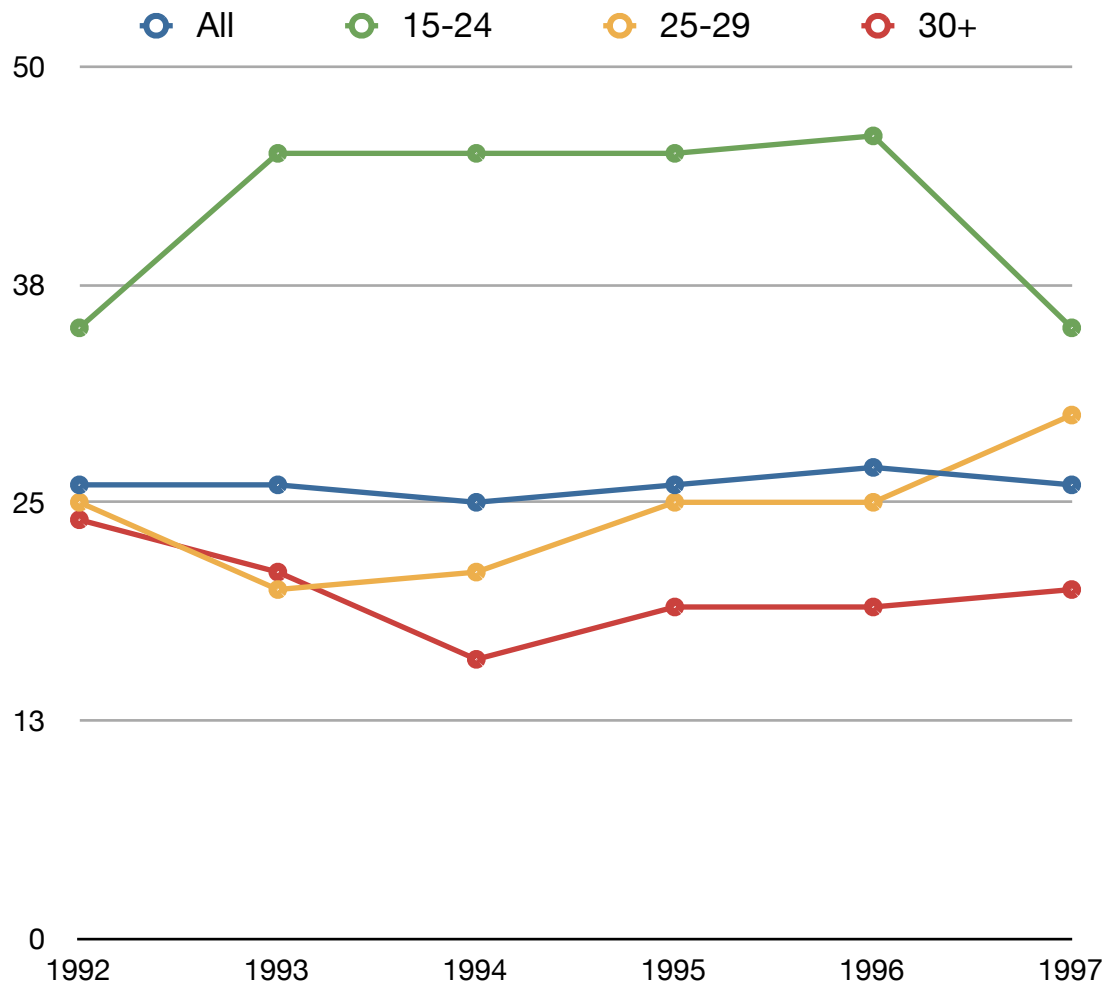
Figure 1.1 is adapted from a report from The British Medical Association (2004). Of 100 pregnant women, the flow chart shows proportionately how many continued to smoke during pregnancy, how many quit and how many cut down. Of 100 women in the UK in 2004, 33 would have been smokers, 20 would have continued throughout pregnancy, and of those who continued, nearly all (18) would have 'cut down' on the number of cigarettes they smoke.

Age-specific trends in smoking during pregnancy (UK)

Figure 1.2 is adapted from a 1998 article published in the British Medical Journal which shows the age-specific patterns of smoking during pregnancy over time. Generally women in the youngest age group (15-24) were most likely to smoke, and older women (30+) were least likely to smoke during pregnancy during the time period from 1992 to 1997, leading up to the first data collection wave for the

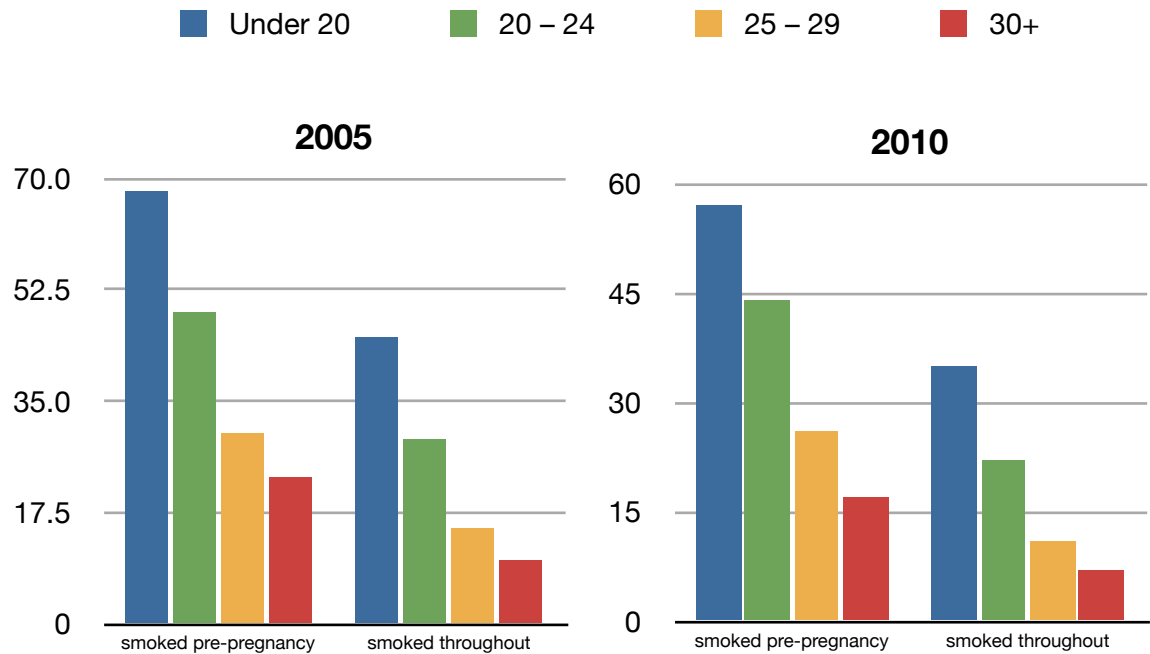
Millennium Cohort Study in 2000. These patterns have persisted in spite of the fact that in the BMJ paper it was reported that the prevalence of smoking in the youngest age group was declining (Owen et al 1998). Figure 1.3 shows data reported from the 2005 Infant Feeding Survey. Smoking prevalence in the youngest mothers was still highest in 2005, and again in 2010 (The NHS Information Centre, 2005, 2011). While overall prevalence is declining, the pattern of higher smoking prevalence among the youngest mothers has remained consistent over time.

Figure 1.2 Prevalence of smoking among pregnant women by age group, England 1992-1997 (Owen et al. 1998)



These strong age-specific trends for smoking during pregnancy provide a clear message for ante-natal care: adolescent mothers and their future offspring are a key demographic requiring special attention.

Figure 1.3 Age-specific patterns of smoking during pregnancy, 2005 and 2010 (The NHS Information Centre 2005, 2011).

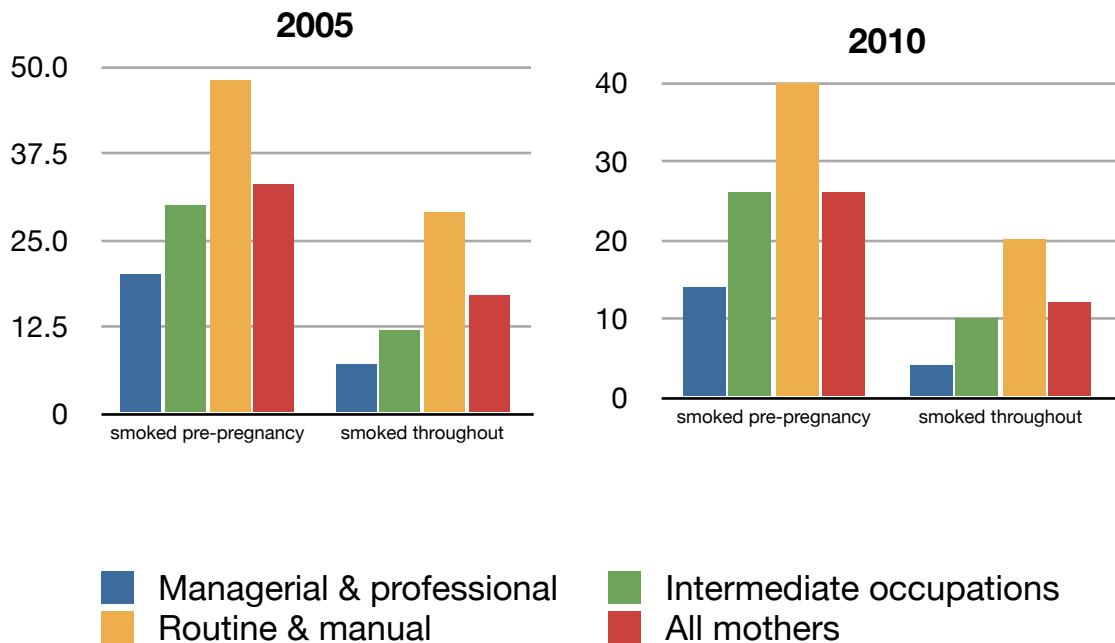


The pattern of an overall decrease in prevalence coupled with a static relative prevalence across age groups also holds true for prevalence patterns of maternal smoking during pregnancy by socio-economic position.

Data from the Infant Feeding Survey show that relative prevalences of smoking during pregnancy across social classes have remained the same since 2005. In other words, women in a lower socio-economic position in the UK are more likely to smoke and more likely to smoke throughout pregnancy than their peers in higher socio-economic positions, even though the overall prevalence of smoking during pregnancy in all groups has decreased over time (Figure 1.4)

Women in routine and manual occupations in the UK represent another key demographic group who may benefit for more focused attention to their health and health behaviours during pregnancy.

Figure 1.4 Socio-economic position and patterns of smoking during pregnancy (The NHS Information Centre 2005, 2011).



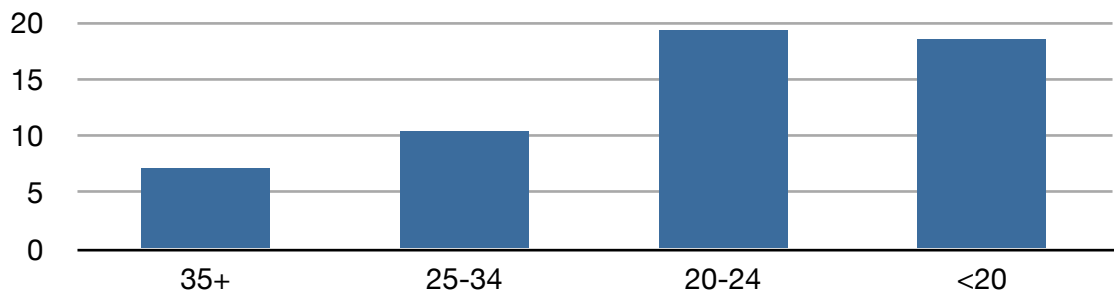
As is apparent from the charts, women from the less advantaged groups are more than twice as likely to smoke compared with more well off mothers. This was the case in 2005 and again in 2010. Though most women attempt to quit and around half of them do quit, the pattern remains the same: the more disadvantaged groups fare worse at both time points and at each level of the scale of socio-economic position.

Considering the age-specific pattern, it is the younger mothers who are more likely to continue to smoke throughout pregnancy, and this is true in the UK and the USA, though the youngest group in the USA was slightly less likely to smoke than the 20-24 year old group in the USA (CDC PRAMS, 2008) (Figure 1.5).

Trends in the U.S. (2008)

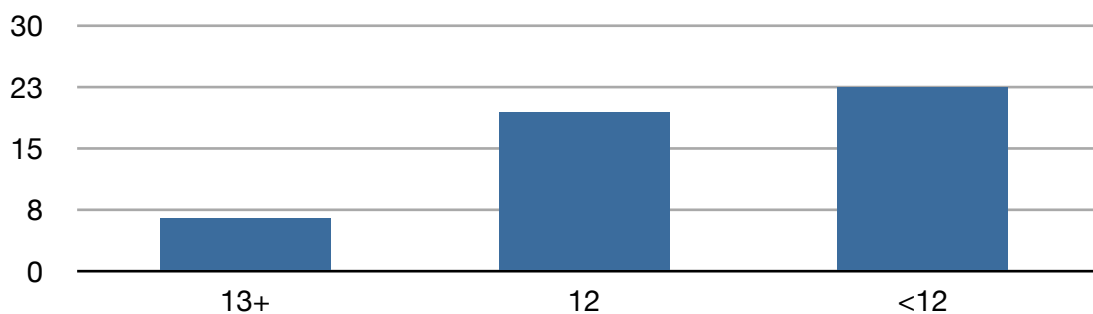
Patterns of smoking during pregnancy are similar in the USA to those in the UK. Younger mothers and mothers with lower levels of educational attainment are more likely to smoke throughout pregnancy. Data from the Centres for Disease Control and Prevention (CDC) Pregnancy Risk Assessment Monitoring System (2008) show these patterns, which generally show that in the two countries, women in the more disadvantaged groups are more likely to smoke throughout pregnancy (CDC PRAMS 2008).

Figure 1.5 Age-specific smoking prevalence, USA (CDC PRAMS, 2008)



Social class by occupation is not as thoroughly defined in the USA as in the UK, but years of education is often used in a similar way since those with more years of education are generally better off socially and economically in the United States, especially at the cut-point of 12 years, which reflects the cut-point between high school and university.

Figure 1.6 Years of education and smoking prevalence, USA (CDC PRAMS, 2008)



1.2 Outcome definitions: epidemiology of child hyperactivity and aggression

Classification of child mental health problems

Hyperactivity and aggression are explored in this thesis. These have been explored previously using data from the Millennium Cohort Study (MCS) at the age of 3 years (Hutchinson et al. 2010) building on previous studies including a study by Pickett et al (2008) that examined difficult infant temperament in the MCS and found that both light and heavy maternal smoking during pregnancy were associated with an increased odds of difficult infant temperament: increased crying, less regularity in daily routine and sleep patterns and less adaptability with new people and novel situations.

Similarly, the Hutchinson et al. (2010) study examined emerging child mental health problems (hyperactivity and aggression) and found that both light and heavy smoking throughout pregnancy were associated with an increased odds of hyperactivity and aggressive behaviour among 3 year olds. The analyses in this thesis build on these two prior studies and link the data for infants with that of the children at ages 3 and also at ages 5 and 7.

These studies are consistent with a large and growing literature (see Chapter 3) that suggests there is an *in utero*, neurotoxic effect of smoking during pregnancy above and beyond the effects of associated social and economic disadvantage on healthy child development and mental health. Intriguingly, both studies found that quitting smoking predicted better outcomes for 9 month olds and 3 year olds. (Hutchinson et al. 2010, Pickett et al. 2008). Four explanatory models of how this may occur and proposed mechanisms are discussed in Chapter 7.

Assessments of child hyperactivity and aggression can be made using several scales that have been developed for physicians, psychiatrists and researchers to use in various settings according to criteria from standard medical diagnosis guides, most commonly the Diagnostic and Statistical Manual of Mental Disorders, currently in its Fifth Edition (DSM-5 2013) from the American Psychiatric Association and the International Classification of Diseases, Tenth Edition (ICD-10) from the World Health Organisation (1992). Those used in the studies of the literature review are listed in Table 1.1 and discussed in more detail in Chapter 3.

Table 1.1 Common scales for child mental health assessment

Outcome measurement tools	
ASEBA	Achenbach System of Empirically Based Assessment
BPI	Behaviour Problem Index
CAPA	Child and Adolescent Psychiatric Assessment
CBCL	Child Behaviour Checklist
CGAS	Children's global assessment scale
ChATTI	Child ADHD Teacher Telephone Interview
CSI	Child Symptom Inventory
BD-DOS	Disruptive Behaviour Diagnostic Observation Schedule
DICA	Diagnostic Interview for Children and Adolescents
DIS	Diagnostic Interview Schedule
DISC	Diagnostic Interview Schedule for Children
DSM-IV	Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition
ITESA	Infant-Toddler Social Emotional Assessment
K-SADS-E	Schedule for Affective Disorders and Schizophrenia for School-Aged Children-Epidemiological Version
SDQ	Strengths and Difficulties Questionnaire
SNAP	Schedule for Non-Adaptive and Adaptive Personality
YSR	Youth Self Report

For this thesis, the Strengths and Difficulties Questionnaire (SDQ) is used to classify cases of hyperactivity and aggressive behaviour. The details of this classification are outlined in Chapter 4. Parents were asked to respond to descriptions such as “*Restless, overactive, cannot stay still for long*” using a 4-point Likert scale.

1.3 Cause and effect in intergenerational health: methodological challenges

Using the Bradford-Hill causal considerations to examine maternal smoking during pregnancy as a potentially causal factor in the development of child mental health problems

The causal criteria set out in 1965 by British epidemiologist and statistician Sir Austin Bradford-Hill are useful for establishing the quality of existing evidence for a causal link between an exposure and outcome (Rothman and Greenland 2005). Sir Bradford-Hill

modernised, formalised and published results of the first randomised clinical trial and set it as the 'gold standard' of epidemiological research (Streptomycin in Tuberculosis Trials Committee, 1948) while also establishing that many exposures cannot be assessed using randomised clinical trials either due to the nature of the exposure or because of ethical reasons. Along with Sir Richard Doll he established the causal link between smoking and lung cancer, a link that cannot be tested ethically using the 'gold standard' randomised trial (Doll and Hill, 1956), but for which sufficient evidence can be extracted from high quality longitudinal studies such as the British Cohort Study or the Millennium Cohort Study which is used for the original analyses in this dissertation.

The Bradford-Hill viewpoints

Sir Bradford-Hill elaborated a set of considerations in thinking about cause and effect in epidemiology--these are often referred to as criteria, but at best they provide a framework for thinking about causation and the quality of measurement of effects that are observed in epidemiological studies--without claiming that meeting them proves definitive proof of cause and effect (Rothman and Greenland 2005).

Strength of the association

Strong associations are generally thought to be more likely to be causal, probably because if the effect size is still large while controlling for other factors, it is likely to be a true effect--though this is not a definitive criteria. This is the case with maternal smoking during pregnancy. Also, a weak association can on its own be a true causal association though it is thought that weak associations are likely to be explainable by undetected co-variables or biases, and they are in themselves more difficult to detect. Large sample sizes and statistically high powered studies improve the chances of detecting weak but true effects.

Consistency

Consistent findings in various contexts and by various researchers are thought to be more likely causal than those without consistency, though lack of consistency does not mean that an association is not causal. Consistency is discussed in relation to existing findings relating to the link between maternal smoking during pregnancy and child mental health in Chapter 3.

Temporality

This criterion is considered to be the most clear and important criterion. For a causal link, the

Maternal smoking during pregnancy and child mental health and wellbeing: evidence, policy and practice

exposure must precede the outcome. Longitudinal studies allow for establishing temporality since the participants begin the study without the disease or outcome of interest and they are followed over time as these develop. In pregnancy studies it is also established because the mother's smoking during pregnancy precedes the development of the outcomes of interest.

Plausibility

Biological plausibility is also important, that is, there must be a mechanism by which the exposure can cause the outcome, though lack of understanding of an underlying, unknown biological mechanism may make a causal link seem implausible when it could be simply that the biological understanding has not yet been established.

Biological gradient

Generally it is thought that if there is a dose-response relationship between exposure and outcome, i.e. that with more exposure there is more outcome, though this is not a necessary criterion to establish a causal link. The biological gradient is reflected in the link between maternal smoking during pregnancy and child mental health in several of the studies that are discussed in the literature review (Chapter 3): the associations are most consistently seen among the children of women who smoked heavily during pregnancy.

Coherence

Coherence refers to epidemiological findings in human research subjects and laboratory evidence, though it is not a necessary criterion for establishing a causal link. In the case of maternal smoking during pregnancy, laboratory studies have also found a link between exposure to nicotine and impaired development of the foetal brain in rats (Eppolito and Smith, 2006).

Experimental evidence

This type of evidence, utilising randomised, controlled trials is considered to be the best type of evidence available, but many exposures and outcomes cannot be investigated

experimentally. The link between smoking and lung cancer is the best known example of a causal link that could not have been established using experimental evidence in humans. Experimental evidence is probably unobtainable for maternal smoking during pregnancy and

child outcomes. It has been suggested that a statistical method (propensity score matching) can be used in place of an experimental design, in order to simulate experimental conditions. This only works where there is significant overlap of other factors between comparison groups (UCLA Medical Imaging Informatics Group 2009), which is not the case with maternal smoking during pregnancy as mothers who smoke consistently during pregnancy have been found to display a constellation of disadvantage-related factors that they do not share with women who quit or do not smoke prior to pregnancy (Pickett et al. 2008).

Methodological challenges and alternative explanations

Given these considerations, it is not straightforward to establish a causal link between maternal smoking during pregnancy and child mental health. The strength of association is one reason to suspect a causal link, as are the consistency and coherence of findings. Temporality is established, as are biological plausibility and biological gradient. The main methodological issue is that experimental evidence is probably impossible to obtain, except in the laboratory with animal models or with statistical simulations of experimental conditions.

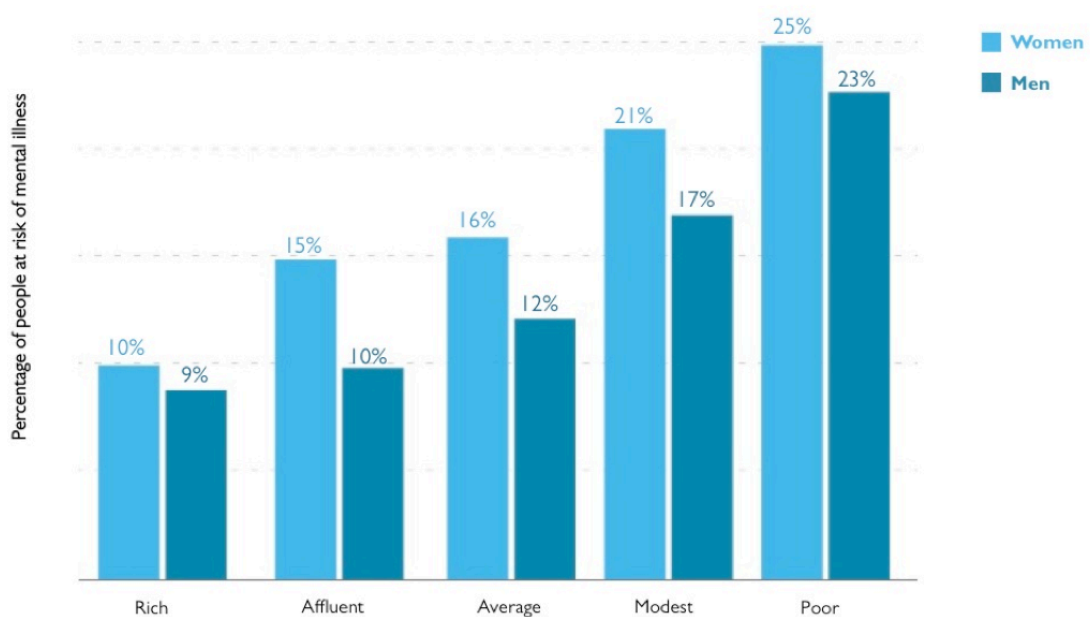
This places the link between maternal smoking during pregnancy and child mental health on similar footing to that of smoking and lung cancer around 1946 when Sir Richard Doll and Sir Austin Bradford-Hill were sketching out their hypotheses. They used longitudinal data and focused on one socio-economic group: British doctors. Discussion of how this thesis attempts to follow their example is found in Chapter 4 and the description of methods used to compare the trajectories of children in distinct socio-economic groups.

Other methodological issues include the difficulty of drawing conclusions across different family generations, genetics, parental mental health and differences in parenting generally. These issues are discussed in more detail in Chapter 4.

Maternal smoking during pregnancy in the context of inequality

Before concluding that mothers who smoke and fail to quit smoking during pregnancy may have chosen to harm their child irreversibly, it is first important to consider that there is also a strong class-based trend not only to educational attainment and smoking during pregnancy, but also to mental illness. According to the Health Survey for England (Health and Social Care Information Centre 2009), there is a strong class gradient to mental illness in the UK; and large gaps between groups according to their affluence: for example about 10 percent of women who are rich are at risk of mental illness while 25 percent of women who are poor are at risk of mental illness in the UK (Figure 1.7). It may be that smoking behaviour reflects either poor health choices that are affected by mental illness, or a way of coping with mental illness--or both.

Figure 1.7 Risk of mental illness by income, Health Survey for England 2008-2009



It has also been established that child educational attainment follows a social class trend (Office of National Statistics, 2010). These trends brings a few questions: (1) How much of these social gradients in mental health and educational attainment are due to unfair biases and opportunities and how much are they due to things like maternal smoking in pregnancy, and

resulting biological effects that influence a child's brain development, behaviour and ultimately success at school?

(2) If maternal smoking during pregnancy is a known predictor of poor child mental health, should exposed children be eligible for disabled status and extra attention to bolster them against the disadvantages that they begin with?

(3) Given that there are also strong social gradients to smoking throughout pregnancy, is it important to look upstream of smoking during pregnancy to consider what else is behind these trends?

Explanatory models of health inequalities

Figure 1.7 shows the social gradient in mental health in the UK: higher socio-economic position predicts better health, for several health outcomes including mental health, drug abuse, infant mortality, cardiovascular disease and overall mortality risk (Wilkinson and Pickett 2009). The social gradient can be explained via 4 different models of health inequalities (see Box 1.1).

Box 1.1 Explanatory models of health inequalities (Bartley, 2004)

1. Peoples' social status declines or gets stuck because they suffer from ill health ([selection model](#)) or both social status and health are determined by common factors ([indirect selection model](#))
 2. People with low social status behave in ways which cause ill-health ([behavioural/cultural model](#))
 3. People with low incomes cannot afford or access resources which promote and protect health ([material model](#))
 4. Low social status itself creates stress that causes ill-health ([psychosocial model](#))
-

Thinking about health behaviours, it is also important to understand that women who smoke throughout pregnancy are much more likely to display a whole constellation of factors related to disadvantage and psychosocial problems, including aggressive, irritable relationships (Pickett et al. 2003).

Going beyond the UK and the social gradient in health and mental health, it is also important to note that mental illness itself is not only more common among poorer groups in the UK, but that mental illness is also more prevalent in the rich, market democracies with a steeper economic gradient generally (Wilkinson and Pickett 2009). So maternal smoking during pregnancy and the link with child mental health explored in this thesis rests within this context: the UK is one of the most unequal countries among the rich, market democracies, and the link between maternal smoking during pregnancy and child mental health may operate differently in a more equal, rich country such as the Netherlands, Denmark or Japan.

Further still, considering other variations of aggressive behaviour: both homicide rates and imprisonment rates are higher in more unequal countries such as the UK and USA, and far lower in more equal countries such as the Netherlands, Denmark and Japan (Wilkinson and Pickett 2009).

This trend also holds for other outcomes such as infant mortality, teen pregnancy, drug use, educational attainment, and child conflict--and it is apparent not only comparing the rich market democracies but also in a separate test bed, i.e that of the 50 individual US states. These outcomes tend to be more common in the more unequal states within the USA (Wilkinson and Pickett 2009).

Establishing biological plausibility

To disentangle the social and economic effects on child mental health from a potentially neurotoxic effect of maternal smoking during pregnancy on the foetal brain, it is necessary to establish the biological plausibility and biological mechanisms that operate to result in child brain developmental deficiencies.

Two reviews are very helpful for understanding the known, likely and suggestive effects of maternal smoking during pregnancy on child mental health. The first is a review by the British Medical Association which generally outlines all known health effects associated with pregnancy smoking and health. This review also discusses the quality of the evidence and

weighs the likelihood that each outcome is truly related to pregnancy smoking (British Medical Association, 2004).

The second is a review recently published in the journal *Nicotine and Tobacco Research*, by Margaret Bublitz and Laura Stroud. This review, from 2012 useful for laying out not only the biological plausibility but also the areas of future research that should be developed for a better understanding of the effect of maternal smoking during pregnancy and child mental health outcomes. It is primarily focused on the brain structure and function in children whose mothers smoked during pregnancy (Bublitz and Stroud 2012).

Known, likely and possible effects of smoking on reproductive health

The British Medical Association review from 2004 lists extensive effects of smoking on reproductive health on both men and women. These include a long list:

... ectopic pregnancy, miscarriage, reduced foetal growth and low birth-weight, perinatal death, placental complications, premature birth, pre-eclampsia, foetal malformation, inner ear disease, increased risk of cardiovascular disease, diabetes and obesity in adulthood, mental health problems, unexplained crying / colic, nicotine withdrawal symptoms, poorer performance at school, lower scores on tests of cognitive function, including language, certain mental health problems, including hyperactivity and shorter attention spans (British Medical Association 2004)."

Maternal smoking during pregnancy and offspring brain structure and function

This review involved a search of the literature about direct effects on the human brain related to smoking during pregnancy. Because animal studies have demonstrated effects on the developing brain among rats exposed to nicotine in utero, this study builds on that starting point for establishing biological plausibility.

Only six human studies to date were found in the review, and five of those examined effects on brain function. In the studies that exist, smoking during pregnancy was consistently linked to decreased thickness and volume of the cerebellum and corpus callosum in offspring. There was also evidence of problems with coordination across brain regions during simulations intended to induce information and auditory processing (Bublitz and Stroud 2012).

This review provides two main results for the purpose of this thesis: (1) it established that there is little published literature about the relationship between maternal smoking during pregnancy and brain function, and (2) it established that among these few studies, an effect on brain structure and function related to information and auditory processing was consistently observed (Bublitz and Stroud 2012).

1.4 Chapter conclusions

Returning to the main thesis question: *should ante-natal care policy include child mental health outcomes such as hyperactivity and aggression as evidence-based reasons to help women to quit smoking during pregnancy?* it is useful to think about the broader issues of methodological challenges in epidemiological research and how the problem of smoking during pregnancy fits in.

This thesis will further explore the relationship between maternal smoking during pregnancy and mental health problems in children. New data is analysed from a longitudinal study of a nationally representative, population-based cohort study and evidence about existing ante-natal care policy and guidance.

It is not possible or ethical to conduct experimental trials in this area, but longer-term follow-up will likely provide more insights into the relationship between smoking and mental health problems as the children in this cohort grow older. Future research could analyse genetic data. Other cohort studies--for example the Sweden family cohort studies--that have extensive data on family members would be useful sources for future analysis and comparison with UK cohorts.

This thesis will focus on the issue of smoking during pregnancy primarily among women in the United Kingdom and in the United States, not only epidemiologically, but with respect to policy, provision of health care, risk communication and the uptake of epidemiological evidence in both countries.

2

Methods

•Aim of this chapter

The aim of this chapter is to outline the methods used in this thesis. The approach of this thesis is to review existing quantitative studies of the association between maternal smoking during pregnancy and child mental health and to classify them according to the quality of methods and to extend the existing evidence via three quantitative analyses using data from the Millennium Cohort Study, a nationally representative birth cohort study of approximately 18,000 children born around the year 2000 in the United Kingdom. Beyond these analyses, relevant antenatal care policy in the USA and UK and qualitative literature on how women perceive the risks of smoking during pregnancy during a 30 year period are reviewed in order to assess whether public policy, discourse and perceptions of the risks of smoking during pregnancy accurately reflect the existing epidemiological evidence.

2.1 Review of existing evidence

2.2 Quantitative analyses

2.3 Review of ante-natal policy, guidance and risk perception

Chapter 1 introduced the issues of maternal smoking during pregnancy and child mental health in the context of health inequalities. In this chapter, the thesis methods are briefly summarised in terms of the three thesis aims:

- (1) To assess and augment the epidemiological evidence of a direct, causal link between maternal smoking during pregnancy and child mental health problems over time, in particular hyperactivity and aggressive behaviour.
- (2) To assess whether current ante-natal policy, guidance and public discourse in two countries, the UK and USA, accurately and appropriately reflect the evidence base.
- (3) To assess whether women's perceptions of risk accurately reflect the evidence base, policy and guidance.

2.1 Review of existing evidence

In Chapters 2 and 4, the first thesis aim is addressed. The epidemiological evidence base is reviewed, summarised and critiqued in order to establish the status of the existing evidence and to assess how the evidence base could be improved. Detailed methods for each of these studies is included in the corresponding chapter.

2.2 Quantitative analyses

Based on the results of the first review, further epidemiological evidence is derived from the Millennium Cohort Study, a large, nationally representative cohort study of children born during 2000-2001 in the United Kingdom. The association between maternal smoking during pregnancy and child mental health is first tested using multivariate logistic regression analyses. The association is then further tested using longitudinal analyses that estimate the average mental health trajectories of children differentially exposed to maternal smoking during pregnancy. Models are constructed to test and to disentangle the effects of maternal smoking during pregnancy and childhood poverty simultaneously.

2.3 Review of policy, guidance and public discourse

In Chapter 5 ante-natal care policy, guidance and popular pregnancy advice guides in the United Kingdom and the United States are reviewed and summarised in terms of the risks of maternal smoking during pregnancy. Similarly, a systematic review of qualitative literature is conducted in order to ascertain what women perceive to be the risks of smoking during pregnancy (Chapter 6).

3

A review of epidemiological studies of prenatal smoking exposure and child mental health problems, 2001-2013

•Aim of this chapter

The aim of this chapter is to identify, classify and critique the existing epidemiological evidence of a potentially causal link between maternal smoking during pregnancy and child mental health outcomes such as aggression and hyperactivity.

3.1 From biological (theoretical) plausibility to evidence

3.2 Search methodology

3.3 Summary of papers and findings 2001-2010

3.4 Update of studies, 2010-2013

3.5 Chapter conclusions

3.1 From biological (theoretical) plausibility to evidence

Since the 1970s there has been increasing interest in smoking during pregnancy, mainly as a result of evidence that smoking during pregnancy can increase the risk of spontaneous abortion, complications in pregnancy and labor, and placental problems. Babies of women who smoke during pregnancy are more likely to be born pre-term, to be underweight, and to die from Sudden Infant Death Syndrome (British Medical Association 2004).

Since 2001, several studies have reported an association between maternal pregnancy smoking and difficult child mental health problems, particularly among boys. These studies range in robustness from retrospective cross-sectional studies that look at mental health problem outcomes in adolescence and measure exposure several years earlier—to longitudinally analysed studies of prospective birth and family cohorts examining mental health problems and attention problems across childhood and into adolescence and young adulthood. Studies prior to Pickett et al (2008) and Hutchinson et al (2010) did not control as extensively for important maternal individual, social, economic and environmental factors—or if they did then they did not also use a very large, nationally representative, population-based sample as Hutchinson et al and Pickett et al did, with the power to detect effects while controlling for detailed maternal factors.

Since 2007 several studies have used genetic information in an attempt to control for potentially confounding genetics as a possible underlying cause for both child mental health problems and maternal smoking during pregnancy.

Studies in more recent years have also increasingly attempted to find out whether there may be long-term mental health problems or cognitive problems resulting from exposure to cigarette smoking in utero not only to piece together what is happening at all stages of development into adulthood but also to understand what puts children at an increased risk for developing mental health problems that do not resolve before adulthood.

There is now a very large body of medium to high-level evidence to suggest that prenatal smoking exposure can cause mental health problems in boys. This is most likely not as a sole cause but as a part of interacting exposures including genetics, family and social environment and other potential environmental exposures such as pesticides; which, like nicotine have been hypothesised to have the ability to act biologically as teratogens on the brain (Park et al. 2006).

To what extent any of these potentially teratogenic effects in utero may persist throughout the child's life into adulthood has not been determined.

Other studies have also attempted to address questions of biological plausibility both by studying prenatal nicotine exposure in animal models and by conducting brain imaging studies to observe structural and functional changes in the foetal brain. It is thought that these changes may be permanent, as has been suggested in some of the imaging studies, but there are examples from other disciplines in which diseases once thought to be irreversible were found to be reversible after all (Lim et al. 2011).

Objectives

Chapter 3 will explore the existing high-quality epidemiological evidence on the link between maternal smoking during pregnancy and child mental health problems that has been published in peer-reviewed scientific journals from 2001 to 2010—beginning with the review of the developmental effects of prenatal smoking exposure by Ernst et al. in 2001 and summarising the conclusions of the published reviews during that time period (Cornelius and Day 2009, Shea and Steiner 2008, Slotkin et al. 2008, Hermann et al. 2008, DiFranza et al. 2004, Wakschlag et al. 2002). This chapter will update the reviews and give greater attention to study quality and criteria by which each study could be judged, to determine how many studies met quality criteria sufficiently to be used to make a causal claim.

Another important area to consider is: what is lacking in the existing studies? What methodologies have not been used that might be more robust and informative, or for what reasons have certain more robust study designs not been conducted? What alternative hypotheses require exploration: genetic confounding, environmental exposures, the mental health problems of the surrounding family, peer group and social context? Also, from an epidemiological perspective, how do case definitions and differences in these definitions influence our understanding of the prevalence and incidence of child mental health problems? These methodological issues are examined further in the discussion of this chapter.

Types of evidence needed to make a causal claim

Ideally, to answer the question of whether prenatal smoking exposure causes child mental health problems, one would have longitudinal data on a large, representative, population-based, prospective cohort of siblings with family environment data, appropriately measured exposure data and consistent, valid case definitions of child mental health problems throughout childhood. Further, to understand epigenetic effects, one would have to be able to measure exposure prior to any epigenetic changes, and then to observe the frequency of genetic changes in exposed and unexposed populations over time. Since the genetics of mental health problems are not well understood, this would be complicated but theoretically possible.

Epigenetic effects could possibly be at play in the observed associations between prenatal smoking exposure and mental health problems. In fact epigenetic changes due to smoking have been observed recently among young women who smoked; i.e those who began smoking were found after follow up to have been more likely to exhibit epigenetic changes in cervical epithelia, a step in the development of cervical cancer. (Ma et al. 2011). Smoking seems to have profound effects on biology, whether due to the chemical exposures directly, to epigenetic changes that result from smoking exposure or to the underlying reasons that a woman chooses to smoke.

Epidemiological evidence is the primary type of evidence examined here because it is the most relevant type of evidence for effects on humans who have been exposed and followed up during childhood rather than studies on animal models whose results have been theoretically extrapolated to humans. For example, a study that found that rats exposed to nicotine in utero displayed more aggressive mental health problems is important (Park et al. 2006) in establishing whether prenatal smoking exposure may plausibly cause mental health problems. However, there are limitations to applying these findings directly to humans whose mental health problems and social contexts are complex and possibly not appropriately simulated by laboratory conditions.

Since biological plausibility has been established in animal models, the important evidence to consider here is epidemiological evidence from human studies. It would not be ethical to conduct a randomised-controlled trial of maternal smoking during pregnancy, and the closest

approximation to a randomised-controlled trial would come from trials of smoking cessation, in which quitting is likely to be associated with several confounders, thereby negating the methodological gains of randomisation. The best possible quality evidence, given existing methods, will come from very large, population-based birth cohort studies with enough participants, data collection and follow-up time to disentangle the effects of prenatal smoking vs. other related exposures such as genetics, family mental health and relative deprivation.

3.2 Search Methodology

A search was conducted in PubMed on 14 December 2010 (and updated on 04 August 2013) using the following search strategy: Smoking AND Pregnancy AND Child Mental health, with the following search terms:

((("Smoking"[Mesh] AND "Pregnancy"[Mesh]) AND ("Attention Deficit and Disruptive Behavior Disorders"[Mesh] OR "Child Behavior"[Mesh] OR "Child Behavior Disorders"[Mesh] OR "Infant Behavior"[Mesh] OR "Crying"[Mesh] OR "Conduct Disorder"[Mesh] OR "Attention Deficit and Disruptive Behavior Disorders"[Mesh])))).

Title and abstract screening and evidence inclusion process

The abstracts of the resulting papers were screened according to the following criteria, as a way of determining which papers to include according to their relevance to the main research questions of this thesis:

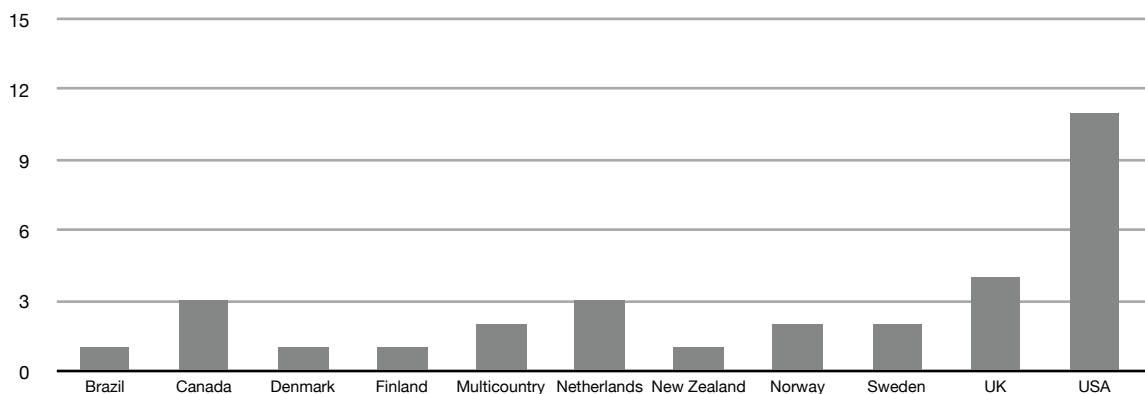
1. Does the paper potentially report epidemiological findings related to pregnancy smoking effects on child mental health OR does it report on important background information?
2. Was it published after January 2001, in English (i.e after the Ernst review) OR was it not reviewed in the Ernst (June 2001) review?

If yes to both, the paper was considered for inclusion. Criteria for inclusion were:

1. Is the study able to control for known confounding factors such as socio-economic position, education, parental mental health and education?
2. Were case definitions clearly defined and consistently applied?

Studies that met the criteria were included in the review. The evidence was considered from the perspective of a null hypothesis that in spite of numerous studies providing evidence for prenatal smoking exposure as a causative factor in the development of mental health problems in offspring the assumption was made that evidence is not due to a causal relationship but rather there is some other explanation for the associations that are observed.

Figure 3.1 Distribution of papers by study site location 2000-2010



From this perspective it is possible to attempt to see other explanations as alternatives to the somewhat established view that there is a causal link between prenatal smoking exposure and child mental health. This attempt at taking a fresh look at the association is warranted because recent studies have called the association into question, using more refined methods and larger sample sizes.

3.2 Findings from 2000-2010: prenatal smoking exposure and child mental health

Ninety-seven studies resulted from the PubMed search beginning in 2001. Of those, 27 papers were found to be relevant to the question of whether maternal smoking during pregnancy potentially causes child mental health problems, on its own or as a part of a cluster of interrelated causes. More papers were identified by searching the citations of the 27 papers, and by expert consultation (6 more papers). Most of the studies were also discussed in the review articles during the 10 year period. Eight review articles were published during the period from 2001-2010: Cornelius and Day (2009), Shea and Steiner (2008), Slotkin et al. (2008), Herrmann et al. (2008), Button et al. (2007), DiFranza et al. (2004), Wakschlag and Pickett (2002) and Ernst (2001). The findings from all studies included in this review are summarised in Appendix 1.

The included papers were drawn from studies that took place in a variety of countries (Figure 2.1): USA (11), UK (4), Netherlands (3), Norway (2), Sweden (2), Brazil (1), New Zealand (1), Canada (1), Finland (1), and Denmark (1). There were also studies conducted in France, Japan, Czech Republic and Germany, but these were not included here because the articles were not in English.

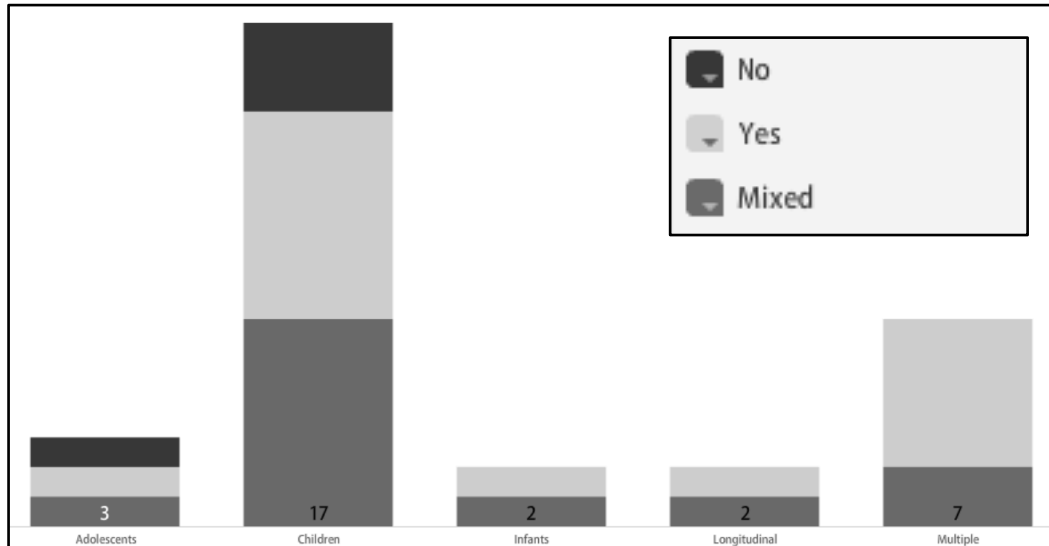
Because the reviews recommended utilising longitudinal analyses of the effects of prenatal smoking exposure on child mental health (Cornelius and Day 2009, Herrmann et al. 2008, Button et al. 2007, DiFranza et al. 2004, Wakschlag et al. 2002) the papers included in this chapter are organised by age group as a way of identifying trends over the course of infancy, childhood and adolescence. There are some studies that attempt to examine the association even into adulthood, and these studies are also summarised in the chapter as a way of beginning to understand how and whether prenatal smoking exposure affects offspring over the life-course. In the next chapter, this organisation of the knowledge base according to age will be used as the foundation for a longitudinal analysis of the Millennium Cohort Study data.

Definitions of child mental health vary according to age. Findings from current studies of prenatal smoking exposure and child mental health are separated by the age of children under study because understanding child mental health, difficult infant temperament, hyperactivity, aggressive behaviour and conduct problems requires an understanding of what is generally defined as normal mental health at any given age in the main regions of interest (wealthy,

developed, market democracies). Comparing publications from different countries may also reveal subtle differences in expectations of child mental health.

Figure 3.2 provides a summary of the papers included in this review. Each bar is shaded according to whether the results of the studies in each age group are supportive of a null hypothesis (No), a positive association (Yes), or Mixed. Several studies reported mixed results, and this probably is reflective of the nature of social epidemiology and the difficulty in defining the outcome (child mental health changes over childhood and the life-course) as well as the potential confounding factors (family and especially maternal adaptive functioning, genetic influences involving multiple genes, environmental effects and interactions). Still, there is consistent evidence of an association, even in studies that were powered to detect subtle effects of extensive confounding factors.

Figure 3.2 Matrix chart of study types: age groups and results, 2000-2010



Infants

Two studies reported on the association between prenatal smoking exposure and mental health among infants only (Stroud et al. 2009, Pickett et al. 2008, Wood et al. 2008, Adamson et al. 2007, DeSouza et al. 2009 and Wakschlag et al. 2008) and one study included infants among other age groups (Martin et al. 2006). One of the three studies found clear evidence of an effect of prenatal smoking exposure on child mental health, and two reported mixed findings; that is, that there was evidence both for and against the hypothesis that prenatal smoking exposure causes child mental health problems.

Martin et al. reported in 2005 significant mental health effects among 6 month olds from a Finnish cohort. In contrast to what would be expected, those infants exposed to heavy prenatal smoking actually had less distress to novelty and less irregularity according to maternal report. This finding is intriguing but could be due to maternal reporting bias if Finnish women in this cohort who smoked were more likely to overemphasise their 6 month old's conforming to expectations. Therefore they may have reported inaccurately because they may have felt uncomfortable with the questions—perhaps being heavy smokers during pregnancy, they also represent a group of women who are more excluded in other ways, since heavy smoking in pregnancy is not a highly acceptable social health behaviour (Martin et al. 2006). But the finding is intriguing because it is only one of two findings among the studies that showed better outcomes for the offspring of smokers.

Pickett et al. reported in 2008 that infants fared worse on 3 dimensions of the Carey Temperament Scale if they were exposed to prenatal smoking—except in the case of women who smoked but then quit during pregnancy. Among this group, infants actually fared even better than infants of women who never smoked. This may reflect the mother's desire to do the right thing for her child and may be a marker for a closer bond in the future, and a more responsive parenting approach. (Pickett et al. 2008, Wood et al. 2008, Adamson et al. 2007, DeSouza et al. 2009 & Wakschlag et al. 2008b). This study was particularly notable because it was drawn from a very large population-based sample (n=18,263), with the power to examine subtle socio-economic effects.

Analyses reported in 2009 from another cohort study—the National Collaborative Perinatal Project of Providence Rhode Island conducted from 1960 to 1966 with 962 mother-infant pairs—indicated greater irritability (on the Graham-Rosenblith Behavioural Examination of the

Neonate scale) and hypertonicity among neonates who were exposed to maternal smoking during pregnancy, after adjustment for maternal age, race and socioeconomic status, infant birth weight and age (Stroud et al. 2009).

Children

The largest group of studies reported on the association between prenatal smoking exposure and child mental health problems during childhood only. The resulting studies in children are listed in Table 2.1, and the full table of all studies is found in Appendix 1.

Table 3.1 Review of studies: Smoking during pregnancy and child mental health

Authors	N	EVIDENCE	ADJUSTED OUTCOMES	QUALITY SCORE*
GRAY 2004	869	Yes	Effects observed for clinically significant behaviour problems at all time points [OR=1.57 (1.20-2.04)]	4
HÖÖK 2006	1,428	Yes	Effects observed for externalising behaviour, destructive/delinquent behaviour at both time points. Equally strong for boys and girls. Height and weight also lower among children whose mothers smoked during pregnancy.	7
CORNELIUS 2007	357	Yes	Effects observed for hyperactivity but not other outcomes	7
CARTER 2007	1,038	Yes	OR for total behaviour problems=1.75 (1.12-2.74), Internalising behaviour (by children of lone mothers) OR=3.35 (1.29-8.67), Externalising (by girls) OR=2.37 (1.12-5.04)	6
HUIJBREGTS 2008	1,745	Yes	Trajectory model estimation showed 3 distinct developmental patterns for physical aggression and four for hyperactivity-hyperimpulsivity. Prenatal smoking predicted child likelihood of following PA trajectories	6
STENE-LARSEN 2009	22,545	Yes	Externalising behaviours 1.32 (1.03-1.70), not moderated by child's sex	7
HUIJBREGTS 2007	1,745	Yes	Prenatal smoking AND PSE X Maternal anti-social behaviour AND PSE X Family income predicted high-risk trajectory. Critical adversities	6
STROUD 2009	962	Yes	Increased irritability (1 pack/day smoking exposure) and increased muscle tone (less than 1 pack/day and 1 pack/day smoking exposure groups)	6
TREMBLAY 2004	572	Yes	Prenatal smoking along with other family factors predicted high-risk trajectory	0
BATSTRA 2003	1,186	Yes	Effects observed for externalising (troublesome) behaviour and attention deficit.	6
BROOK 2006	208	Yes	Maternal unconventionality, maternal warmth and pregnancy smoking associated with child aggressive behaviour	5
WAKSCHLAG 2006A	448	Yes	Effect observed for ODD+ADHD [OR=2.66, p<0.05]	4
ASHFORD 2008	396	Yes	The negative effects of prenatal smoking exposure on child behaviour did not diminish over time	4
OBEL 2008	20,936	Yes	Effects observed but association was not strongest in the cohort with the fewest smokers, suggesting that the association cannot be entirely due to genetic confounding	7
WAKSCHLAG 2002	77	Mixed	Effects observed for CD among boys but not girls. Maternal responsiveness accounted for some of this effect.	8
Authors	N	Mixed	Effects observed for externalising behaviours only at age 2 years.	9

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MARKUSSEN LINNET 2006	1,355	Mixed	Effect of prenatal smoking 10+ cigarettes/day observed for hyperactive-distractibility behaviour [OR=1.6 (1.0-2.3) but not aggressive or anxious behaviour	6
JOHANSSON 2008	8,850	Mixed	Effects observed for excessive crying OR 1.31 (1.13-1.51) and irritability OR=1.27 (1.09-1.48) in children exposed pre and postnatally. For children only exposed prenatally, only effects observed for use of broncho-dilating drugs OR=1.45 (1.03-2.04) and poor sleep OR=2.06 (1.09-3.87)	6
DONOFRIO 2008	8,889	Mixed	Effects (CP and ODP) were non-significant after comparing differentially exposed siblings. Effects (ADHD) were attenuated after comparing siblings.	4
BRION 2010B	509	Mixed	Effects observed for conduct/externalising only after adjustment 1.82 (1.19-2.78).	4
BRION 2010A	6,735	Mixed	Effects observed for conduct/externalising only after adjustment 1.24 (1.07-1.46)	5
PICKETT 2008	18,263	Mixed	Effect of heavy smoking OR=1.17 (p=0.09). Prenatal smoking followed by quitting during pregnancy was associated with improved outcomes among offspring at 9 months of age	5
MAUGHAN 2001	5,770	Mixed	OR for conduct problems 1.53.	4
THARPAR 2003	2,054	Mixed	Effects observed for ADHD	4
MARTIN 2006	2,001	Mixed	Effects observed for temperament, behaviour and academic problems. Contrary to expectation, infants exposed to heavy prenatal smoking had less distress to novelty and less irregularity.	5
SEN AND SWAMINATHAN 2007	8,395	No	Found that alcohol but not smoking predicted behaviour problems in children.	4
THARPAR 2009	815	No	Significant differences observed for genetically related vs. unrelated offspring, suggesting inherited effects rather than prenatal smoking effects	0
ROZA 2009	4,680	No	Associations accounted for by controlling for parental socioeconomic status and psychopathology	6

*Quality score on Newcastle-Ottawa Scale

Null results (children)

An example of evidence in favour of the null hypothesis comes from a 2009 paper from a study of 18 month old children from the Netherlands. This study initially observed the effect of prenatal smoking exposure to be OR=1.45 [1.15-1.84] for externalising mental healths and OR=1.59 [1.21-2.08] for total problems using the Child Mental Health Checklist (n=4680). After controlling for parental socioeconomic and mental health factors, the observed effects disappeared, providing evidence that residual confounding may be responsible for the effects that have been observed among children whose mothers smoked during pregnancy (Roza et al. 2009). One strength of this study was that both mothers and fathers provided data about their child's mental health, thereby minimising some maternal reporting bias.

Positive association (children)

On the other hand, there were high-quality studies that found clear evidence of an effect of prenatal smoking exposure and child mental health problems, even after controlling for socioeconomic and parental mental health factors. In Norway in 2009, smoking during pregnancy was reported to be associated with externalising mental health problems among 18-month old children, after adjusting for relevant confounding variables including maternal education, mood and child birthweight. (n=22,545). Smoking was reported by the mother during the 17th week of pregnancy. The effect (OR=1.32, 1.03-1.70) was observed in both boys and girls. The study authors estimated a population attributable risk of 1.75% for smoking 10 or more cigarettes per day during pregnancy for externalising mental health problems (Stene-Larsen et al. 2009). Still, the study did not control for more extensive maternal and family socioeconomic factors, and more subtle residual confounders could have been at work.

Mixed results

An example of a study of children with mixed results is a Swedish study published in 2008 (n=8850) which separated groups of 3 year old offspring exposed only prenatally from those exposed prenatally and postnatally to cigarette smoke in the household and those exposed postnatally only. In terms of mental health outcomes, children exposed both pre- and postnatally to smoking had a higher odds of excessive crying (1.31; 1.13-1.51) and irritability

Maternal smoking during pregnancy and child mental health and wellbeing: evidence, policy and practice (1.27; 1.09-1.48) compared with unexposed children. Increased odds of suffering from poor sleep (2.06; 1.09-3.87) and increased odds of being given broncho-dilating medication (1.45; 1.03-2.04) were observed in children who were exposed prenatally only (Johansson et al. 2008).

Adolescents

Three papers reported on studies focused specifically on adolescents (Silberg et al. 2003, Indredavik et al. 2007, Nigg and Breslau 2007). Of these, one study observed effects for externalising mental health problems, one study did not, and one study found mixed results—effects were observed for some outcomes and not for others.

A Norwegian study of 14 year old adolescent offspring, published in 2007 (n=84) examined pregnancy smoking and child mental health problems and reported that children exposed prenatally to cigarette smoke were more likely to fare worse on four scales of adolescent mental health and cognition: The Achenbach System of Empirically Based Assessment, the ADHD-Rating Scale IV, the Autism Spectrum Screening Questionnaire and the Children's Global Assessment Scale. The follow-up period was 14 years, and though the sample was small, the investigators were still able to detect effects of prenatal smoking exposure on mental health after adjusting for maternal mental health and socioeconomic factors, as well as the child's birthweight. Interestingly this study observed effects for both externalising and internalising mental health problems (Indredavik et al. 2007).

Another paper from a study of adolescents reported effects among 17 year old adolescents (n=713) in a cohort from Detroit, USA with smoking history 6 years after pregnancy. Results were mixed. Effects were significant for ODD and for CD but not for ADHD. Outcome data were collected from mothers, teachers and the adolescent's self report (Nigg and Breslau 2007).

An analysis of a cohort study of adolescent twin boys from Virginia USA using retrospective exposure reports 12-17 years after the pregnancy found no effects for mental health problems after adjusting for socioeconomic and maternal factors. Maternal CD was also assessed (retrospectively), and was found to be strongly associated with having smoked more than 10 cigarettes per day while pregnant. The authors concluded that this evidence does not indicate

that maternal smoking during pregnancy may have no effect on mental health during infancy, but simply that it did not seem to have an effect on whether a child exhibited CD symptoms during adolescence—but that maternal smoking 10+ cigarettes a day possibly acted as a marker for an intergenerational transmission of antisocial mental health (Silberg et al. 2003).

Young adults

One of the strongest pieces of evidence in favour of the null hypothesis comes from a 2010 study of Swedish young adults (born between 1983-1989). The study looked at whether young adults (n=609,372) prenatally exposed to cigarette smoke were more likely to have become violent criminal offenders. Effects were observed, including a dose-response relationship between increased prenatal smoking and violent criminal behaviour. In spite of this, differentially exposed siblings (n=50,339) were found to be just as likely to engage in violent criminal behaviour, leading to the conclusion that familial factors were the underlying cause in this age group, rather than prenatal smoking exposure (D'Onofrio et al. 2010).

Adults

A similar study, however, found the opposite: a Providence, Rhode Island USA study of adults who were at least 33 years of age found an effect of prenatal smoking exposure on criminal offending. At birth, data were collected on 3766 babies, and they were followed up via criminal record checks using names, dates of birth and social security identification numbers where possible. Propensity score matching was used to simulate experimental-style comparisons. After adjustment for socioeconomic and family background factors, effects were observed for prenatal smoking exposure. Exposed offspring had greater odds of having criminal arrests (OR=1.31, 1.06-1.62). Effects were observed for both men and women (Paradis et al. 2010). This study's reliance on propensity score matching means that its controls for confounders may not be as reliable (UCLA Medical Imaging Informatics Group 2009) as that of the Donofrio et al. study from 2010 mentioned above, and other biases may have been introduced using this method.

Longitudinal analyses

Longitudinal analyses have been suggested by prior reviews of studies (Cornelius & Day 2009, Herrmann et al. 2008, Button et al. 2007, DiFranza et al. 2004, Wakschlag et al. 2002). The

following 9 studies have analysed the association of prenatal smoking exposure and child mental health problems over time. Of these, 7 found clear evidence that prenatal smoking exposure predicted child mental health trajectories, and 2 studies found mixed evidence. There were no longitudinal studies whose results supported the null hypothesis alone.

An American study published in 2006 reported on whether there is an association between prenatal smoking and a “developmental pattern” of conduct problems in boys. Exposed children in the Pittsburgh Youth Study (448) were found to be more likely to develop oppositional disorder and oppositional defiant-attention deficit/hyperactivity co-morbid disorder but not attention-deficit/hyperactivity disorder alone. They were also more likely to begin to develop these problems at an earlier age than non-exposed children. (Wakschlag et al. 2006a).

Another American longitudinal study of 77 African-American 10 year olds from Chicago found that maternal pregnancy smoking was associated with “low sociability / negative emotionality” in infancy and with conduct disorder at the age of ten; however the early caregiving environment was seen as mediating the relationship—boys exposed to pregnancy smoking but who had “responsive” mothers in early infancy did not experience the same increased risk of CD as exposed boys with “unresponsive” mothers during infancy (Wakschlag et al. 2006b).

A study of 203 African American and Puerto Rican children (mean age 8.6, SD 0.87) conducted by the New York University School of Medicine published in 2006 found that not only pregnancy smoking but also maternal warmth and maternal unconventional mental health were associated with aggressive behaviour among offspring (Brook et al., 2006).

Huibregts, et al. (Quebec, Canada) analysed their cohort data longitudinally and found 3 trajectories for the development of physical aggression and hyperactivity—and they reported in 2007 that prenatal smoking exposure predicted following high-risk trajectories.

A longitudinal study of 396 children from the Netherlands reported in 2008 that maternal smoking during pregnancy was associated with both externalising and internalizing mental health problems during childhood at ages 5, 10, 11 and 18—after controlling for potential confounding variables including demographic, maternal mental health and child social and attention problem variables (Ashford et al. 2008).

A Finnish study from 2006 examined the relationship between smoking during pregnancy and the offspring's temperament, mental health and academic performance at the ages of 6 months, 5 years and 12 years. It concluded that several mental health outcomes might be attributable to smoking during pregnancy, after adjusting for maternal hospitalisation (for accidents or psychiatric reasons), distress, nausea or respiratory infections during pregnancy, socioeconomic status, and maternal age (Martin et al. 2006a).

Gray et al. observed clinically significant mental health problem effects on the Child Mental Health Checklist in an American cohort of children born with low birth weight, at the ages of 3, 5 and 8 in Boston (n= 869). Statistically significant predictors of increased odds of mental health problems at each age were: maternal psychological distress at 40 weeks of pregnancy (1.59, 1.21-2.09), maternal cigarette smoking during pregnancy (1.57, 1.20-2.04), Hispanic ethnicity (2.0, 1.24-3.24) and maternal age (0.94, 0.94-0.99). (Gray et al. 2004)

Issues raised by the current review and prior review papers

Review papers published during the period from 2001 until 2010 have emphasised the following areas that should be improved in order to clarify whether it is prenatal smoking exposure or effects of residual confounding that is so consistently observed in the studies of the effects of prenatal smoking exposure on child mental health over the life course. None of the studies to date have been able to disentangle perfectly the effects of prenatal smoking with genetic and social confounders (Herrmann et al. 2008), but beginning around 2009, several studies have focused specifically on disentangling any potential biological / teratological effect of the chemical exposure of prenatal smoking from other factors.

The major issues that remain are: to resolve questions about potential confounders: genetics, family mental health and home environment, socioeconomic status, chemical exposures, and low birth weight—all of which are known to be associated with child mental health problems. Interaction effects can also be addressed in future high quality studies in order to understand interactions with gender and with various mental health outcomes such as hyperactivity and aggressive behaviour.

Study quality is another area of concern raised by the reviews. It is necessary to use sample sizes that are large enough and powered to detect effects after introducing controls for extensive and complicated potential confounding factors.

3.4 Update of studies, 2010-2013

During the two years since the original review was conducted, there has been an increase in the number of studies that aim to disentangle the associated exposures from prenatal smoking during pregnancy. The same search methodology was used to find relevant papers published since 2010, and 43 relevant papers were found. The increase in papers likely reflects the increase in interest in the topics of maternal smoking and child mental health and its determinants. This preoccupation has grown in step with an emphasis on individual responsibility for health and increasingly prevalent behavioural health problems such as obesity.

Of the 43 studies, nearly all found positive associations between maternal smoking during pregnancy and either hyperactivity or aggression in childhood. Sixteen of the studies used data from longitudinal studies, as was recommended in the review papers from the previous 10 years (though few of these used longitudinal, as opposed to cross-sectional regression analyses of the data).

The results of these longitudinal studies from seven different countries were consistent: prenatal smoking exposure predicts child mental problems but social, economic, environmental and familial factors attenuate the effect so that what remains seems to be a subtle but reliable effect on child neurological development (Cornelius MD et al. 2012, Hernández-Martínez C et al. 2011, Galera C et al. 2011, Sciberras et al. 2011, Motlagh MG et al. 2011, Fang H et al. 2010, Boden JM et al. 2010, Murray J et al. 2010, Hsieh et al. 2010, Nomura et al. 2010, Brion MJ et al. 2010).

Still, there are three good quality studies that give reason to question this effect. One study replicates the finding that quitting smoking predicts the best child outcomes above and beyond those of non-smoking mothers. This finding was first observed by Pickett et al. (2008) and indicates that if there is a neurotoxic effect, it is not irreversible if exposure is limited (Robinson M et al. 2010).

The second reason to question the effect is a paper that controls for maternal smoking during pregnancy, in which the authors report that maternal depression in pregnancy predicts child aggression (Hay DF 2010).

The third and most important reason to question the effect is a study from Finland (Obel C et al. 2010) that includes all births across a 20 year period. This study found that the effect of

maternal smoking during pregnancy was not a significant predictor after extensive controls for social, economic, demographic and familial factors were taken into consideration together.

3.5 Chapter conclusions

Not only are there many studies looking at the association between prenatal smoking exposure and child mental health problems, but there are also a variety of ways of defining mental health problems, at various time points over the course of childhood and into adulthood. This heterogeneity complicates the picture. By separating studies according to age group it is possible to see that at any given age the evidence for a causal claim is mixed. There is certainly consistency in that there are several studies that show negative effects on child mental health, and biological plausibility has been shown in animal models. What is less clear is whether closely related maternal and family mental health factors can explain the entire association as has been observed in some studies, or whether there is a true effect of prenatal smoking exposure that may even persist into adulthood and be a key factor in the path leading to criminal offending, as one study has suggested (Paradis et al. 2010).

Two papers that resulted from consulting with experts in this field have added to the complexity of the issue. The first paper examines and reports on a genetic-sex-exposure interaction—in other words, having a certain genetic phenotype was found to interact with sex (boy/girl) in the presence of prenatal smoking exposure (Wakschlag et al. 2009). The second paper provides evidence that smoking predicts aggression and noncompliance but that paternal responsiveness moderates smoking effects on behaviour.(Wakschlag et al. 2011). In light of these, it is understandable that other studies might have differing findings and that appropriate policy responses might be difficult to develop.

Methodologically, there are several challenges to finding the truth about the real association between prenatal smoking exposure and child mental health problems. The first is study design. Studies of siblings differentially exposed would provide the best evidence for or against a true association since the family background and social context can be controlled for, and it is one of the most important potential confounders. Given the scarcity of such studies, the next best are longitudinal studies that measure smoking exposure prospectively. Robust studies of high-quality, population based cohorts over time can compare groups of children

whose family and social contexts change over time, to see whether those who fare better also experienced positive social and economic changes over time relative to comparison groups.

Another methodological issue is that of exposure measurement. Smoking patterns are not as straightforward as would be required for robust confidence in measurement. Women, especially when pregnant, will attempt to quit smoking several times, and perhaps they will also have spikes in the number of cigarettes smoked during stressful times. These may or may not correspond to critical periods of development during the pregnancy, and there are many unknowns that remain about exposure. Further, for older generations it is bewildering to think that maternal smoking during pregnancy could truly cause hyperactivity and conduct problems since so many mothers, across the entire income scale, smoked during pregnancy in previous generations while hyperactivity at least seems to have increased more recently, as smoking during pregnancy has decreased in higher income groups and concentrated among lower income groups. This thesis is concerned with the effects of smoking during pregnancy on the current generation of children, not only because possible cohort effects for older generations would be different, but also because the cigarette smoke that this generation is exposed to is vastly different, more chemically altered, than the cigarette smoke that previous generations were exposed to.

Outcome measurement also presents challenges. Choosing which outcomes are of most importance remains an open question. The studies in this chapter emphasise the fact that many outcomes and definitions of outcomes, at different time points, and of differing severity have been studied. Few studies have shown a link to internalising problems such as depression and anxiety, yet such a link would be expected if the association between prenatal smoking exposure and child mental health problems were explained by maternal mental health problems alone.

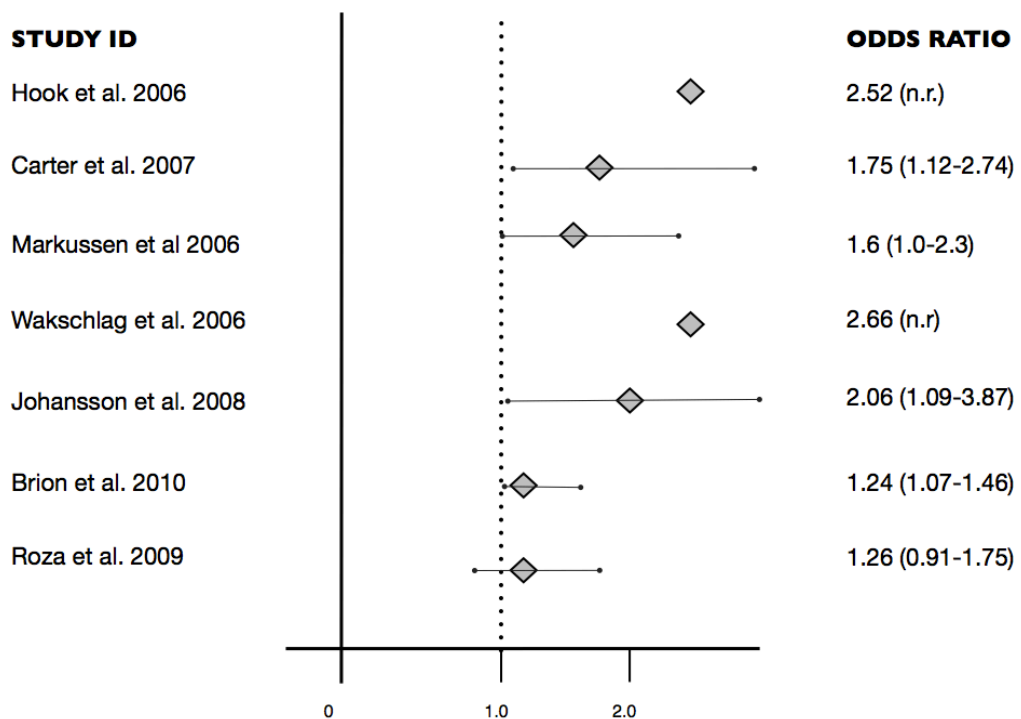
Finally, alternative explanations should be tested and ruled out if possible. These include genetic confounds, environmental and family context factors, along with maternal social, economic and psychological factors which may mediate or moderate the relationship.

Because of this heterogeneity of methods, age groups, outcomes and results, we remain in a state of equipoise about the association between prenatal smoking exposure and child mental health problems. The next chapter will attempt to answer some of the remaining questions by

introducing more longitudinal analysis in a very large, population-based sample, powered to detect effects after extensive controlling for potential confounders.

Considering the existing studies that are most relevant to this thesis, i.e. good quality studies scoring 7 or higher on the Newcastle-Ottawa scale (Wells et al., 2014) that report findings relevant to child mental health, a summary of the findings of these studies reveals the following pattern: most studies report significant associations between maternal smoking during pregnancy and child mental health problems after controlling for potentially confounding variables, but the confidence intervals that are reported all originate very close to one or cross one (Figure 3.3).

Figure 3.3 Forest plot of findings



Discussion

Many studies have found positive associations between prenatal smoking exposure and child mental health problems, which leads one to assume that there might be a causal link. The same findings—that prenatal smoking exposure is a precursor to mental health problems in offspring—have been found in many cohort studies, in several different countries, using a wide range of mental health checklists from different professional psychological bodies.

In spite of this consistency, many of these studies suffer from the same methodological issues. These phenomena should be examined over time, ideally over the entire life course so that other influences can be sifted out for a real comparison of individuals whose mothers smoked during pregnancy to those whose mothers did not.

Longer-term follow-up, though not available in the current literature base, will likely provide more insight into the relationship between smoking and mental health as the children in the Millennium Cohort Study grow older and genetic data are gathered. Other cohort studies that have more extensive data on family members, including genetic information and long-term follow up data on the mothers and other significant family members would be very useful sources for future studies.

4

Prenatal smoking exposure and child well-being in the Millennium Cohort, United Kingdom, 2000-2008

•Aim of this chapter

The aim of this chapter is to assess whether children whose mothers smoked during pregnancy are more likely to display hyperactivity and aggressive behaviour compared to their peers whose mothers did not smoke during pregnancy, taking a longitudinal perspective to observe change over time using birth cohort data from a large, nationally representative, population-based sample from the United Kingdom.

4.1 Study design and methods

4.2 Cross-sectional analyses, 7 years of age, hyperactivity

4.3 Cross-sectional analyses, 7 years of age, aggressive behaviour

4.4 Longitudinal analyses, aggression and hyperactivity across 5 years

4.5 Chapter conclusions

In this chapter the effect of maternal smoking during pregnancy on child mental health is analysed directly. Data from the Millennium Cohort Study are used to determine whether the findings of the review in Chapter 2 are supported in the context of children who were born during a one year period from October 2000 to September 2001 whose mothers smoked during pregnancy in the United Kingdom. These analyses are unique in that they utilise high-quality longitudinal data from a very large population-based sample.

The findings of this chapter are relevant to answering the thesis question: ‘Were children born in the United Kingdom in the year 2000 more likely to experience mental health problems such as hyperactivity and aggressive behaviour if their mothers smoked during pregnancy?’ Taking a longitudinal perspective allows for a better understanding of change over time. Multi-level models are utilised here in order to track both intra-individual and inter-individual change over time, simultaneously.

Introduction, questions and study aims

Given the scarcity of studies available that have been able to examine the relationship between prenatal smoking exposure and child mental health problems in sufficient detail—i.e (1) controlling for extensive and known potential socio-economic confounders, (2) utilising a population-based, nationally representative, prospective study design with sufficient sample size to allow for the power to detect real associations and to rule out erroneous ones, and (3) analysing the data longitudinally so as to follow the children over time to see how they fare, to see what predicts the resolution of mental health problems and what predicts the persistence of mental health problems—this analysis is intended to add weight to the balance of evidence. It will first analyse the most recent data collection wave (when the cohort members were seven years old), then utilise four data collection waves over the course of five years.

A longitudinal approach is important to the study of child mental health and development, especially in light of recent findings that brain structure and function are far more plastic than previously thought (Merzenich and Buonomano 1998)—indicating that mental health disorders may come and go, in flux with the environment an individual lives in and that environmental causes may be as important to consider as genetics and biochemical exposures. Longitudinal analyses are particularly important in furthering this line of research in order to discern what changes are due to treatments and what changes would have happened with or without treatment.

Longitudinal analysis

A true longitudinal analysis is different from a cross-sectional analysis of longitudinal data. Most studies in the literature (as summarised in Chapter 2) that utilise longitudinal data are superior to cross sections because they establish a temporal distinction between cause and effect, but they mostly perform standard logistic regression analyses. This involves defining the exposure at one time point and the outcome at a later time point, without controlling for the time element statistically. By contrast, multi-level models are able to account for changes within individuals and between individuals over time, simultaneously, thereby maintaining the element of time in the statistical analyses. As a result it is possible to observe the average trajectories of different exposure groups over time, to observe whether the severity of problems increases, decreases or remains static over time.

Defining hyperactivity and aggressive behaviour

Hyperactivity in the past has often been popularly perceived as an American phenomenon or social construction, though a systematic review found the prevalence to be generally stable across populations, including reports from 30 other countries (Polanczyk 2007). Prior to 1970, differences in case definitions may have caused American youth to be classified as having attention and hyperactivity problems, while British youth with similar mental health profiles were classified as having aggressive behaviour problems, but currently most diagnostic systems use the DSM diagnostic system, and using this, prevalence seems to be similar across national populations for defining hyperactivity (Attention Deficit-Hyperactivity Disorder) and aggressive behaviour (Conduct Disorder) (Polanczyk 2007). In North Carolina (USA), a population-based study found rates as high as 10% of children with a diagnosis for Attention Deficit-Hyperactivity Disorder, and 7% of all children receiving medication to treat the condition (Rowland 2002).

Theoretically there is good reason to suspect that structure and function vulnerabilities in the brain would lead to social vulnerabilities, for example if auditory processing is impaired, but only in a subtle way that isn't detected as hearing loss, then anyone with this vulnerability would be at risk for not developing normally in a social environment that is heavily dependent on auditory processing.

Analyses in this chapter will examine whether hyperactivity and conduct problems are more common among children who were exposed to cigarette smoking during gestation. The

question here is not to ask whether hyperactivity is a real problem outcome or not but rather to ask whether this issue, which has become of substantial social concern during the past 20 years is accurately associated with smoking during pregnancy.

Rise in violent crime among youth, increased interest in child aggression

In some countries, as many as 5.8% of the population are classified as having conduct disorder (CD) (Polanczyk 2007). Increasing rates of violent crime arrests for juveniles—for example, in the United States during the ten year period from 1983 to 1992 (Frick 1992)—has led to an increased interest in the causes of child mental health problems, how exposures during pregnancy may impact child mental health, and what happens in-between—i.e between a toxic exposure during pregnancy and violent crime, or more broadly, between exposure during pregnancy and any mental health problems during childhood.

Is smoking during pregnancy the risk factor or a marker of risk?

As mentioned in Chapter 2, many studies have found associations between maternal smoking during pregnancy and child mental health problems. Two other studies of this association analysed data from the Millennium Cohort, and a relationship was observed between maternal pregnancy smoking and child temperament at the age of 9 months (Pickett et al. 2008) and child mental health problems (hyperactivity and aggressive behaviour) at 3 years (Hutchinson et al. 2010). Both of these studies controlled for extensive social and economic co-variables within a very large, nationally representative, population-based sample. Many of the social and economic factors were found by Hutchinson et al. (2010) to predict child mental health outcomes, but maternal smoking during pregnancy remained a key predictor even after adjustment for these factors.

More recently a cohort study by researchers at Harvard University (USA) found that pregnancy smoking was associated with a 1.25-fold increased odds of criminal arrests among adult offspring at age 33 years or older (Paradis et al. 2010); on the other hand, a Swedish cohort study (Donofrio et al. 2010) found that comparing differentially exposed siblings resulted in no association between maternal pregnancy smoking and adult criminal mental health, suggesting the effect to be either genetic or related to the home environment.

In spite of these extensively detailed existing studies, there are questions that remain. I was interested in finding out whether the data from the most recent sweep of the Millennium Cohort Study from the United Kingdom supported the hypothesis that maternal smoking during pregnancy was associated with persisting child mental health problems at 7 years of age, and whether there were discernible longitudinal trends in the severity of mental health problems that could be observed and tested within this cohort.

One of the most important aspects of this study is to consider the social and economic forces that may also create vulnerabilities in children. It may be that children born with healthy brain structure and function will still be at risk for mental health problems if their environment during childhood puts them at a disadvantage, and work on brain plasticity supports the idea that it is not simply the *in utero* period that matters (Merzenich and Buonomano 1998).

It has been established that not only prenatal smoking exposure, but also a long list of social and economic factors are strongly associated with child mental health problems, including: poverty, low maternal educational achievement, maternal well-being during her own childhood, maternal mental health, maternal feelings about the pregnancy and her competence as a parent, and infant factors such as low birth weight (Pickett et al. 2008, Hutchinson et al. 2010). Considering all of this is worrying in itself, and illuminates the possibility that prenatal smoking exposure may have a direct effect on foetal brain biology, or it may be a marker of intergenerational processes of the transmission of mental health and mental health problems—or it may be both.

Tobacco use during pregnancy is one of the few of these factors that is modifiable at the individual level; that is, the mother herself could in theory improve the chances of transmitting good mental health if she can find a way to quit smoking during pregnancy. In fact previous research indicated that women who quit during pregnancy were more likely to have children with easy-going infant temperaments (Pickett et al. 2008), and children with less risk of mental health problems at the age of three (Hutchinson et al. 2010).

This study aims to shed more light on the relationship between maternal smoking during pregnancy and child mental health by looking at trends over time.

4.1 Study design and methods

Data from the UK Millennium Cohort Study were used for this analysis. The cohort is a nationally-representative, population-based birth cohort which began in the year 2000. Data for the first wave were collected when cohort members were 9 months of age, via interview with the mother and father (when possible). Areas with greater proportions of ethnic minorities as well as areas with higher deprivation rates were over-sampled so as to recruit/obtain a nationally representative number of cohort members in these groups over time, given that these populations were expected to have higher relative attrition rates. Data are being collected every three years and are available from the Centre for Longitudinal Studies. The first wave included more than 18,000 participants (Centre for Longitudinal Studies 2010).

Sequence of studies

The first analyses serve as an update to prior research and publications which have looked at the association between smoking during pregnancy and child mental well-being within the same cohort, when the children were nine months and three years of age (Pickett et al. 2008, Hutchinson et al. 2010). This analysis will examine how the same children have fared at 7 years of age. Data from all four waves will then be analysed longitudinally in order to examine the role of prenatal smoking exposure as a predictor for the persistence of child mental health problems over time.

Study population

The Millennium Cohort Study is a birth cohort study, meaning that all cohort members were born around the same time, in this case during the period of one year beginning on the first day of September, 2000 in England and Wales and beginning on the first day of December, 2000 in Scotland and Northern Ireland. When the cohort member (CM) was nine months old, mothers were contacted and invited to participate. All children born during this time in the UK were eligible to participate. The study was designed to provide longitudinal data on nearly 20,000 individuals and their families.

Questions related to exposures during pregnancy were collected at that first time point, when the baby was nine months old. The study was designed to gather detailed information about childhood, child development and to provide data on whether government policies aiming to

reduce child poverty had an impact on children and their families.

For this chapter, the analyses were conducted using only data from natural birth mothers of the singleton cohort members. After counting the participants who answered the questions relating to the main outcome at each wave, the final study population included is reported in the appropriate section, later in this chapter.

Data collection methods

The mothers of cohort members (and fathers, or mother's partners) were interviewed at home and data entry was conducted onsite using a computer during interviews. Mothers were able to answer questions about sensitive information such as drug use using a direct data entry method on the computer itself as a way of minimising shame or embarrassment with the interviewer (Londra 2007).

Questions about exposure to prenatal smoking were asked during the first data collection wave, when the child was 9 months old. Questions related to mental health outcomes were asked of both mother and mother's partner when the children were 9 months old and 3, 5 and 7 years of age.

Selection of subjects

Selection of families was initially made via the Child Benefit Register of each of the four countries of the United Kingdom. It is estimated that this register includes 97% of all births that take place in the UK and therefore serves as a source of nationally-representative information about UK families. 72% of the families who were contacted agreed to participate (Dex and Joshi 2005).

Because more families from disadvantaged wards were included in the sample, to allow for higher attrition among disadvantaged families over time, the cross-sectional analyses in this chapter are weighted. Survey weighting variables are included in the dataset available from the Centre for Longitudinal Studies (Hansen 2012). These survey weights were applied to the analyses in this chapter.

Sample size and follow up

The original sample size included 18,819 children in 18,552 families. As of wave 2, there were 14,898 families and by wave 3 the number of families was 15,246. Some new families entered at wave 2 (692) and 1,444 families who attrited at wave 2 rejoined the study at wave 3. The total sample size as of wave 4 was 13,857 families (Hansen 2012). For the analyses in this chapter, singleton births whose biological mothers participated as the main respondent in the first data collection wave and who completed the questions about the main exposure (maternal smoking during pregnancy) and the relevant questions about child mental health from the Strengths and Difficulties Questionnaire (SDQ) were included, and the final sample included 13,161 children.

Ethical considerations

The consent of each interviewee was obtained by the Millennium Cohort Study staff. Signed consent was obtained as outlined by Hansen 2012. Ethical approval for the original study was given at each wave of data collection by the National Health Service Ethical Authority (reference number: MREC/01/6/19) at wave 1, the London Multi-Centre Research Ethics Committee (MREC/03/2/022) at wave 2 and again at wave 3 (05/MRE02/46) and by the Northern and Yorkshire Multi-Centre Research Ethics Committee of the NHS (07/MRE03/32) for wave 4.

Methodological limitations

As mentioned above, a birth cohort study is the strongest known study design that can be used to examine the relationship between prenatal smoking exposure and mental health problems in childhood. A randomised controlled trial is a stronger study design overall, but it is not currently thought to be ethical, to randomise women to smoke during pregnancy.

Trial results, for example from randomised controlled trials of the effectiveness of nicotine replacement therapy could be analysed post-hoc, but then the strength of the design is lost because mothers are not being allocated randomly to different treatment groups but rather those who quit in one group would be compared to those who didn't quit in another group, so this is not true randomisation—and the work of balancing potential confounders randomly among treatment groups is not achieved.

For this reason, the best study design for the UK is a large population-based longitudinal study that allows for establishing temporality, as the outcomes can be tracked over time as they develop during childhood.

Measurement issues: prenatal smoking exposure

One issue that is of concern with these data is that the smoking exposure data were gathered via maternal report as opposed to biological assay. There are legitimate concerns about this because there is a stigma to smoking during pregnancy, and mothers may have lied about their true smoking status because of the stigma, or they may have had other difficulties with recall.

There are a few reasons that this concern is of less importance in this case than in other studies. First the interviews were conducted in a non-clinical setting where the women interviewed may have felt less guilt or worry of being perceived as having poor health behaviours in a health-oriented setting. Second, being interviewed at home improves the expectation that these data are reliable for two reasons: one is that the interviewer will be able to smell smoke in the house, to see ashtrays, to smell the mother even, and because of this the mother would be less likely to lie about a question whose answer that might seem obvious. The other reason that the mother's being interviewed at home helps is that she is in her own environment, not in a perceived position of disadvantage as she might feel in a clinic or doctor's office, for example.

A third reason that these data can be thought to be reliable for assessing true smoking status is that there have been studies that gather this data in both ways: via mother's report and via biological assays, and these studies make it clear that the differences between the two methods are not large (Pickett et al. 2005, 2009a, 2009b).

Further, relying on biological assay, while temptingly suggesting a more true result because of the impossibility of lying—is not a perfect solution. Women who truly would like to lie about their smoking status, or more realistically, women who are trying to quit and would feel ashamed about being known as smoking while pregnant very possibly abstain the day or two before an ante-natal care visit or research visit, obtain a negative score on the assay, and return to smoking. So in practice relying on maternal report, in a trusted environment, with a trusted and impartial interviewer is likely to provide a similarly accurate assessment to the use of biological assays.

Exposure assessment

Nearly all mothers in the study responded to and provided valid responses to the questions on smoking during pregnancy in the MCS. Of a total of 18,552 mothers participating in the first data collection wave, 99.87% provided a valid response. Achieving this high response rate for sensitive information may have been facilitated by the direct data entry method used for gathering sensitive information. The mother was able to answer the questions using on-screen prompts directly on the computer without the interviewer's knowledge of her replies.

Exposure measurement variable

Wave 1 of the MCS included variables for assessing cigarette smoking among the mothers of cohort members. Mothers were first asked whether they smoked before pregnancy, then asked how many cigarettes they were smoking before pregnancy, then whether they changed the number of cigarettes they smoked during pregnancy, and finally if they had changed, they were asked how many cigarettes per day they smoked after the change. The coding for the variable is in the table below. Four prenatal smoking exposure levels were created: none (0), light (1-9), heavy (10+) and quit (changed to 0).

Outcome variables

For the present study outcomes are compared at three comparable time points: ages 3, 5 and 7. Data on infant temperament is available from the first wave, when cohort members were 9 months old, but not used here since infant temperament is not comparable with child

behaviour. At ages 3, 5, and 7, the Strengths and Difficulties questionnaire (SDQ) was given to mothers for private self-completion using direct data entry to using computer-assisted technology. The questionnaire includes 5 questions about the child's risk for hyperactivity and 5 questions about the child's risk for conduct problems. The developers of the questionnaire provide guidelines for scoring the questionnaire at "normal," "borderline," or "high" levels for both hyperactivity and conduct problems separately (SDQ 2012). More detail of the questions and how they were used for this analysis have also been reported previously (Hutchinson et al. 2010). The questions relevant to hyperactivity and aggressive behaviour are outlined in Box 4.1.

Box 4.1 Coding for Cases of Hyperactivity and Aggression

The Strengths and Difficulties Questionnaire (SDQ) is a widely used scale for identifying children with hyperactivity and aggressive behaviour. There are 25 questions in total, and ten of these are relevant to this study (SDQ 2009).

The parents are asked: “*What is your child like?*”

The responses for hyperactivity are:

1. *“Restless, overactive, cannot stay still for long”*
2. *“Constantly fidgeting or squirming”*
3. *“Easily distracted, concentration wanders”*
4. *“Can stop and think things out before acting”*
5. *“Sees tasks through to the end, good attention span”*

The responses for conduct problems are:

1. *“Often has temper tantrums or hot tempers”*
2. *“Generally obedient, usually does what adults request”*
3. *“Often fights with other children or bullies them”*
4. *“Often argumentative with adults”*
5. *“Can be spiteful to others”*

The respondent can choose from four possible responses:

- A) *“Certainly true”*
- B) *“Somewhat true”*
- C) *“Not true”*
- D) *“Can’t say”*

Each response is assigned a numerical value and children who score in the top 10% of the scale are counted as cases. This classification follows on from analyses by Hutchinson et al. (2010).

Because one aim of this chapter is to update and augment the analyses conducted by Hutchinson et al. (2010) in 3 year olds, this analysis structures the variables in the same way so that results can be compared and so that conclusions can be drawn about whether effects of prenatal smoking exposure are attenuated over time, whether they persist or become

aggravated as the child ages. The cut-point used by Hutchinson, and recommended by the authors of the SDQ is the top 10% of scores; that is, children scoring in the top 10% of both hyperactivity and conduct problem scales were classified as having these problems. Derived variables were created by summing the scores on each scale (0-10). Dichotomous “problem” variables were created for hyperactivity and conduct problems and these were used in the multivariate logistic regression analyses at 7 years of age.

In the longitudinal analyses the outcome variable is continuous rather than dichotomous. This structuring allows for observing changes in the average values on the SDQ scales over time.

For example, with a continuous variable observed over time, it is possible to see not only whether or not the exposed group has a greater odds of exhibiting problems as in cross-sectional regression analyses but also how high the score is and how that score changes as a trajectory over time in the exposed group compared to the unexposed group.

Social, economic and psychological covariates

Previous work by Pickett et al. (2009) proposed that there is a constellation of factors that can be drawn around pregnant women who continue to smoke, comparing them to pregnant women who had the ability to quit smoking, or those who never smoked. Strikingly:

“Among women living in poverty, around one in five smoked throughout pregnancy, whereas among women not living in poverty less than one in 10 smoked continuously.”

The fact that around one in five women living in poverty smoked throughout pregnancy, while less than one in ten not living in poverty smoked throughout pregnancy, coupled with the fact that 80% of women overall report wanting to quit smoking during pregnancy signals that poverty weakens the grip that a mother has on her own health behaviours, as a result of the difficult life circumstances she is faced with. It is important to keep in mind that a mother who smokes almost always wishes to quit smoking during pregnancy. But her ability to do so is weakened by her economic well-being and related factors, and not because she is unaware that she might harm her own health and the health of her baby. This point is re-visited later, in Chapter 5.

Box 4.2 Potential co-variables tested in multivariate logistic regression models, maternal smoking during pregnancy and child mental health outcomes, Millennium Cohort Study, United Kingdom, 2000-2008

Maternal smoking during pregnancy

Maternal age

Maternal education

Maternal family stability during childhood

Maternal relationship with own parents

Maternal relationship with friends

Maternal social support

Maternal life satisfaction

Maternal domestic partners

Maternal experience of intimate partner violence

Maternal sense of parenting competence

Maternal sense of control

Maternal experience of homelessness

Maternal adaptive functioning (managing finances and household)

Maternal depression

Maternal experience of limiting long-term illness

Ethnicity

Partner/couple status of mother

Family stability

Family poverty

Whether the pregnancy was planned

Entry to ante-natal care

Whether the mother breastfed the cohort member

Whether the cohort member was immunised

Whether post-natal smoking was allowed near the cohort member during infancy

Whether the cohort member had a low birthweight

Whether the cohort member's birth was a pre-term delivery

These co-variates were chosen so that the results could be compared with the results of previous studies by Pickett et al. (2009) and Hutchinson et al. (2010). Pickett et al (2009) examined the relationship between maternal smoking during pregnancy and infant temperament among 9 month old infants using the same sample of mothers and children studied in this thesis. Similarly, Hutchinson et al (2010) examined the relationship between maternal smoking during pregnancy and child mental health (hyperactivity and aggressive behaviour) among 3 year old children from this sample.

In both of these studies, the potential covariates listed above were included in the analyses for this chapter so that the results of this chapter build on previous work conducted with this cohort of mothers and children.

Data analysis plan

Cross-sectional analysis, multi-variate logistic regression, 7 year olds

Models were constructed for 7 year olds to see whether the relatively strong associations observed at nine months and 3 years of age observed in the studies by Pickett and Hutchinson are still observed in the cohort at age 7. Logistic regression models were estimated in Stata version 12 to calculate the crude and adjusted odds ratios for childhood mental health problems in exposed and unexposed groups, and in a partially exposed group (children whose mothers quit smoking during pregnancy).

Longitudinal analysis

The next step was to analyse the data longitudinally; that is, to examine how individual children fared over time, to test whether prenatal smoking exposure predicted the persistence of mental health problems over time, or the likelihood of belonging to a trajectory group whose mental health problems are worse than those of differentially exposed peers, at 3, 5 and 7 years of age.

For this analysis a multi-level model of change over time was utilised. This model combines two types of estimating equations: the level 1 equation estimates change within each individual over time. The level 2 equation estimates change between individuals with respect to the outcomes over time. The multi-level model combines these equations mathematically and allows for an analysis of where children start (y-intercept) in terms of severity of problems on the Strengths and Difficulties Questionnaire (SDQ) scales, by exposure status--and how the trajectories change during the five year period by exposure.

Generalised least squares (GLS) and maximum likelihood estimation (MLE) are currently the dominant methods for fitting multi-level models. In Stata version 12, the xtmixed package uses an MLE approach. The STATA code for variables and model building are included in Appendix 3.

4.2 Results

Prevalence of the exposure in the study population (pre-pregnancy)

Because more families from disadvantaged wards were included in the sample, to allow for higher attrition among disadvantaged families over time, the descriptive statistics and analyses in this chapter are weighted. Survey weights are included in the datasets as provided by the Centre for Longitudinal Studies (Hansen 2012).

Table 4.1 provides a comparison of key characteristics of the families who participated in the analyses when cohort members were 7 years of age with the original baseline cohort. The families who participated in the survey when children were 7 years of age were similar to families in the cohort at baseline. The mean age of mothers had changed, as expected during the seven year period, from 29.1 to 36.1.

Table 4.1 Comparison of Baseline and Seven Year Follow up Socio-Demographic Characteristics, Millennium Cohort Study, United Kingdom, 2000-2008

	Baseline	Seven year follow up
Mean age of mother (years) (SD)	29.1 (6.0)	36.1 (6.0)
Ethnicity		
White British, Irish or other white background	82.6	83.8
Black	3.6	3.3
Indian	2.5	2.5
Pakistani and Bangladeshi	6.8	6.4
Other	4.4	4.1
Below 60% median poverty indicator	32.7	30.0
Employed (in paid work)	62.0*	62.4
Current smoker	13.5	12.8

*during pregnancy

In this cohort, 10% of mothers were light smokers (<10 cigarettes per day) before pregnancy, 25% of mothers were heavy smokers (10+ cigarettes per day) before pregnancy and 65% of women did not smoke during pregnancy. Counting light and heavy smokers together, 35% of mothers in this sample reported smoking before pregnancy.

Comparing before pregnancy to during pregnancy, this 35% who reported smoking changed shape: the heavy smoking group decreased in size, from 25% pre-pregnancy to 10% during pregnancy. The light smoking group increased in size, from 10% pre-pregnancy to 13% during pregnancy, perhaps indicating that women in the heavy smoking group moved into the light smoking group.

The prevalences of smoking and quitting smoking before and during pregnancy in the Millennium Cohort Study are similar to those reported in the Infant Feeding Surveys of 2000, 2005 and 2010.

In the Infant Feeding Survey, as mentioned in Chapter 1, 25% of women smoked during pregnancy in 2010. Of these, 54% quit smoking during pregnancy, and 12% smoked throughout pregnancy in 2010. In 2005, the Infant Feeding Survey reported that 17% of women smoked throughout pregnancy, and that 19% of women smoked throughout pregnancy in 2000.

By comparison, the results here show that in the Millennium Cohort Study, 23% of women were heavy or light smokers throughout pregnancy in 2000-2001 when the first data collection wave took place.

Table 4.2 describes the sample studied. For all covariates, the “yes” response is shown. The Stata 12 coding used to define all variables can be found in Appendix 3. The full version of Table 4.1 and all potential co-variables, as defined previously by Pickett et al. (2009) is found in Appendix 4. An abbreviated version with key variables is included below.

Table 4.2 Distribution of Exposure, Outcome and Key Co-variables, Millennium Cohort Study at Baseline, United Kingdom, 2000-2001

N=13,161	No.	%
Mother heavy smoker (10+ cigarettes per day) during pregnancy	1,882	10.32
Mother light smoker (1-9 cigarettes per day) during pregnancy	2,333	12.80
Mother quit smoking during pregnancy	2,319	12.72
Child hyperactivity at 7 years of age	4512	7.8
Child conduct problems at 7 years of age	3378	5.9
Mother's age at cohort member's (CM) birth <20 years	1,580	8.67
Mother completed GCSE qualification grades A-C at time of CM's birth	6,092	33.40
Mother ethnic minority	2,924	16.06
Mother had no partner at time of CM's birth	1,747	9.60
Family below 60% median poverty	6,429	35.25
Mother doesn't have other parents to talk to	4254	23.32
Mother's life satisfaction	2,438	18.52
Partner perpetrated violence	476	2.61
Mother ever lived with more than one partner	4,885	28.30
Mother reported lacking parenting competence	385	2.11
Mother smacks child daily or weekly	119	0.90
Low sense of control	1,856	10.18
Mother depressed when CM was 9 months old	1637	8.98
Late entry to antenatal care	695	3.81
Low birth weight (CM)	1,231	6.75
Preterm birth (CM)	1,468	8.05

4.3 Multivariate logistic regression analyses, hyperactivity and aggressive behaviour in seven year olds

Results are given below for the multivariate logistic regression analyses at 7 years of age. The full results of all multivariate logistic regression models, including the results for 27 potential co-variables (Box 4.2) are included in Appendix 6. The 27 co-variables included here are modelled after the analyses of Pickett et al. (2008) and Hutchinson et al. (2010) who previously published the results of the effects of maternal smoking during pregnancy in 9 month olds and 3 year olds.

Table 4.2 Crude odds of hyperactivity, 7 year olds, Millennium Cohort Study, United Kingdom, 2007-2008 (N=13,161)

Maternal smoking during pregnancy	Odds Ratio	p-value	95% CI
Light smoker during pregnancy	1.8	<0.01	1.6 - 2.0
Heavy smoker during pregnancy	2.2	<0.01	2.0 - 2.5
Quit smoking during pregnancy	1.4	<0.01	1.3 - 1.6

The logistic regression models were adjusted for the potential co-variables listed in Box 4.2 simultaneously. Potential co-variables that were not statistically significant in the model were removed in a step-wise fashion, until only the significant potential co-variables remained. The full results of the final models are included in Appendix 6, and the results for the main exposure are presented here, in Table 4.3. After adjustment for 27 potential co-variables, both heavy and light smoking during pregnancy were associated with hyperactivity in the offspring at 7 years of age.

Table 4.3 Adjusted odds of hyperactivity, 7 year olds, Millennium Cohort Study, United Kingdom, 2007-2008 (N=13,161)

Maternal smoking during pregnancy	Odds Ratio	p-value	95% CI
Light smoker during pregnancy	1.3	0.01	1.1 - 1.5
Heavy smoker during pregnancy	1.4	<0.01	1.1 - 1.7
Quit smoking during pregnancy	1.2	0.12	1.0 - 1.4

Table 4.4 Crude odds of conduct problems, 7 year olds, Millennium Cohort Study, United Kingdom, 2007-2008 (N=13,161)

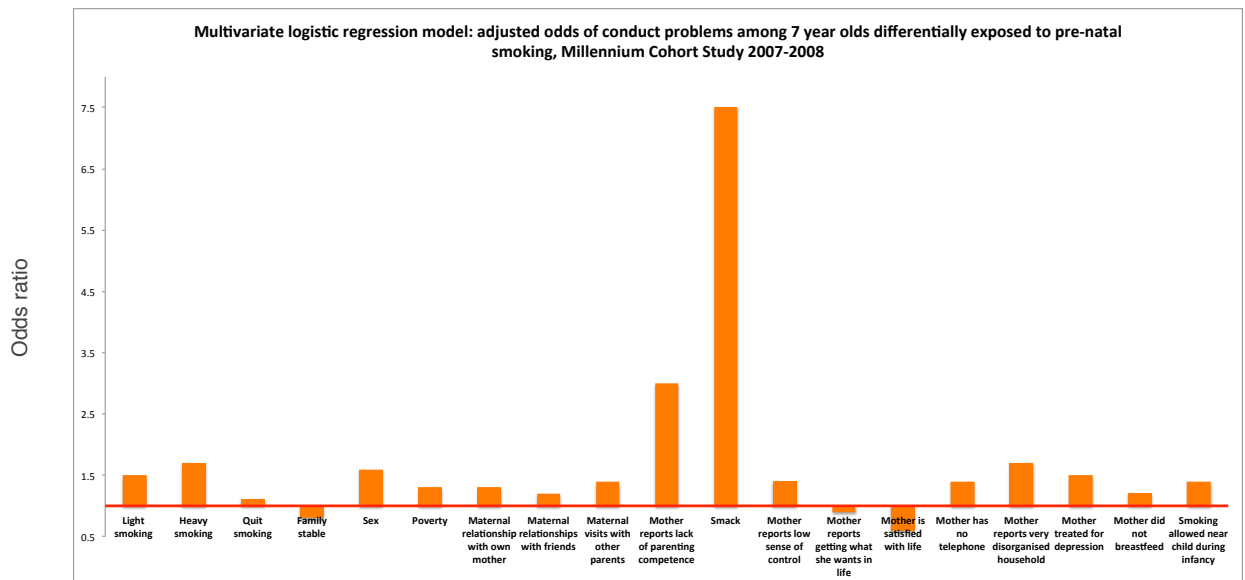
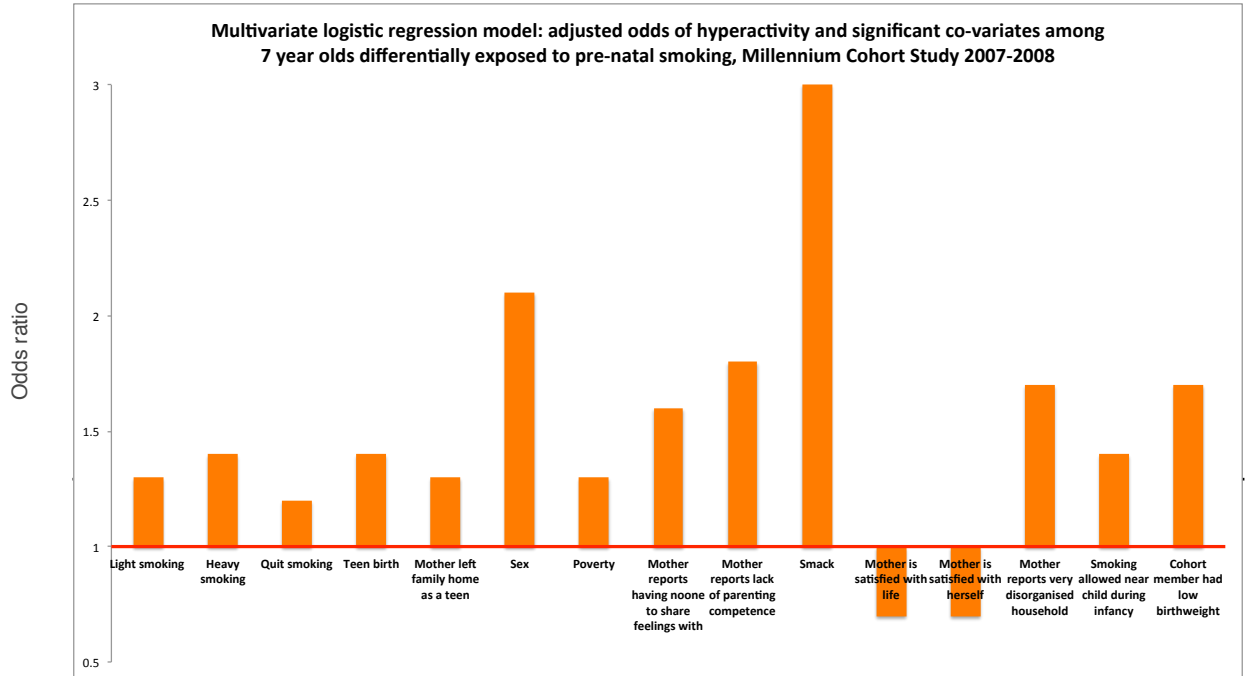
Maternal smoking during pregnancy	Odds Ratio	p-value	95% CI
Light smoker during pregnancy	2.1	<0.01	1.8 - 2.4
Heavy smoker during pregnancy	3.2	<0.01	2.7 - 3.7
Quit smoking during pregnancy	1.3	<0.01	1.1 - 1.6

The logistic regression models for conduct problems were constructed in the same way as for hyperactivity and all potential co-variables that were not statistically significant in the model were removed in a step-wise fashion, until only the significant potential co-variables remained. The full results of the final models are included in Appendix 6, and the results for the main exposure are presented here, in Table 4.5. After adjustment for all potential co-variables, both heavy and light smoking during pregnancy were associated with conduct problems in the offspring at 7 years of age. The final models are illustrated in Figure 4.4.

Table 4.5 Adjusted odds of conduct problems, 7 year olds, Millennium Cohort Study, United Kingdom, 2007-2008 (N=13,161)

Maternal smoking during pregnancy	Odds Ratio	p-value	95% CI
Light smoker during pregnancy	1.5	<0.01	1.2 - 1.8
Heavy smoker during pregnancy	1.7	<0.01	1.4 - 2.1
Quit smoking during pregnancy	1.1	0.22	1.0 - 1.4

Figure 4.4 Adjusted multivariate models, main exposures and co-variables, maternal smoking during pregnancy and child mental health among 7 year olds, Millennium Cohort Study, United Kingdom, 2007-2008



After adjustment, prenatal smoking exposure remains statistically significantly associated with both hyperactivity and conduct problems, though many of the co-variables remain significant predictors as well. A particularly strong association with both outcomes is observed in the very small group (n=119) where mothers reported “smacking [the child] daily or weekly.”

Two maternal factors (mother reports satisfaction with her life and mother reports satisfaction with herself) appear as protective factors against both hyperactivity and conduct problems.

A further sensitivity analysis was conducted, in a sub-sample of the two highest levels of the National Statistics Socio-Economic Classification (NS-SEC 1 and 2) in order to ascertain whether the effect of maternal smoking during pregnancy was observable in socially advantaged families. The results show that there is a statistically significant association for both hyperactivity and conduct problems, even among the best off socio-economic groups in the UK (Table 4.6).

Table 4.6 Sensitivity analysis: Crude odds of hyperactivity and conduct problems, 7 year olds, Millennium Cohort Study, United Kingdom, 2007-2008 (N=5410)

Maternal smoking during pregnancy	Hyperactivity: Odds Ratio p-value (95% CI)	Conduct Problems: Odds Ratio p-value (95% CI)
Light smoker during pregnancy	1.4, p = 0.04 (1.1-2.1)	1.6, p = 0.45 (1.0-2.5)
Heavy smoker during pregnancy	2.3, p < 0.01 (1.6-3.4)	4.1, p < 0.01 (2.7-6.2)
Quit smoking during pregnancy	1.4, p = 0.87 (0.84-1.5)	1.1, p = 0.74 (0.7 - 1.6)

4.4 Longitudinal analyses of prenatal smoking exposure and child mental health problems, Millennium Cohort Study, United Kingdom 2000-2008

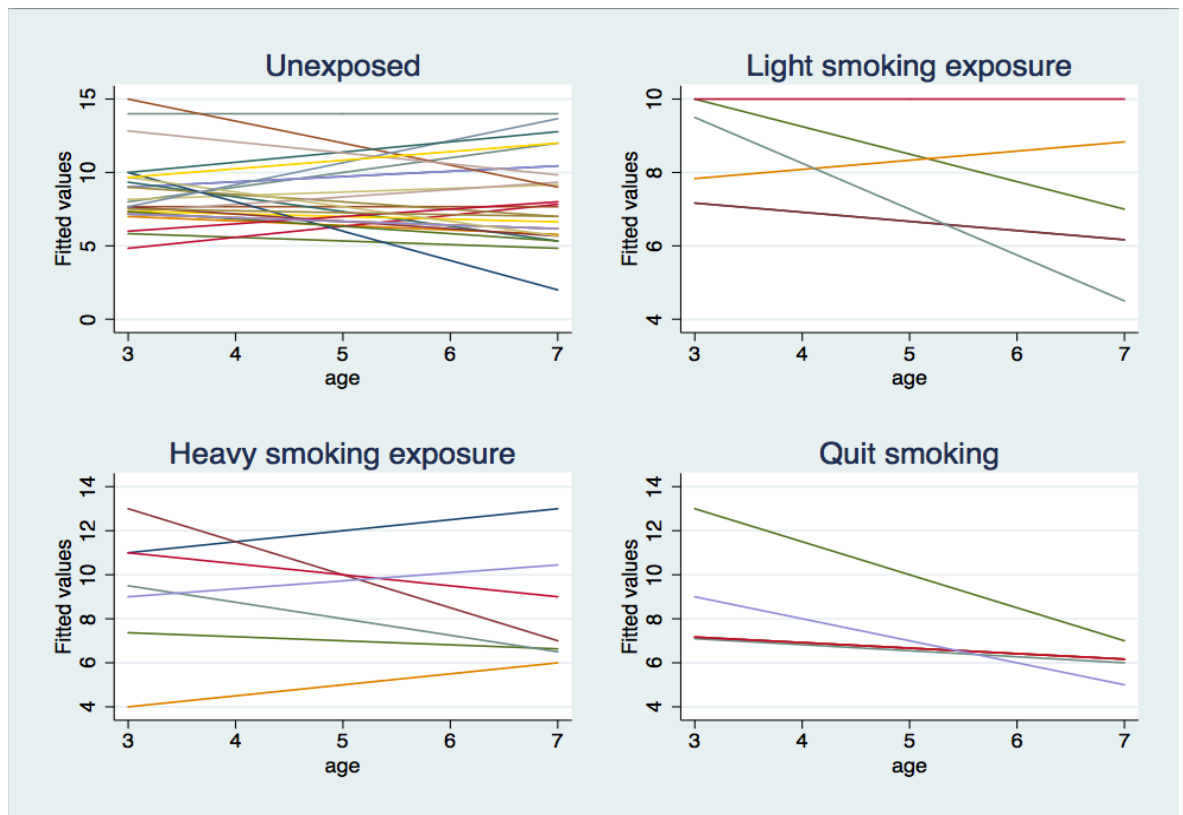
As mentioned previously, the longitudinal analysis takes into account the degree of hyperactivity and aggressive behaviour on the SDQ scales, thereby going beyond dichotomised hyperactivity and aggressive behaviour outcomes.

For the longitudinal analysis, to take into account intra-individual change over time and inter-individual change over time simultaneously (the estimating equations are combined to provide a single regression coefficient) The methods outlined by Willett and Singer (2010) were followed. To begin, Willett and Singer recommend visualising a random sample of trajectories from the data set. Are the slopes of individual trajectories generally zero, positive or negative? Figure 4.5 shows some sample trajectories from the data set, separated by exposure status.

For a quadratic trajectory, i.e. to identify a curved trajectory, $d+2$ repeated measures are needed, where d is the degree of the polynomial (i.e. quadratic is x^2 so $2+2=4$ waves of data are required). Given that there are currently 3 comparable waves of data available from the Millennium Cohort Study, the trajectories compared here will necessarily be linear. With 3 waves of data this is the most accurate estimation that can be made. Once the next wave of data becomes available, it will be possible to ascertain whether the true trajectories are typically curved or linear.

The multi-wave data set was transformed into one data set by reshaping it into “wide” format. This transforms the data so that each individual has a variable that measures, for example, hyperactivity at age 3, hyperactivity at age 5 and hyperactivity at age 7 as distinct variables within one data set.

**Figure 4.5 Longitudinal methods:
Summary of sample trajectories of hyperactivity**

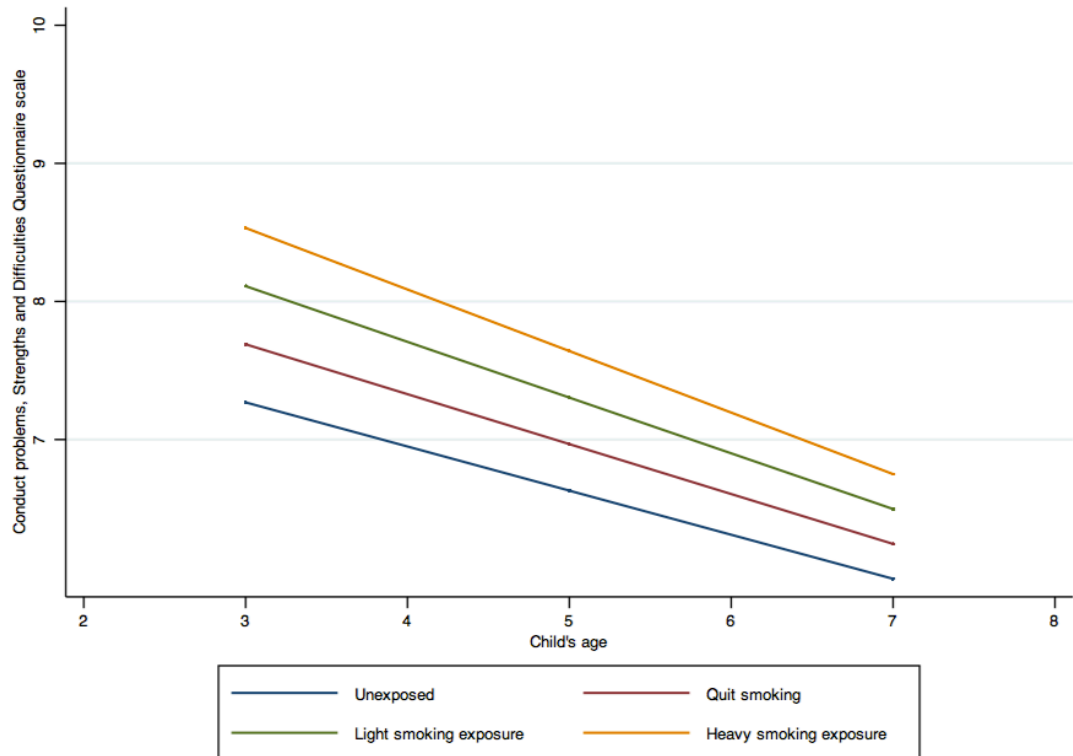


Longitudinal results and trajectories by exposure

After observing the sample trajectories, full longitudinal analyses were conducted. It was observed that the severity of both outcomes (hyperactivity and aggressive behaviour) generally decrease over time during childhood. That is, in all exposure groups the average level of hyperactivity and aggression is lower.

For both hyperactivity and conduct problems, children whose mothers smoked heavily throughout pregnancy fared worst. While all groups became less hyperactive and aggressive over time during childhood, on average the children exposed to maternal smoking during pregnancy started out scoring highest on the SDQ problem scales and continued to score higher than the less exposed and unexposed groups. The results for conduct problems are presented in Figure 4.6, and results for hyperactivity are presented in Appendix 6.

Figure 4.6 Trajectories of conduct problems over a 5 year period among children differentially exposed to maternal smoking during pregnancy, Millennium Cohort Study, United Kingdom, 2000-2008



After observing the persistence of the association between maternal smoking during pregnancy and child aggression in both cross-sectional and longitudinal analyses, the role of poverty in the longitudinal relationship between maternal smoking during pregnancy and child mental health was further examined, as family poverty is likely to be one of the drivers of many of the other social and economic co-variables that are associated with both smoking during pregnancy and child mental health.

A persistent poverty variable was created to reflect persistent poverty across childhood. To illustrate clearly how poverty influences the trajectories, Figure 4.7 displays the result of this further analysis for conduct problems, and the results for hyperactivity are reported in Appendix 6. Children whose mothers smoked during pregnancy and who were also poor

Maternal smoking during pregnancy and child mental health and wellbeing: evidence, policy and practice
 throughout childhood were most at risk for conduct problems, at 3 years of age and across the 5 year period of study.

Two groups stand out for their similarities and differences. The trajectory of the group that was exposed to smoking but not poverty is nearly identical to the trajectory for the group exposed to poverty but not smoking (green and red trajectories). The worst-faring group is that of the children whose mothers smoked throughout pregnancy and who were also poor. The best-faring group is that of the children who were exposed to neither poverty nor maternal smoking during pregnancy (Figure 4.7).

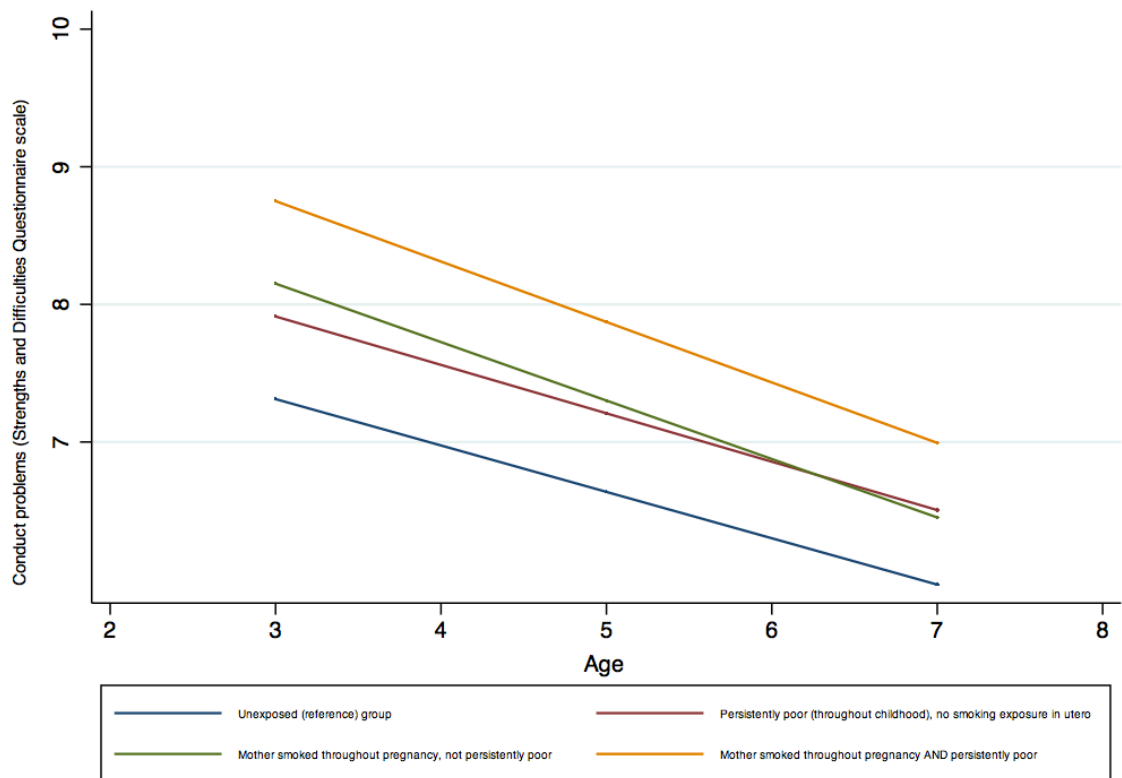
Table 4.7 Longitudinal trajectories of conduct problems, 3, 5 and 7 year olds, Millennium Cohort Study, United Kingdom, 2007-2008

Maternal smoking during pregnancy	Coefficient	P-value	95% Confidence Interval
Mother smoked throughout pregnancy	0.62	p<.001	0.57 - 0.67
Family poverty during childhood	0.67	p<.001	0.56 - 0.75
Average rate of change	-0.76	p=.002	-0.12 - -0.27

Controlling for the effects of persistent poverty, the estimated differential in initial child aggressive behaviour between children of mothers who smoked during pregnancy and those who did not is 0.617 (p<.001) and controlling for the effect of maternal smoking during pregnancy, for each 1-point difference in persistent poverty: the average initial child aggressive behaviour score is 0.659 higher and the average rate of change is 0.756 lower (Table 4.7.)

Children of mothers who smoked during pregnancy exhibit more aggressive behaviour initially than children of mothers who did not smoke during pregnancy but their rate of change in aggressive behaviour scores between ages 3 and 7 is no different. Persistent poverty is positively associated with aggressive behaviour and negatively associated with the rate of change in aggressive behaviour scores.

Figure 4.7 Trajectories of conduct problems over a 5 year period among children differentially exposed to prenatal smoking and family poverty, Millennium Cohort Study, United Kingdom, 2000-2008



4.5 Chapter conclusions

Main findings: not irreversible, not likely to be reversed

Across childhood the increased odds and dose response relationship between smoking during pregnancy and child hyperactivity and conduct problems seen at age 3 continues to be observable at 7 years of age in a large, nationally representative, population-based cohort study that includes extensive controls for social and economic co-variates.

In longitudinal analysis the effect is also observable: children whose mothers smoked during pregnancy begin life at with higher scores on scales of both hyperactivity and conduct problems. Though both problems attenuate over time in all exposure groups, children whose mothers smoked during pregnancy and children whose mothers were persistently poor relative

to their peers fared worse throughout the 5 year period of study. Children exposed to maternal smoking during pregnancy, especially heavy smoking start out childhood at a disadvantage in terms of hyperactivity and aggression compared to children with lighter exposure levels and to those not exposed to maternal smoking during pregnancy.

The chapter comprises a longitudinal epidemiological analysis of smoking during pregnancy and child mental health outcomes using cohort data for UK children from before birth to 7 years of age. The data analysed are from the Millennium Cohort Study. Data for 13,161 mothers and children, analysed longitudinally, were used to link exposure to maternal smoking during pregnancy to child mental health outcomes (hyperactivity and aggressive behaviour) at 3, 5 and 7 years of age. The multivariate logistic regression analyses and the longitudinal analyses of trajectories confirm the link between smoking in pregnancy and the development of disruptive behaviour problems in children in a large population-based sample from the United Kingdom. At the same time these analyses provide evidence that suggests that these effects may not be irreversible.

Limitations

Timing, dose and duration issues with respect to smoking during pregnancy are important. Smoking itself may be damaging to gametes (Zenzes 2000) and therefore there is also a need to study women who have ever smoked in addition to those who currently smoke. There is, for example, evidence that smoking initiation causes epigenetic changes in cervical epithelia in women (Ma et al. 2011) and smoking may have other profound effects on the biology of

women and their offspring. This recent evidence of epigenetic effects is important for beginning to understand the profound effects that smoking, or something else that smoking is a marker for, has on the biology of women. While pregnancy is a useful intervention time, when women may be more motivated to quit smoking, a woman's smoking at any age is potentially bad for her health and the health of her future children.

With a better understanding of smoking and epigenetics, it may be that quitting smoking during pregnancy is too late to make a difference, though more than one study has found that there is good reason to focus on quitting smoking during pregnancy for better child outcomes (Pickett et al, 2008, Hutchinson et al. 2010).

Future methods: observational v. experimental design

A nationally representative, population-based cohort study is the strongest possible study design for examining the association between prenatal smoking exposure and child mental health problems that is currently possible. Current and future studies of this association can additionally seek to add more refined genetic information and data on multiple generations in order to further disentangle real effects from potential confounding effects of family genetics and family environment. The use of the next most robust study design, a randomised controlled trial (an experimental as opposed to observational design), would be unethical in this case because it would not be ethical to randomise a pregnant woman to a smoking group in order to follow up the effects on her offspring—given that smoking is already known to be a health hazard, especially during pregnancy.

It is possible to examine the association experimentally in a post-hoc way by observing the effects over time in children of pregnant women who are already enrolled in a smoking cessation trial but who fail to quit smoking and compare them to the children of women who successfully quit, though results may be influenced, for example, by the presence of nicotine replacement therapy (NRT). Since nicotine may be the brain teratogen at work in the association between prenatal smoking exposure and child mental health problems, such a method would not solve the experimental design problem. In other types of smoking cessation trials that do not use NRT, where women are randomised to get help quitting or not, compliance with the intervention is unlikely to be random, and so the problem remains.

Another possible way to obtain experimental results would be to look at trials where NRT is compared to placebo, to see whether nicotine alone is a problem, as has been done in animal studies. This approach, if linked to child mental health outcomes over time, would be useful for further disentangling the neurotoxic and socio-economic effects.

5

Review of policy, guidance and discourse in the United Kingdom and United States

•Aim of this chapter

The aim of this chapter is to summarise ante-natal care policy towards smoking during pregnancy, official guidance and public discourse in the United Kingdom and the United States and to determine whether it accurately and appropriately reflects the existing evidence for a link between exposure to cigarette smoking in utero and mental health problems during childhood. This is done by first analysing documents from the National Centre for Clinical Excellence (NICE) in the UK and the Surgeon General's office in the USA, then analysing the advice contained in the most popular and commonly read pregnancy guides in both countries, to assess whether there is mention of the risks of smoking during pregnancy on infant irritability and child mental health problems such as aggression and hyperactivity.

5.1 Review of policy and official guidance: United Kingdom

5.2 Review of policy and official guidance: United States

5.3 Leading guidance accessed by pregnant women: United Kingdom

5.4 Leading guidance accessed by pregnant women: United States

5.5 Chapter conclusions

Background

Smoking during pregnancy is a leading cause of preventable disease in the peri-natal period (BMA, 2004) and as such is an important point of intervention for both maternal and child health. To prevent or cease smoking during pregnancy has proved to be difficult, and there are indications that it will become increasingly difficult to continue to reduce the overall rate of smoking during pregnancy as it becomes increasingly concentrated in the most socio-economically disadvantaged groups (Graham 2011). In fact, in the US, the prevalence of pregnancy smoking in some States is on the rise (CDC, 2008), in contrast to general trends in the United Kingdom (the NHS Information Centre, 2011).

As mentioned in previous chapters, there are strong socio-economic gradients to smoking during pregnancy, and these become even stronger considering who continues, or is unable to quit smoking during pregnancy (Graham 2011). Generally, women in lower socio-economic groups are twice as likely to smoke at all, and 3-4 times more likely to continue to smoke during pregnancy compared to their better-off peers in both the UK and the USA (The NHS Information Centre 2011, CDC 2008).

Chapter 1 deals more extensively with the specifics of these trends and how they play out in different age-specific and socio-economic groups in the two countries. The aim of this chapter is to summarise ante-natal care policy toward smoking during pregnancy, official guidance and public discourse in the United Kingdom and the United States, and to determine whether they accurately and appropriately reflect the existing evidence for a link between exposure to maternal smoking during pregnancy and child mental health problems. This is done by focusing first on documents produced by the relevant national official sources of scientific advice, National Institute for Health and Care Excellence (NICE) in the UK and the Surgeon General's office in the USA, then analysing the advice contained in the most popular and commonly read pregnancy guides in both countries, to assess whether child mental health problems are presented among the risks of smoking during pregnancy.

Health policy and complex epidemiological evidence

Whether smoking cessation during pregnancy alone can prevent the many peri-natal health problems associated with it, without also addressing the contextual social and economic relative deprivation that go hand in hand with the likelihood of smoking during pregnancy is not well understood. Evidence about the effectiveness of quitting smoking during pregnancy

for improving health outcomes is difficult to derive since conducting good quality randomised trials to answer this question would be unethical. The first evidence to show an effect of quitting smoking during pregnancy on the risk of infant crying and difficult temperament comes from a study by Pickett et. al (2008) using longitudinal data. In this study it was observed that women who quit smoking during pregnancy were more likely to have children with easy-going infant temperament, after considering extensive social, economic and maternal mental health co-variates, in spite of having smoked during part of pregnancy, in a population-based sample of more than 18,000 children in the UK (Pickett 2008).

A clear epidemiological understanding of the benefits of smoking cessation during pregnancy is still being developed, including the critical time point during pregnancy to quit, and from what level of smoking (heavy, light, infrequent). Therefore, it is even more difficult to connect peri-natal health outcomes to the smoking cessation services that are typically available in publicly provided ante-natal care in the UK and USA.

It is within this context that this chapter examines the existing ante-natal care policy and guidance. This issue is also reflected clearly in the next chapter (6), where one of the strongest messages that comes across from assessing women's perceptions of the risks of smoking during pregnancy is that doctors and midwives did not give clear advice about the risks of smoking during pregnancy or what would be likely to happen if they quit, cut down, or quit intermittently.

This is partly due to confusion about the nature of risk. Epidemiological studies can only provide accurate risk estimates at the population level, not at the individual level. (Davey Smith G 2011). Because front line ante-natal care staff are not typically specialists in statistical methods, their ability to articulate the differences between population and individual risks may be limited. This leaves women in a potentially vulnerable state if they are smokers when they become pregnant, since smoking is highly addictive, and they may have trouble maintaining the will to stop from day to day throughout pregnancy unless they have a clear understanding of what is at stake.

To complicate the picture more, recent studies provide evidence that as an indicator, the most commonly used indicator of peri-natal health currently in use (low birthweight) may become less useful in the future, as population weight and body mass index trends change. Currie and Almond (2011) have argued that high birthweight may be as important an indicator now as low birth weight (Currie 2011, Almond and Currie 2011). A broader understanding, with refined indicators for healthy peri-natal outcomes may be needed.

Given such a complicated picture, this chapter's aim to describe the existing policy and guidance, to ascertain whether that guidance appears in the most commonly read pregnancy advice guides and to evaluate the fidelity of scientific evidence that is currently presented in these sources, keeping in mind that the scientific knowledge is constantly being refined and improved.

Most important is that the official policy, guidance and diffused advice in popular sources of pregnancy advice be evidence-based given these constant refinements. In the UK guidance is written by the NICE.

NICE guidance is distilled from systematic reviews and expert reviews of the literature on topics chosen by the Department of Health. In the US official guidance is distilled by the Office of the US Surgeon General, drawing on expertise from the Centres for Disease Control and Prevention (CDC) and experts in public health and epidemiology--and then distributed to the States via the Centre for Medicaid Services through to publicly provided care. States then work within their local budgets to provide reimbursements to physicians and hospitals for relevant services.

One last consideration is that policy environments matter (Baumgartner and Jones 2007), and the agility of policy making in the two countries differs. Good policy and policy making can be responsive to the external environment; the opposite is true where there are deep divisions and inequalities, which may act as blocks to progress and cooperation, in-fighting and short-term approaches to policy.

The current universal coverage of smoking cessation for pregnant women in the US is only a recent result of the effort by the Obama government to reform health policy in the US (Centre for Medicaid Services, 2011). The pay-off for resolving such large-scale problems could be large. A 2007 study by the American Legacy Foundation estimated that if all smokers enrolled in Medicaid programs stopped smoking, the Medicaid system would save \$9.7 billion

after 5 years (American Legacy Foundation 2007).

Two environments, two policy contexts: ante-natal care and smoking cessation United Kingdom and United States

Though there are differences between the two national contexts, there are also similarities and good reasons for comparison. The standard of living and Anglo-Saxon economic traditions are somewhat similar in the UK and USA (OECD 2010) more so than between the UK and Sweden, for example though in the UK there is extensive social protection beyond that which has existed in the USA during the past 30 years; for example there has been a free universal health care system in the UK since 1947 which acts as a buffer to protect health and large unexpected household expenditures and other forms of social and economic stress.

In the US this buffer does not exist, and even basic primary care, including peri-natal care is typically a large household expenditure either directly or via monthly insurance payments (OECD 2010). In both countries the least well off should be comparable since in the US there is Medicaid for the poor—though access is patchy and varies from state to state. This will change under the Obama health care reforms, and already universal access to smoking cessation services has been made available for those who are enrolled in Medicaid (Centre for Medicaid Services 2011).

It is difficult to draw a clean comparison between the two countries, but there is value in comparing the two given the known similarities and differences, and since smoking among pregnant women in the US is on the rise in some states, those states may be able to look to the UK for policies that are effective at reducing smoking rates at the population level. As mentioned, a key difference between the US and the UK is the nature of ante-natal care. In the United Kingdom all ante-natal care is free, while in the United States it may be free if the mother is living in poverty, and eligibility criteria vary across the individual States.

For that reason this paper will compare only policy and guidance for publicly provided care. In other words, the ante-natal care that is available to all women in the UK is compared to the ante-natal care that is theoretically available to all poor women across the US generally, after the Obama health care reform of 2010.

Table 5.1 Summary of documents analysed for content relating to guidance for pregnant women who smoke in the United Kingdom and the United States

Source	United Kingdom	United States
Official policy and guidance	NICE Guidance	Surgeon General's Report
Publicly available ante-natal care	National Health Service (NHS) Ante-natal care packet	Women, Infants and Children (WIC) pre-natal care packet
Leading pregnancy advice book	Your Baby and Child / The New Pregnancy and Childbirth	What to Expect when you are Expecting
Leading pregnancy magazine	Mother and Baby	Fit Pregnancy

Sources of policy, guidance and advice, UK and USA

The starting point for this review departs from three questions:

- (1) What has been the scope and amount of policy action to reduce smoking in pregnancy in two health care systems - the UK and the US?
- (2) Have the overall policy responses in the two countries been influenced by the research evidence on the mental health impact on children from smoking in pregnancy?
- (3) Have health policy actions influenced health professional approaches to ante-natal smoking advice?

To answer these, three types of sources were considered for each country: official policy and guidance, publicly available ante-natal care packets, and the leading pregnancy advice guides from each country.

Analysis of documents

Analysing guidance for pregnant women who smoke is especially complex for the US where there are local and state actions and policies as well as federal ones. The UK is more fragmented now than in the past, and there are different health policies in the four countries, but fundamentally the public health care system is uniform. To gain a general understanding of guidance and advice, the comparison is made at the national level.

Considering that preference for the most popularly read pregnancy advice books currently follow national lines in the US and UK, this approach provides a general picture of how broad national policy diffuses into the more popular literature that women read in each context.

The purpose of this chapter is to summarise what is said about the risks of smoking during pregnancy for child behaviour, temperament, mental health, intelligence and learning: are the risks mentioned framed as proven or speculative risks? How are professionals being encouraged to use the guidance to screen, refer and treat women?

Box 5.1 Summary of sources reviewed (UK)NICE guidance

1. NICE Guidance: Antenatal and postnatal mental health: draft scope for consultation, 2012.
2. NICE Public Health Guidance 26: Quitting smoking in pregnancy and following childbirth, 2010.
3. NICE Guidance: Antenatal care: Routine care for the healthy pregnant woman, 2008.

National Health Service (NHS) Ante-natal care packet
York District Hospital, UK (2011)Leading Pregnancy Guides

1. Your Baby and Child by Penelope Leach, 2010.
2. The New Childbirth by Sheila Kitzinger, 2011.
3. Mother and Baby Magazine, 2012.

Box 5.2 Summary of sources reviewed (USA)Surgeon General's guidance

1. Centres for Medicaid Services 2011. New Medicaid Tobacco Cessation Services. Letter to State Medicaid Directors: Department of Health and Human Services 24 June 2011.
2. U.S. Surgeon General's Report: How Tobacco Smoke Causes Disease: The Biology and Behavioral Basis for Smoking-Attributable Disease, 2010.
3. CDC Pregnancy Risk Assessment Survey (PRAMS). Quitting smoking during pregnancy in the USA, 2008.

Women, Infants and Children (WIC) pre-natal care packet
Bernalillo County Hospital, USA (2011)Leading Pregnancy Guides

1. What to Expect when you are Expecting by Heidi Murkoff, 2008.
 2. Fit Pregnancy Magazine, 2012.
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5.1 United Kingdom: What is the official (NICE) Guidance about maternal smoking during pregnancy?

In the UK, the National Institute for Clinical Excellence (NICE) produces guidance on all aspects of clinical practice and public health that are relevant to the population. The NICE Guidance reports that are relevant to smoking during pregnancy include Antenatal Mental Health, Smoking and Pregnancy, and Pregnancy and Complex Social Factors. The link between maternal smoking during pregnancy with child mental health outcomes appears in official guidance “How to Stop Smoking in Pregnancy and Following Childbirth.”

NICE Guidance documents: Smoking during pregnancy

NICE Guidance: Antenatal and postnatal mental health: draft scope for consultation 10 October–7 November. NICE, London 2012.

NICE public health guidance 26: Quitting smoking in pregnancy and following childbirth. NICE, London 2010.

National Institute for Health and Clinical Excellence (2008) Antenatal care: routine care for the healthy pregnant woman. CG62. NICE, London 2008.

UK Policy and guidance:

1. NICE Guidance: Antenatal and postnatal mental health: draft scope for consultation, 10 October–7 November 2012.

This document mentions the use of drugs, alcohol and tobacco during pregnancy. It notes that cigarette smoking is common, but cannabis use is as well. In the cities this document claims that about 15% of women screen positive for drugs, mostly cannabis. It mentions that 10% of women binge drink and that 13% of women smoke during pregnancy. It states that smoking is thought to be the most harmful of these exposures, but this may simply be because there is evidence about smoking while evidence for other drugs would be difficult to obtain and not population based. The problems it mentions as being associated with smoking are foetal distress, growth restriction and prematurity. There is not a mention of child mental health outcomes.

2. NICE Guidance: Antenatal care: routine care for the healthy pregnant woman, Clinical Guidance 62, 2010.

This document clearly outlines the actions that should be taken by general practitioners (GPs) and any other National Health Service staff who interact with pregnant women. The guidance is quoted in the box below.

Smoking in pregnancy (NICE Clinical Guidance 62)

“At the first contact with the woman, discuss her smoking status, provide information about the risks of smoking to the unborn child and the hazards of exposure to secondhand smoke. Address any concerns she and her partner or family may have about stopping smoking. Pregnant women should be informed about the specific risks of smoking during pregnancy (such as the risk of having a baby with low birthweight and preterm birth). The benefits of quitting at any stage should be emphasised.

Offer personalised information, advice and support on how to stop smoking. Encourage pregnant women to use local NHS Stop Smoking Services and the NHS pregnancy smoking helpline, by providing details on when, where and how to access them. Consider visiting pregnant women at home if it is difficult for them to attend specialist services.”

Smoking in pregnancy (NICE clinical guidance 62, continued)

“Monitor smoking status and offer smoking cessation advice, encouragement and support throughout the pregnancy and beyond.

Discuss the risks and benefits of nicotine replacement therapy (NRT) with pregnant women who smoke, particularly those who do not wish to accept the offer of help from the NHS Stop Smoking Service. If a woman expresses a clear wish to receive NRT, use professional judgement when deciding whether to offer a prescription.

Advise women using nicotine patches to remove them before going to bed. This supersedes NICE technology appraisal guidance 39 on NRT and bupropion. This recommendation has been withdrawn. See 'How to stop smoking in pregnancy and after childbirth (i.e if women cannot quit, advise that they cut down).'”

This clinical guidance does not specifically mention the risks of maternal smoking during pregnancy for child mental health and development.

3. NICE Public Health guidance 26: Quitting smoking in pregnancy and following childbirth, 2010.

This guidance provides extensive detail about the effects of maternal smoking during pregnancy, state of the art assessment of the effectiveness of interventions and guidance on what everyone who interacts with a pregnant woman should know and do about smoking during pregnancy.

It notes that this includes advice for midwives, stop smoking specialist advisers, health care professionals, GPs, practice nurses, health visitors, obstetricians, paediatricians, sonographers, family nurses, staff of fertility clinics, dental clinics and community pharmacies.

It details that all should know what services are available to help pregnant women to quit smoking during pregnancy and that all should know and understand about the impact that smoking and also second hand smoke can have on the woman’s child(ren).

This also includes the suggestion that all the named professionals have training in how to

approach the subject of smoking cessation during pregnancy without damaging the relationship with the pregnant woman.

The NICE public health guidance 26 mentions several risks of smoking during pregnancy including that respiratory infections and problems are more common in children whose mothers smoked during pregnancy and among those children who are brought up in a household where someone is a smoker. The Guidance then discusses the risk to child mental health:

“Exposure to smoke in the womb is also associated with psychological problems in childhood such as attention and hyperactivity problems and disruptive and negative behaviour. In addition, it has been suggested that smoking during pregnancy may have a detrimental effect on the child’s educational performance.”

The document mentions extensive risks of smoking during pregnancy including that smoking during pregnancy increases the risk of infant mortality by 40%.

5.2 USA: What does the US Surgeon General's Report advise about maternal smoking during pregnancy?

In the US, the Office of the Surgeon General provides analysis and guidance on clinical practice and public health. The Surgeon General's Report that is relevant to maternal smoking during pregnancy and long-term child mental health is "How Tobacco Smoke Causes Disease: the Biology and Behavioural Basis for Smoking Attributable Disease." (CDC 2010). This report is an extensive summary of all that is understood about smoking and includes a large section about pregnancy.

Two other official documents are relevant: *Quitting Smoking during Pregnancy*, from the Centres for Disease Control and Prevention (CDC), the national laboratories and agencies responsible for disease prevention in the USA (with local offices in each state), and "New Medicaid Tobacco Cessation Services" from the Centres for Medicaid Services, the national office responsible for publicly provided health care in the US.

1. Centre for Medicaid Services: New provision for pregnant smokers in the United States

Effective 1st October 2010, the Obama Administration directed all Medicaid (means-tested) programmes to expand Medicaid coverage of tobacco cessation services, including for pregnant women (Similar services were already previously available in 39 states.)

A study found that in spite of existing provision, neither physicians nor enrollees were previously especially aware of the benefits available to them, and a study of found that generally approximately 36% of enrollees were aware that treatment in the form of smoking cessation services were available. (McMenamin et al., 2004). The services available include comprehensive coverage for both counselling and medication.

2. Surgeon General's Report: How Tobacco Smoke Causes Disease

This document mentions cognitive and neurobehavioral effects, citing experimental evidence from studies of rhesus monkeys exposed to nicotine in utero. (Sekhon et al. 2001). Results from an experimental laboratory study using chickens as animal models is also mentioned: chickens exposed as embryos to nicotine were more likely to display hyperactivity at low doses and *hypoactivity* at high doses. (Ejaz et al. 2005).

Finally, the report mentions speculative thinking that nicotine affects the outer hair cells in the ear, influencing language ability (McCartney 1994), leading to poorer performance scores on assessments that rely heavily on verbal abilities. According to this report there is evidence of similar effects as well as endocrine-disrupting effects from smokeless tobacco (Agrawal et al. 1983, Gupta and Sreevidya 2004, Gupta and Subramoney 2006).

3. Centres for Disease Control and Prevention (CDC): Quitting Smoking during Pregnancy

This document is intended for clinical audiences who interact with pregnant women and outlines the risks of smoking during pregnancy before providing information that pregnant women can access for help with smoking cessation. Child mental health and development are not mentioned with the risks included here (CDC 2008).

“Women who smoke during pregnancy are more likely than other women to have a miscarriage. Smoking can cause problems with the placenta—the source of the baby's food and oxygen during pregnancy. For example, the placenta can separate from the womb too early, causing bleeding, which is dangerous to the mother and baby. Smoking during pregnancy can cause a baby to be born too early or to have low birth weight—making it more likely the baby will be sick and have to stay in the hospital longer. A few babies may even die. Smoking during and after pregnancy is a risk factor of SIDS, an infant death for which a cause of the death cannot be found. Babies born to women who smoke are more likely to have certain birth defects, like a cleft lip or cleft palate.”

5.3 Leading guidance accessed by pregnant women: United Kingdom

What are women given when they present for publicly provided antenatal care in the UK?

In NHS packets given to women, and in leading pregnancy books and magazines, how is official guidance being reflected and framed for readers? How much attention do the risks of smoking during pregnancy get? What is the language style? These questions were considered looking at the most commonly available pregnancy advice sources including ante-natal care packets and popular pregnancy advice guides.

National Health Service (NHS) ante-natal care packets

In the United Kingdom nearly all women use publicly provided care, and most private health insurers do not offer routine antenatal care (Abbott, 2012). Women are typically booked in directly for their antenatal care with an NHS midwife from week 10-12 of pregnancy, and they receive a pregnancy advice packet with official advice and many other publicly oriented materials related to all aspects of pregnancy and infant care, including promotional materials for the NHS Stop Smoking Service, which includes materials and services for pregnant women.

An NHS ante-natal care packet was obtained from York, United Kingdom (2011) in order to examine a sample of advice that is contained for pregnant women who smoke. The packet contained a set of brochures for public and commercially available information relevant to new mothers. Two of the brochures were related to smoking:

- (1) An introduction to the extensive and free NHS Stop Smoking Service, which includes a website, counsellors, individual and group cessation counselling, films, PSAs and special advice dedicated specifically to pregnant smokers.
- (2) A brochure advising on ways to stop smoking. It recommended, instead of smoking, for the pregnant woman to do something to pamper herself: to go shopping, or to book in for a massage to help her to relax.

Given that most pregnant smokers who are unable to quit smoking are less well-off economically, the suggestions do not seem to be especially well tailored to the target audience.

Your Baby and Child (2010) by Penelope Leach and The New Pregnancy and Childbirth (2011) by Sheila Kitzinger

Recent evidence suggests that about one third of pregnant women read pregnancy advice books (Kennedy, 2009). The most popular of these in the UK and USA were read for all references to smoking and any risks of smoking during pregnancy.

Your Baby and Child by Penelope Leach (2010)

This popular advice guide begins with a very positive message to mothers in general:

"Whatever you are doing, however you are coping, if you listen to your child and to your own feelings, there will be something you can actually do to put things right or make the best of those that are wrong."

and also, placing focus on the happiness of the child:

". . . the happier you can make your baby, the more you will enjoy being with her, and the more you enjoy her, the happier she will be." (Leach 2010).

There is one reference to smoking and its association with cot death (Sudden Infant Death Syndrome) postpartum:

"Try not to expose your baby to smoke before or after birth. Failing a non-smoking household, her sleeping place should be kept smoke free 24/7 whether she is in it or not." (Leach 2010).

The link between maternal smoking during pregnancy and child mental health problems is not mentioned.

The New Pregnancy and Childbirth by Sheila Kitzinger (2011)

This popular UK pregnancy advice book includes nine references to smoking during pregnancy and the associated risks for child health and development: (1) cessation and ultrasound, (2) nicotine's effect on foetal heart and breathing, (3) placenta, (4) pumping "poison" into the blood stream, (5) constricting blood vessels to the placenta so that less oxygen and other nutrients enter, (6) the baby will be more likely to be healthy and easy to care for, (7) prematurity, bleeding and miscarriage, (8) birth complications including infant death in first week of life, and (9) preterm birth and other complications.

Presumably by advising women that their babies will be “more likely to be healthy and easy to care for” the author is drawing on the evidence of easy-going infant temperament by Pickett et al (2009), but there isn’t a specific reference to the research. It is also possible that the reference is a more general one, that if the baby is healthy then s/he will be easier to care for.

Mother and Baby Magazine (UK)

Print issues of the best selling pregnancy magazine in each country spanning a one year period (2012) are archived online (Bauer 2012), and these were scanned to ascertain whether the link between maternal smoking during pregnancy and child mental health problems and/or excessive crying during infancy were mentioned as possible effects of smoking during pregnancy. In the United Kingdom the best known and best selling pregnancy magazine (published monthly) is called “Mother and Baby.” Five articles were found that discussed the risks of smoking during pregnancy.

Article 1: Smoking during pregnancy is related to behavioural problems in children

This article specifically refers to work by Hutchinson et al (2010) about “the risk of damage to foetal brain if mothers smoke, which could result in behavioural conditions – especially in boys.”

“Recent research shows that women who smoke during pregnancy are much more likely to have children with behavioural problems because of harm to the still-developing brain in the foetus. The study, published in the Journal of Epidemiology and Community Health, was carried out on more than 14,000 mother and child pairs from the UK and US; the children were all around 3 years old. Mothers that had smoked when they were pregnant divided into ‘heavy’ and ‘light’ smokers, depending on how many cigarettes they had per day during pregnancy. They were then asked to record their children’s behaviour, such as temper, behaviour towards adults and whether they bullied other children. Findings took into account factors such as the mother’s age when the child was born, her socioeconomic status and family stability. ‘Light’ smokers were 44% more likely than non-smokers to have boys with conduct problems; this figure rose to 80% in ‘heavy’ smokers.”

There are a few notable mistakes in this summary. Though it is surprising to see so much detail about study design and publishing journal, the authors of the article make mistakes about the study population. They state that the study was conducted on mother and child pairs in the US and UK. In reality this study was an analysis of only mothers and children in the UK. The article continues:

“All of the mothers that smoked when they were pregnant were more likely than non-smokers to have boys who were hyperactive or had attention deficit disorders. Girls were also significantly more likely to have problems with their conduct,

but not display hyperactivity or attention deficit problems. Professor Kate Pickett, of the University of York, led the research. She said that the results showed that smoking during pregnancy is associated with “direct effects” on development to the structure of the foetal brain, explaining that similar results had been found in studies on animals.

The words ‘direct effect’ are presented as a quotation, but they are taken out of context. The actual discussion from the paper treats the issue of direct effects in context with both smoking as a marker and likely gene-exposure-environment interactions:

“Smoking during pregnancy may have direct effects on the development of behaviour problems, most plausibly via adverse teratological effects on the foetal development of brain structure and functioning, which is well-characterised in animal models. If boys’ foetal development is more sensitive to these insults, then this would indicate why sons of smokers were more likely to have behaviour problems than daughters of smokers. Alternatively, smoking may be a marker for the intergenerational transmission of processes associated with both smoking during pregnancy and problems in offspring. If daughters of smokers are susceptible to genetic or family environmental influences linked to conduct problems but not to hyperactivity–inattention, then this may explain the significant risk of girls displaying conduct-only problems at this age. Rather than genes, exposure or environment being sole causes, the aetiology of disruptive behaviour disorders most likely involves gene–exposure–environment interactions” (Pickett et al, 2008; emphasis added).

Further, the statement that “all of the mothers that smoked . . . were more likely . . . to have boys who were hyperactive or had attention deficit disorders . . .” is misleading. By using “all” the authors ignore that the measure of association is an odds ratio and they don’t explain that this is an approximation of a relative risk, and further there is not explanation that a relative risk applies to the population and not the individual, i.e. “all of the mothers.”

This difference represents another gap between what the scientific literature reports and how the information is translated and presented in popular media for pregnant women.

Article 2. Are you struggling to quit smoking for your little one?

The focus of this article is not specific to the risks of maternal smoking during pregnancy and child mental health but rather provides advice for quitting smoking during pregnancy. The advice is nested in a list of the risks of smoking for the mother and child, but long-term child mental health is not mentioned as one of the risks here (Bauer 2012).

“Now you’re pregnant, your baby’s health is the most important thing. When you smoke your unborn baby receives less oxygen meaning his heart has to beat faster. Even if you’ve been smoking through most of your pregnancy, stopping in the last few weeks will have a positive impact.”

The other benefits to smoking cessation mentioned in the article are reduced risk of stillbirth, less chance of premature birth and suffering from related breathing, reduced feeding and health problems, and reduced risks of low birthweight and cot death.

Article 3. The truth about smoking health issues

This article outlines extensive risks to mothers and children of smoking, not only during pregnancy but also postpartum, and includes the dangers to children who grow up in homes with parents or others who smoke (Bauer 2012).

You probably know that smoking causes lung cancer, but you may not have taken in the sheer scale of the deaths it causes: 114,000 deaths a year, which is equivalent to a plane crash every day killing 300 passengers. Smoking has more than 50 ways of making your life a misery through illness, and more than 20 ways of killing you . . .”

The article continues on to list the dangers to child health:

“Smoking in pregnancy can increase your risk of miscarriage, premature delivery and stillbirth. When you inhale smoke, you take over 4,000 chemicals into your body, including carbon monoxide, which gets into your bloodstream and cuts down the amount of oxygen reaching your baby.

More than 42 per cent of British children live in a household where somebody smokes, and every year 17,000 children are admitted to hospital with illnesses caused by their parents smoking. Babies and children exposed to smoky atmospheres are twice as likely to have asthma attacks and chest infections; are more likely to need hospital care in their first year of life; will be more sickly and will miss more school; and are more susceptible

to infections such as coughs and colds. Research has proved that children of smokers have a higher rate of cot death, an increased risk of meningitis, and more chance of getting ear infections and 'glue-ear' which can lead to hearing loss."

The article stands out particularly for its use of quantitative information to influence mothers. Typically in this type of publication quantitative information is avoided or inaccurate. In this case the numbers are used well, alongside comparisons to every day examples in relevant contexts (e.g. plane crashes and British households).

Article 4. Quit smoking

This article addresses the issue of quitting smoking and the safety of using pharmacotherapy such as nicotine replacement patches and lozenges. First the article treats the risks of smoking and advises quitting, but goes on to suggest that pharmacotherapy is not without risks (Bauer 2012).

"If you don't quit, you will be more likely to vomit, get urinary infections and suffer bleeding and your risk of miscarriage is increased. Your baby has an increased risk of cot death and she is more likely to develop a respiratory illness such as

asthma. When you smoke, your baby smokes too, she gets less oxygen, which restricts her growth and weight gain, making her more prone to infections when she's born. Smoking during pregnancy has also been linked to preterm labour."

The importance of quitting is emphasised, as is the current advice that pregnant women should use nicotine replacement therapy in the UK if they cannot quit by other means, but the safety of this is questioned:

"... a large Danish study of over 75,000 women backed up previous research that any nicotine replacement therapy may lead to cleft palates, heart problems and digestive disorders, so use of nicotine patches is best avoided during pregnancy."

This is the only instance where the popular advice was observed to contradict official guidance, by using the scientific evidence directly to override the official guidance.

Article 5. 5 things you need to know about smoking during pregnancy

The fifth and final article is a basic summary of why women should quit combined with advice and encouragement to achieve quitting smoking during pregnancy (Bauer 2012).

“Even if you are near the end of your pregnancy, your baby's health and development will benefit from no longer being exposed to the harmful substances that tobacco smoke contains.”

It concludes, unlike the previous article, that pharmacotherapy is better than smoking because it only contains nicotine, and not all the other harmful chemicals found in commercially available cigarettes.

In this article, clearly stated and unequivocal advice about maternal smoking during pregnancy and the risks to child development appears:

If you continue smoking you are at risk of your baby being stillborn, being born prematurely and having breathing difficulties. Your baby is also at greater risk of having learning difficulties or being hyperactive.

5.4 Leading guidance accessed by pregnant women: United States

In the packets given to women, in leading pregnancy books and magazines, how is the guidance being reflected and framed for readers? How much attention do these risks get? These questions are explored here for pregnancy advice in the US as a comparison to the UK.

United States: Women, Infants and Children (WIC) prenatal health packets

In the United States the picture of publicly provided care is different, and publicly provided care is only available for poorer women, though similarly to the United Kingdom, women accessing Medicaid are typically booked in with a midwife from weeks 10-12 of pregnancy, and they also receive a pregnancy advice packet with official advice and publicly oriented materials for pregnant women, including locally available smoking cessation services information, which varies from state to state, but which is currently universally available under the Obama Health Care Reforms of 2010 (Centre for Medicaid Services 2011).

A WIC prenatal care packet was obtained and analysed from Bernalillo County Hospital, New Mexico, USA (2011) in order to ascertain what advice it contained for pregnant women who smoke. In the packet were brochures and photocopied fliers for publicly provided services related to pregnant women. There was one flier related to smoking cessation, referring women to the 1-800-QUIT-LINE, a free telephone counselling service available to all pregnant women who smoke (WIC 2011).

The risks mentioned included loss of the pregnancy, premature birth, health problems after birth, low birthweight and increased chance of needing special care, a longer time in the hospital postpartum and a higher risk of sudden infant death syndrome (SIDS) and more colds and other lung problems later in life. The materials in the packet did not refer to specific risks of smoking during pregnancy on the child's behaviour and development (WIC 2011).

What pregnancy advice book is most commonly read in the US and what advice about the risks of smoking does it mention?

What to expect when you are expecting (2008) by Heidi Murkoff

In this widely popular pregnancy advice guide, there are 34 mentions of smoking during pregnancy. The risks associated with maternal smoking during (and before) pregnancy include: fertility, "ageing of eggs," miscarriage, sperm count in fathers, smoking is extra stress "you don't need," obesity and post-gastric bypass surgery complications, avoiding cigars as celebration because "your baby will thank you" (suggests passing out chocolate cigars instead), increased heart rate, insufficient oxygen, ectopic pregnancy, placental abnormalities, premature delivery, low birthweight, shorter stature and lower head circumference, cleft palate, cleft lip, birth defects, hyperactivity and aggression. It concludes its advice about smoking (Murkoff 2008):

"and being born too small is the major cause of infant illness and peri-natal death, inc SIDS, apnoea and low Apgar scores."

Fit Pregnancy Magazine (USA)

In the United States the best known and best-selling pregnancy magazine is called "Fit Pregnancy." Issues are published every two months, and the print editions are archived online (American Media, 2012). The six issues from 2012 were selected in order to make comparisons with the United Kingdom with respect to what is communicated in the popular

press about maternal smoking during pregnancy and the link to infant crying and child mental health.

Article 1. Consequences of Pregnancy Smoking

This article brings attention to a less known reason not to smoke during pregnancy, and summarises the Paradis et al. 2008 study of maternal smoking during pregnancy and adult offspring criminal arrests (American Media 2012).

“A study by researchers at Harvard and Brown universities has found that men and women born to mothers who smoked one pack or more per day during their pregnancies were more than 30 percent more likely to have been arrested later in life.”

The authors of the article used an interesting way to explain controls for confounding by socio-economic status:

“In addition, the link between heavy smoking in pregnancy and future criminal activity of children held up across all socio-economic lines.”

The article concludes with suggestions for help with smoking cessation. Obviously this is a clear mention of the link between maternal smoking during pregnancy and child mental health and behaviour, though it does not discuss the issues of study quality across such a long period of time, nor does it explain what “30 percent more likely” means in population terms.

Article 2. Secret - Smoking Cigarettes

The second article about smoking during pregnancy in Fit Pregnancy lists several risks to the pregnancy and child health, and also questions the safety of pharmacotherapy (American Media 2012).

“Smoking robs a foetus of oxygen, which can cause slow growth and inadequate weight gain. Smoking also contributes to miscarriage and preterm birth, as well as sudden infant death syndrome (SIDS), impaired lung function and other complications in babies. Up to 41 percent of all SIDS cases and 10 percent of all infant deaths are attributable to smoking, according to the National Partnership to Help Pregnant Smokers Quit.

Nicotine gum and patches have not been proven safe during pregnancy--in fact, a recent Obstetrics & Gynecology study found that nicotine substitutes such as these appeared to increase the risk of congenital malformations. However, that study has generated controversy among researchers, who say the potential benefits of quitting outweigh the possible risk of nicotine replacement products.”

Maternal smoking during pregnancy and risks to child mental health and development were not mentioned in this article alongside the other risks.

5.5 Discussion

The key issue for this chapter has been to ascertain what is said about the risks of maternal smoking during pregnancy for child behaviour, mental health, intelligence and learning and to discover how these risks are framed.

Three types of sources from two countries were examined here: official policy and guidance, publicly available ante-natal care packets and leading popular pregnancy advice guides in the United Kingdom and the United States.

Comparison of official guidance

In both countries, the risk of child mental health problems was mentioned in official policy and guidance and in the leading pregnancy advice guides, but not mentioned in the selected ante-natal care packets. In both countries the official policy and guidance for clinical practice appropriately reflects the existing evidence base, is up to date, referencing the most recent studies, and rather than overstating or underplaying the evidence, mentions the links, the research methods and reports that there is evidence of a link, without claiming the link as conclusive. Though this is an accurate reflection of the existing evidence, there may be scope for suggesting how clinicians can translate the ambiguity appropriately and clearly for pregnant women.

Given the state of the evidence, that there is likely an effect on the developing brain among children whose mothers smoked during pregnancy, but that the effect is likely subtle and reversible, especially among children whose mothers quit smoking during pregnancy, it seems that the official guidance reflects this complexity well. What could be improved is greater attention to the issue of nicotine replacement therapy use during pregnancy, especially during the third trimester of pregnancy. If nicotine has been found to act as a teratogen on the developing brain in animal model studies (Dwyer et al. 2009), then it seems that this therapy should be treated with caution. Reasoning that nicotine replacement is better than smoking is not sound, since the application involves a constant absorption of nicotine when used as a patch, including during sleep—though the recommendations state that pregnant women should remove patches during sleep.

The guidance could be better reflected in the ante-natal care packets in the UK if the packet from York District Hospital is a good representation of the information that women are

given. The known risks of smoking during pregnancy could be updated to include the potential risks to child mental health.

These risks are addressed in the official guidance and in the popular pregnancy guides. It would be reasonable to add them to ante-natal care packets and other NHS resources for pregnant smokers.

Comparison of popular pregnancy guides

The most popular pregnancy advice guides read by women in the US stated the link between maternal smoking during pregnancy and risks to child mental health unequivocally, and this is probably an overstatement. In the UK the link was described as a potential link; in the US the link was presented more forcefully.

The reason for looking at popular guides in both the UK and US is that this is where most all of the relevant research has been conducted, and the intention of this chapter was to ascertain and summarise how the research is filtering through into official guidance and popular advice in these two countries.

In the United States, the leading pregnancy advice book, “What to expect when you are expecting” strongly emphasises the link between smoking during pregnancy and child aggression and hyperactivity, and this approach seems to be intended to motivate women to quit. There is an emphasis on risks, and the language used is strong and direct.

In the United Kingdom, the leading pregnancy magazine included advice based on the Hutchinson et. al study published in 2010, and advised that smoking during pregnancy could lead to aggressive behaviour in boys, but not girls. In contrast to the style of presentation of evidence in the USA, the article in the UK-based Mother and Baby magazine ended with a quote from a representative from the Faculty of Public Health saying that women should quit smoking, “ideally before they become pregnant.” The evidence of a link was presented but not strongly emphasised, and not in frightening language but rather in somewhat more encouraging language.

Communication of risks

While the official guidance in both the UK and USA communicate the potential risks using language that reflects the complexity of the issue, the popular pregnancy advice guides in the USA sometimes present the potential risks using a less subtle approach. This approach perhaps originates from a concern that without this approach, women may not take the advice seriously, and then be less likely to quit smoking. In the most widely read popular advice guides from the UK, information about risks is presented with more equivocal language while in the USA the potential risks tend to be presented less subtle way, with an emphasis on the risks rather than the uncertainty around the risks, and mother's individual responsibility to minimise the health risks to her child.

This culture of preoccupation with risk is also reflected in the number of times that the leading books mention risks. In the USA the leading pregnancy advice book mentions the risks of smoking during pregnancy 34 times. In the UK the leading book mentions the risks of smoking during pregnancy only 9 times.

One reason for this difference may be the culture of medical malpractice and the emphasis on health care as a commodity in the USA. If the product is bad and someone is harmed as a result, then the medical provider has to prove that he or she clearly laid out the risks. Perhaps this culture permeates into the way that the popular pregnancy advice guides are written: better to fill them with cautionary tales (accurate or not) than to risk being criticised for not giving clear warnings, but definitive conclusions about the reasons for these differences are beyond the scope of this thesis.

Smoking during pregnancy and perspectives on risk

One reason for differences in tone between the two countries can also be derived from the differences in the health care systems. In the UK, for example, there is a strong motivation for brief (not mentioning risks) advice for smokers, because the cost-effectiveness argument is so compelling. According to cost-effectiveness studies of brief advice generally (not during pregnancy) if as few as 1/40 women who receive this advice quit as a result of it, provision of this advice is still highly cost-effective in the UK (Godfrey et al., 2010), though the efficacy of health professional brief advice against smoking during pregnancy has not been established.

In the USA, by contrast, the calculation would be more complicated because a given pregnant woman may not be eligible for public health care once her baby is born since pregnant women count as two individuals during pregnancy and so become eligible for means-tested public health care when they are pregnant, but not after (Centre for Medicaid Services, 2011). Such interventions are still likely to be cost-effective, but because of the complicated picture of health care, the argument for a brief, non risk-focused advice is less compelling.

It could be suggested that the UK has the right approach and that changing to a more USA style approach could be pointless, and possibly detrimental. It depends, though, from whose perspective the question is asked. If the question is one of societal cost-effectiveness, then to rely on brief advice from the GP and other health care providers, it is likely a good approach for antenatal care given the evidence of its cost-effectiveness in the general population. If, on the other hand, the question is one of fulfilling one's individual responsibility, then it makes sense that the pregnancy guides would list as many risks as possible, with detailed instructions on avoiding them, since the idea is that each woman should protect her own health and that of her child.

It has been suggested that since pregnancy is 'embedded in a social and cultural setting' (van Tijingen, 2003), that it is useful to outline more clearly how medical model approach versus a social model approach influences decisions about how to present risks to individual pregnant women (van Tijingen, 2004). Generally, the tone of risk communication in the popular US pregnancy guides follows from the medical model approach, with a more biomedical focus, whereas the tone of risk communication in the UK follows from both the medical model approach and the social approach, with as much focus on the mother, baby and couple's needs as on statistical and biological information. The differences in availability of health care provision may be the source of the differences in risk communication observed in the most widely read pregnancy guides from the USA and UK.

Conclusions

This chapter's aim has been to describe and evaluate existing ante-natal care policy, guidance and advice about smoking during pregnancy in the USA and UK and to determine whether and how appropriately the risks of smoking during pregnancy, grounded in the scientific literature, are reflected in the guidance, ante-natal care packets and most commonly read pregnancy advice guides.

Future research could involve conducting interviews with authors of the popular pregnancy advice articles and books to attempt to gain an understanding of how they review and present scientific literature, to summarise this process and to reflect on whether the process could be improved. In general there seems to be a high level of awareness of scientific findings in the popular pregnancy advice guides in both countries and good sources for their findings, if not a clear understanding of a hierarchy of epidemiological evidence. It may be in the interest of publicly provided ante-natal care systems to play a role in the drafting of the most popularly read pregnancy advice guides.

Similarly, publicly available ante-natal care packets could be analysed more comprehensively, and they could be revised, where appropriate, to include the potential risks to child behaviour, mental health and well-being whether or not knowledge of these additional risks would motivate more women to quit smoking during pregnancy.

The next chapter will focus on individual mothers, assessing what women perceive to be the risks of smoking during pregnancy, and how these perceptions of risk have changed since the 1970s.

6

Perception of risk: smoking during pregnancy and effects on children

•Aim of this chapter

The aim of this chapter is to review the literature that has addressed the question, *What do women perceive to be the risks of smoking during pregnancy?* The qualitative literature base is searched in order to ascertain to the extent to which relevant results include mentions of the risks of smoking during pregnancy, and in particular, child mental health outcomes such as hyperactivity and aggressive behaviour, in order to gauge whether these risks appear prominently among the risks with which mothers are familiar.

6.1 Critical perspectives on how risk is perceived

6.2 Nested study from a systematic review of qualitative studies, 2012

6.3 1976-1997: Early confusion about risk

6.4 1998: The year of the Master Settlement Agreement

6.5 1996-2005: Risk becomes prominent

6.6 2007-2012: Bird nests and backlashes

6.7 Chapter conclusions

Background

As discussed in the last chapter, the link between exposure to maternal smoking during pregnancy and child mental health problems such as hyperactivity and aggressive behaviour appears in the official guidance in both the United Kingdom and the United States, from the National Centre for Clinical Excellence (NICE) in the UK and the Surgeon General's office in the USA. Further downstream, the link does not figure prominently in the ante-natal care packs for smokers from the National Health Service (NHS) in the UK or in publicly provided ante-natal care (Medicaid/WIC) for pregnant smokers in the USA.

By contrast, the popular pregnancy books and magazines in the UK and USA do mention the potentially increased risk of infant irritability and child mental health problems such as hyperactivity and aggression (Kitzenger 2011, Leach 2010, Murkoff 2008, Bauer Media 2012, American Media 2012). This chapter looks beyond these sources to the qualitative research base to ascertain what is known about how women have perceived the risks of smoking during pregnancy across a period of nearly four decades, and whether the potentially increased risk of infant irritability and child mental health problems in children whose mothers smoked during pregnancy has begun to appear in the published qualitative literature base.

As discussed in the previous chapter, the potentially increased risk of infant irritability and child mental health problems is presented clearly to women through official channels in the United Kingdom and United States. What then do women take away from the official guidance, ante-natal care packets and popular pregnancy books and magazines reviewed in Chapter 5? Could knowledge of the potential risks, and therefore potential benefits of quitting be used to help mothers to see clear and compelling reasons to try to quit? These questions are addressed in this chapter.

To answer these, a database of qualitative research findings relating to smoking during pregnancy was accessed. This database was constructed by a team of researchers at the University of York, Centre for Reviews and Dissemination between 2010 and 2012 and includes the findings of all qualitative research on smoking during pregnancy from 1976 (inception) and 2012. Both the original methodology used to construct the database and the specific methodology used to access findings related to women's perceptions of the risks of smoking during pregnancy are described later in this chapter.

6.1 Critical perspectives on how risk is perceived

Recent sociological work has focused some attention on risk perception and how risk perceptions are regulated in modern societies. The sociologists Deborah Lupton from Australia and Ulrich Beck from Germany are key to this area of work, and their work intersects around risk discourses which individualise risk, implying that individuals are responsible for the risks to which they are exposed.

Deborah Lupton: The Quantified Self

Deborah Lupton's 'Quantified Self' concept explores the ideas behind risk, perception of risk and the individual as a locus of individual risks, and how this is somewhat disconnected given that epidemiological measures of association involve comparisons of groups and therefore cannot be applied directly to individuals. This issue is also addressed in a 2011 paper by George Davey-Smith (Epidemiology and the Gloomy Prospect) about the nature of risk estimation in epidemiology. Lupton discusses how individual health risks are, in everyday life, lay-estimated and that individuals have become accustomed to estimating their own health risks in their own ways, and to attempt to modify them by modifying their behaviour, particularly using new technologies that feed the fascination with self-quantification:

“Weird and wonderful devices such as self-tracking devices for dogs to wear to monitor their exercise levels, smartphones that could detect bad breath and other odours and a ‘smart fork’ embedded with sensors that could warn people they were eating too fast all received media attention in the early days of 2013 (Lupton 2013).”

The fact that currently no good methods exist for estimating individual level risk complicates risk communication and the public's understanding of health risks. The proliferation of technologies to track one's own health data only more the picture more complicated.

Ulrich Beck: the Risk Society

Another leading figure in the area of risk and risk perception, Ulrich Beck, has written about risk and technology extensively, and proposes that a “risk society” is one where technology is used to attempt to quantify the world that we live in, and that this quantification is a way of soothing anxieties and insecurities about modern life:

“ . . . surges of technological rationalization and changes in work and organization . . . the change in societal characteristics and normal biographies, changes in lifestyle and forms of love, change in the structures of power and influence, in the forms of political repression and participation, in views of reality and in the norms of knowledge. In social science's understanding of modernity, plough, the steam locomotive and the microchip are visible indicators of a much deeper process, which comprises and reshapes the entire social structure (Beck 1992).”

Beck's perspective that quantification is an approach that humans use to cope with the inevitable risks and uncertainties of life is useful in understanding the gaps between risk estimates and individual women who smoke during pregnancy. It may be that different social groups are more or less able to utilise quantitative information in a way that they feel comfortable with, and that this may lead some socio-economic groups to reject risk information if they are unable to see how it applies to them or to their social groups directly.

Risk, Fear, Blame, Shame and the Regulation of Public Safety

In 'Risk, Fear, Blame, Shame and the Regulation of Public Safety', the philosopher Jonathan Wolff brings together the issues of objective risk and risk perception by exploring the role of risk, fear, blame and shame. He uses this as a basis for proposing that these factors are as important for understanding how risk operates in public perception and why studying objective risk alone is not sufficient for understanding risk. He suggests that there are primary and secondary variables that can be elaborated in attempts to understand objective risk and subjectively perceived risk, and the role that blame, shame and outrage play in risk and risk perception:

“One convenient way of understanding the various factors in play is to divide them into “primary variables” and “secondary variables.” On the present analysis the primary variables are three: cause, hazard, and probability. The secondary variables so far introduced are fear/dread and blame/outrage. They are called secondary because they take the primary variables as their object. In the standard cases fear attaches to hazard and probability – the “bigger” the risk, the more it is feared – whereas blame or outrage attaches to cause, as illustrated. But note that each of fear and blame/outrage can take as their object each of cause, hazard, and probability.

Outrage can attach to the hazard, independently of cause. If a hazard will involve many deaths, or deaths in a particularly frightening manner, this may create pressure to do more to mitigate the hazard, even from those who are not personally at risk and so have no fear for themselves or on behalf of family and friends. Here,

then, it must be a sense of moral concern, rather than personal dread, that moves such people. Finally, outrage can attach to probability. Even if the cause and the hazard do not generate outrage, the fact that something is happening “too often” may do so. Note that it is not claimed here that everyone will react the same way, but rather that broad trends may be detectable (Wolff 2006).”

How do these sociological and philosophical underpinnings match up with the advice given about smoking during pregnancy? Also, given that perceptions change over time, specifically,

what are perceptions more recently? The next section of this chapter will present results from a nested study from a systematic review of qualitative studies in order to begin to answer these questions and to ascertain whether awareness of the increased risks of hyperactivity and aggression in children of mothers who smoked during pregnancy have been taken up by individual women. Risk and outrage in particular will be explored in light of these sociological and philosophical perspectives, to explore how they influence women’s perceptions of the risks of smoking during pregnancy.

6.2 Nested study from a systematic review of qualitative studies, 2012

A broader systematic review of smoking during pregnancy was conducted at the University of York (Kate Flemming, Hilary Graham, Morag Heirs, Dave Fox and Amanda Sowden) during 2010 and the searches were updated in 2012 (Flemming et al 2013). The papers from this systematic review were further analysed for this chapter in order to explore aspects of the findings that were relevant women’s perceptions of the risks of smoking during pregnancy, and whether risks to child mental health appeared among the risks of smoking during pregnancy mentioned by the women who participated in the studies.

Research questions of the systematic review

1. How do the circumstances of mothers’ lives influence their smoking behaviour prior to and during pregnancy?
2. What are the perceived barriers to, and facilitators of, quitting in pregnancy and sustained quitting postpartum?
3. What are the gaps in the evidence base for tobacco control policies which qualitative research could help to fill?

The review followed the University of York's Centre for Reviews and Dissemination protocols and the search terms included were:

Smoking- terms as used by Cochrane Tobacco Addiction Group to identify studies in Medline for their Register.

Pregnancy - terms as used by Cochrane Pregnancy and Childbirth Group to identify studies in Medline for their Register.

Disadvantage – developed by the research team's information specialist (Flemming et al, 2013).

The sets of terms were combined in the following way: (1) Qualitative AND Smoking AND Pregnancy (2) Qualitative AND Smoking AND Disadvantage

There was no date limit set on the searches and the resulting studies were drawn from the inception of the databases until 2012.

Inclusion criteria

Published and unpublished studies reported in English were eligible for inclusion providing they met the inclusion criteria:

1. The research was undertaken in high income countries matching the stage of the smoking epidemic in the UK (i.e. a strong association between social disadvantage and cigarette smoking among women and men)
2. The paper was published in English
3. The research was identified by the authors as using qualitative research
4. The paper includes reporting on smoking in pregnancy, smoking in disadvantaged female populations, or smoking in disadvantaged, pregnant women.

Two reviewers independently screened the titles and abstracts, and any discrepancies were resolved by discussion. The potentially relevant studies identified from screening were

obtained in full text and independently assessed by two reviewers to determine whether they met the inclusion criteria (Flemming et al. 2013).

For the purpose of this chapter, the database of included papers from the systematic review was accessed. The database captured all published papers with qualitative findings relevant to smoking during pregnancy since inception of the databases of scientific journals. The database was searched for all findings related to women's perceptions of the risks of smoking during pregnancy.

All mentions of risk in the database of papers, either as framed by the study authors or as mentioned for other reasons by study participants were identified, were collected and summarised for the purpose of this chapter. The results in this chapter represent the complete set of published qualitative findings related to women's perceptions of the risks of smoking and pregnancy that have been published in the scientific literature in English since 1976 when the first scientific paper about smoking during pregnancy was published (Graham, 1976).

RESULTS:

In total 29 papers were included in the systematic review. These papers all reported on the results of qualitative studies exploring smoking during pregnancy. Of the 29 papers included in the main review, 20 papers included mentions of women's perceptions of the risks of smoking during pregnancy. In these papers the idea of risk as a reason for a woman to re-think smoking during pregnancy was central. Though the potentially increased risk of child mental health problems such as hyperactivity and aggression was consistently mentioned in official guidance in the UK and USA, it was not mentioned by the study participants in any of the papers resulting from the systematic review.

Table 6.1 Results of nested review: papers that mention of risks of smoking during pregnancy

Year	Authors	Country of study	Number of participants	Methodology
2008	Wood, L. et al.	Australia	40	Not reported
2007	Bull, L. et al.	UK	38	Not reported
2007	Nichter, M. et al.	USA	53	Ethnography
2006	Bottorff, J.L. et al.	USA	28	Grounded theory
2005	Abrahamsson, A. et al.	Sweden	17	Phenomenology
2004	Thompson, K.A. et al.	UK	15	Not reported
2004	Lowry, R.J. et al.	UK	Not reported	Not reported
2003	Tod, A.M.	UK	11	Naturalistic approach
2002	Lendahls, L. et al.	Sweden	24	Phenomenology
2001	Haslam, C. & Draper, E.S.	UK	40	Not reported
2001	Hotham, E.D., Atkinson, E.R. & Gilbert, A.L.	Australia	19	Not reported
1998	Wakefield, M. et al.	Australia	14	Not reported
1998	Dunn, C, Pirie, P. and Lando H.	USA	57	Not reported
1998	Edwards, N. & Sims-Jones, N.,	Canada	21	Symbolic interactionism
1997	Arborelius and Nyberg.	Sweden	13	Client-patient-centered
1996	Haugland, S., Haug, K. & Wold, B.	Norway	33	Hermeneutic
1994	Lawson, E.J.	USA	20	Not reported
1991	Maclaine, K. & Clark, J.M.	UK	22	Not reported
1989	Oakley, A.	UK	13	Not reported
1976	Graham, H.	UK	50	Not reported

In the first report from the systematic review of qualitative studies of smoking in pregnancy, there were four main findings highlighted by the study authors (Fleming et al, 2013).

1. The embeddedness of smoking in women's lives, questioned only because of pregnancy
2. Quitting for pregnancy rather than for good
3. Quitting had significant costs for the woman and cutting down was a positive alternative
4. The role of partners and the broader dynamics of the couple's relationship in influencing women's smoking habits

The authors of the first report from the systematic review concluded that synthesis of qualitative research can play an important role in informing public health policy and practice. In light of this, the issue of risk perception is explored further in this chapter, building on the authors' identification of risk perception as a key issue.

Across the studies risk is generally presented in terms of women's reactions and responses to questions. In most cases risk was not a focus of the studies but it was mentioned by women as they explained, for example, that they knew smoking was harmful but that they had not been able to quit in spite of this knowledge. Given this, the results of the review for this chapter are presented in terms of how they have changed over time, from 1976 to 2012.

Both the reported risks and the investigators' approach to risks changed over time. Also noteworthy is that among the women represented in these studies, it was broadly reported that doctors and midwives did not tell them unequivocally to quit smoking, or if they did, they did so in such a way that was not specific about the risks of smoking during pregnancy.

Though there were studies conducted regularly across the 36 year period from 1976 to 2012, there were spikes in 1998, 2004 and 2007. Though the spikes are not large, they do correspond with key events in tobacco control and wider changes in risk perception globally, and there may have been somewhat more interest than usual in the topic of smoking during pregnancy on the part of journal editors, thus influencing their choices of papers to publish. Political events such as the Master Settlement Agreement of 1998 and the public smoking bans that were introduced around 2007 in several contexts may have influenced these small spikes.

Figure 6.1 QUALITATIVE PAPERS REPORTING ON PERCEPTION OF RISK BY PUBLICATION YEAR



6.3 1976-1997: Early confusion about risk

Leading up to 1998 and the Master Settlement Agreement, which required the major tobacco sellers to pay 28 billion dollars to US public health authorities and made extensive news and stimulated extensive attention to smoking as a major public health problem, the scientific literature had already established certain milestones with respect to specific risks of maternal smoking during pregnancy, for example, that 10 or more cigarettes per day during pregnancy could be considered as a useful cut-point for predicting poor peri-natal outcomes relative to lower levels of smoking (Maclaine and Clark 1991). Without suggesting that there is any causal effect on women's perceptions of risk, it is nonetheless useful to consider what women were reporting in multiple national contexts as the perceived risks around that time.

For example, more than half of the women in a small study conducted in London mentioned that they thought smoking was harmful for their pregnancy. Three quarters were familiar with low birth weight as a potential risk of smoking during pregnancy and 16% mentioned such risks as premature birth, miscarriage and 'handicap', though it is not clear exactly what is meant by handicap. Most women in the study reported that they believed that smoking low-tar cigarettes would be less harmful for to their child's health (Maclaine and Clark 1991).

The studies prior to this, from 1976 to 1989 included few mentions of specific physical, biological or health risks related to smoking during pregnancy (Graham, 1976 and Oakley et al. 1989), and it seems that there was less preoccupation with the risks of smoking during pregnancy. Similarly, a 1994 study of low-income pregnant adolescents did not mention specific risks of maternal smoking during pregnancy on the child's health.

During this period leading up to the Master Settlement Agreement of 1998, a Norwegian paper in 1996 sought to explore whether women thought that smoking during pregnancy was harmful and if so what the specific risks were. In 33 semi-structured interviews these questions were explored along with "Which is the most serious aspect of the [risks] you have mentioned?" "How many cigarettes do you think you can smoke without harming the foetus?" and "Are there any advantages to smoking during pregnancy?"

One of the responses that brought attention to the primary care setting was this: *"The doctor has never even asked me (about smoking), not even once. He should have said something about it. I know at he smokes himself, and that his wife smoked when she was pregnant. So, I don't know . . . he might have another picture of it all."*

In this study perceived risks were examined in depth, and the study aimed to ascertain how much women knew about the potential risks of smoking during pregnancy and what their peri-natal care advice about the risks had been. The authors were surprised to find that though there was a general acceptance that there were risks, these were not well understood by women, and women reported perceiving that the risks were also not well understood by their peri-natal care providers:

"The smokers had the impression that the harmful effects were still debated among doctors, and that some doctors think you can smoke a certain amount of cigarettes without any harm. The pregnant women were also uncertain of the doctors' and midwives' attitudes towards stopping, and thought that it might be dangerous to stop smoking in pregnancy if withdrawal symptoms are experienced."

"The doctor thought it was better to smoke fewer cigarettes, and then gradually cut down, than just suddenly. I have the impression that doctors' opinions on this differ." (Haugland, 1996).

On the other hand some women's perceptions of the risks smoking during pregnancy were clearer, in the sense that they believed it was clear that smoking during pregnancy would be harmful to the child.

"I can't say that I know what happens to the foetus when I smoke. I know it is dangerous."

"The doctor scared me at the ante-natal clinic when she said that there were new studies showing that the baby flinches every time you puff the cigarette, that is really painful (for the foetus). I didn't think i was that serious. So every time I smoke and I fee the baby move, I think of this. That makes me stop smoking at once." (Haugland, 1996).

Approaching the 1998 Master Settlement Agreement and widespread public knowledge about the harms of smoking, a 1997 study by Arborelius and Nyberg pointed out not only that there are risks that women perceived of pregnancy smoking, but also that women harbour many fears that may or may not be expressed about smoking during pregnancy. One woman poignantly expressed her feelings at delivery: her first thought was whether her child would have physical deformities due to her smoking.

In this study women were asked what they perceived to be the risks of smoking during pregnancy as well as what feelings they had about smoking:

"The thought suddenly struck me: My God! What am I doing . . . a defence mechanism . . . when I was lying in the delivery ward, that's when the thoughts came . . . I asked what she looked like, if she had ears . . . then it all started to come, everything you had suppressed during the whole . . .how it would be if her arms and legs . . ."

In this study from 1997, the authors reported that most women could report at least one risk of smoking during pregnancy. Most frequently they mentioned low birth weight. At the same time the authors reported that many women misunderstand the concept of risk, which is evidenced by the fact that many women in the study were keen to point out that they knew of individual examples of women who smoked during pregnancy (including themselves) who had healthy babies.

At the same time, several women in this study had direct experience with perceived hazards of smoking and connected maternal smoking during pregnancy with miscarriages, placental abnormalities and frequent infant infections with maternal smoking during pregnancy.

Women in the study were both blaming outcomes on behaviours that may not have caused the outcome and at the same time excusing behaviours that are strongly linked to health outcomes. This conflict may result from the existing methods of risk estimation which are

probabilistic and so difficult to understand without an underlying numeracy and understanding of probabilities.

The authors of this study (Aborelius and Nyberg 1997) reported that many women claimed that they would stop smoking if they had been given unequivocal proof of the harms of smoking during pregnancy, or that their own child would definitely be harmed. This common way of thinking reveals a misunderstanding of risk and an unfair expectation of doctors and midwives. The problem lies in not understanding probabilities and increased or decreased probabilities under certain conditions. Risk communication could focus on this problem and work to improve and perhaps even to discover methods of estimating individual risks. Other methods of risk communication such as colour-coded graphic displays of information can also aid in attempts to communicate what an increased risk means without the need for women to comprehend the risks numerically.

“...if they had said that something was wrong, that the baby wasn't growing enough or if they suspected the slightest little deviation”

“If they had told me during pregnancy that I 'was absolutely not allowed to smoke because it was bad for the baby,' then I would probably have stopped, I think.”

“In a way I wish there had been someone who had said: 'You have to stop NOW or else!’” (Aborelius and Nyberg, 1997).

6.4 1998: The year of the Master Settlement Agreement

In 1998 there was a spike in the number of papers published on the topic of maternal smoking during pregnancy in the qualitative literature, and was second only to 2007 in terms of number of relevant papers, possibly reflecting external events with respect to smoking--the Master Settlement Agreement in 1998 and the widespread introduction of public smoking bans internationally, most prominently in 2007.

The three studies published during 1998 (Wakefield et al., Dunn et al., Edwards et al.) may have been published by peer-reviewed journal editors because of the wider relevance and interest in the topic of the harms of smoking to public health coming together in 1998—or it may have been a simple coincidence that there were more relevant papers published during 1998. All three studies here mentioned women's perceptions of the risks of maternal smoking

during pregnancy. The first set in Australia, by Wakefield et al. discussed pregnancy smoking with two focus groups of adolescent pregnant smokers from low socio-economic areas in Australia.

In contrast to a previous study from 1994 of attitudes toward smoking among adolescents which the authors report found that adolescents perceived low birth weight to be a positive outcome (Lawson, 1994), making the labour and delivery easier at the time of birth, by 1998 the adolescents in this study were aware that low birth weight as a problematic outcome. Still they were unable to articulate what the implications were and the reasons that low birth weight predicted potential problems for their child. The adolescents in this study reported having received very little information about the risks of smoking during pregnancy (Wakefield et al. 1998).

The next study published during this significant year for tobacco control was conducted among low-income multi-ethnic group in the United States. This paper reported on the ambiguity and conflict in the minds of pregnant smokers, and brings forward the issue of addiction and health behaviour, beyond the question of whether women have accurate perceptions of the risks of smoking during pregnancy:

“I feel bad when I smoke. I’m like ‘God, my baby’s smoking.’ and I’ll put my cigarette out. But later I’ll rub it off and keep smoking my cigarette.”

The authors of the study found several examples of this dilemma, and some women reported that the stress and anxiety resulting from knowing that smoking was risky for the pregnancy resulted in their smoking more, rather than less.

On the other hand, the authors reported that several women in this study felt confident that cutting back was a good way to protect their child’s health if they found it impossible to quit altogether.

The specific risks that were mentioned by women in this 1998 study were:

- Low birth weight
- Colds
- Asthma and bronchitis

Though many women in the study reported experiencing these outcomes with their own children from prior pregnancies during which they smoked, this knowledge was not enough to help them to quit smoking

Finally, the third relevant study published during 1998 (Edwards et. al) focused on smoking relapse during pregnancy and the postpartum period. Specific risks of smoking during pregnancy were not the focus of the paper. In the context of media campaigns of the time that emphasised the mother's responsibility to stop, one of the study participants commented:

I would come home and I could smoke a pack a day, and this I did sporadically, knowing it was very bad for the baby, knowing everything about the ill effects of smoking on the baby, but I knew it was my only link to sanity."

Though the specific risks that this study participant had in mind are not mentioned, she reports that she knows what the risks are, and at least it seems apparent that she knows that smoking during pregnancy is harmful. The study authors commented that there was a need at the time for a

differentiation between negative forms of psycho-social support such as nagging and criticising (in particular from partners and family members who were themselves also smokers) and positive support such as encouragement and praise (Edwards et al. 1998); it is possible that this recommendation may have been taken up and in some way influenced the rationale for empathetic approach used in the UK NHS Stop Smoking Services for pregnant women.

6.5 1999-2006: Risk becomes prominent

During this time period there were 9 relevant studies, regularly across the 7 year period, with a small spike in 2004. Going along with the increase in frequency and regularity of relevant studies across time is an increasing focus on the risks of smoking during pregnancy, and this figures prominently in each of the studies from this period.

One study (Haslam and Draper 2001), for example, included 40 women from the UK and reported that all 40 women in the study could recount a list of risks related to pregnancy smoking, including:

“... Cot death, stunted growth, asthma, chest infections, prematurity/ low birth weight, miscarriage, stillbirth, congenital deformities and low intelligence. When asked if they were concerned about the risks, half of the sample said that they were not worried. Many refuted the risks by citing previous uncomplicated pregnancies experienced by themselves, female relations and friends. Low birth weight was not considered a serious health problem but was believed to be associated with an easier labour.”

This is the first mention of cot death and low intelligence, and in spite of the 1998 study in Australia where mothers reported knowing that low birth weight was an undesirable outcome, in this case in 2001 in the UK some mothers still viewed low birth weight as a potentially good thing, leading to an easier labour (Haslam and Draper 2001).

Another study from the same period (Lendahls et al. 2002) focuses on the conflict between risk, guilt and addiction:

“I’ve never met anyone that has had a problem. My friends have big, healthy babies and smoked, so... why should I put my cigarettes away? G1: You’ve got a 50±50 chance of having a healthy kid.”

“It’s so bad for your health. I smoke quite a lot... it’s not good when you’re pregnant. At the moment, I smoke because I’m worried that something might happen to the baby, but it’s smoking that causes that.”

“I’ve experienced the anti-smokers full-on... and then the family... ‘Suppose she’s just sneaked out the back for a cigarette.’ As if I was out there stabbing someone.” (Hotham 2002)

This particular mother had clearly internalised the sense of risk and guilt, and resorted to a little humour to defend her addiction.

Here also mothers in interviews proved knowledgeable, both in their reasoning (given lack of official information) about nicotine replacement patches and biases among their own antenatal care providers:

“I don’t know enough about them... they [patches] are not really tested and the baby is used to me having a cigarette and she’s made it this far. I’ll leave it at that.”

About biased antenatal care:

“Depends on whether your doctor or midwife smokes . . . a midwife who smokes . . . said, ‘In all my years, I’ve never seen a baby be smaller because of a mother who smokes.’ . . . that undoes every- thing that you are told.” (Hotham 2002).

The 2002 Hotham study is the first among the papers where risks related to nicotine replacement therapy are discussed.

In 2003 (Tod), the wrestling with specific risks continued. This study from the UK about barriers to smoking cessation included comments from mothers who considered the risks:

“I know that like there’s chance of low birth weight, cot death, all sorts. Bleeding in your pregnancy. Yeah all sorts. Asthma in the baby when it’s born.”

“She [a midwife] said to me she’ll always be tiny. I mean I wish she could see her now because she’s, like, huge and five feet four, you know what I mean?”

“To be able to stop, you’ve got to have a . . . a bloody good life.”

Here again, women in the study prove knowledgeable, astutely pointing out that quitting would be easier with a “good life” and also indignant, perhaps as a result of their addiction to smoking and the sense of guilt reflected in one mother’s wishing she could see the midwife who told her many years earlier that her baby would always be small, to prove to her that in fact her daughter had turned out healthy.

6.6 2005-2012: Bird nests and backlashes

Beginning with a study from Sweden in 2005 (Abrahamsson et al.), a new thinking seems to emerge. In this study the authors categorise women’s responses about challenges to smoking cessation during pregnancy. They clearly present the idea that women’s perception of the risks of pregnancy smoking could be likened to nest-building, in the same way that a bird brings together available materials to build a nest, women who mostly have no scientific training put together their own risk stories given what advice they have received along with their personal

experience and that they have read (Abrahamsson 2005). This idea has been reflected in previous studies, but is presented more formally here.

The authors also point out that this may be a kind of “resistance activity” which puts the woman’s own perception of risk in the forefront of her decision making, differing perhaps in 2005 from the period 1999-2004 when it seemed women were taking a more passive role to scientific evidence. There isn’t evidence that the perceptions of risk were affecting smoking cessation rates at all, but there does seem to have been a shift to more preoccupation with risks during 1999-2004 and a backlash beginning with studies published beginning in 2005.

Perhaps this is simply the result of a residual uncertainty on the part of both mothers and antenatal care providers. Though there are many risks to pregnancy smoking, it is very difficult for anyone without an understanding of probabilities and odds to understand how these risks apply to them, and when the issue is one of addiction, the lack of clarity is perhaps a welcome reason for women who smoke during pregnancy to defend the smoking habit.

One of the 2007 studies, conducted in Surrey, England by Bull et al. reported that the risks of maternal smoking during pregnancy mentioned in the study group included “medical risks, respiratory disorders, cancers and heart disease,” but that there was a sense, especially among respondents from more disadvantaged backgrounds, that the risks were exaggerated, and not personally relevant. One of the male respondents, a partner of a pregnant smoker commented: *“I don’t know if they have proved it, I mean there is a lot of scare-mongering with children”* (Bull et al. 2007).

In the other studies from 2007 risk and risk perception are not prominent, rather there is an emphasis on the symbolic of meaning of smoking in women's lives. This perhaps also reflects the policy environment where a major shift was in progress toward a health protection approach and the introduction of widespread public smoking bans. This may reflect the backlash against the emphasis on individualised risk.

This may also reflect a change in the motivation for conducting these studies. Rather than attempting to establish what women’s knowledge is, there seems to have been a shift to attempting toward attempting to understand what women’s attitudes, motivations and values are with respect to smoking. This may have developed as it became clear that simple knowledge is not enough to motivate a pregnant woman to quit smoking, especially considering that smoking is highly addictive and that smoking during pregnancy has become

most common among disadvantaged groups (Graham 2011) who have fewer resources, more stress and more personal problems (Pickett et al. 2009).

Discussion and conclusions

Interestingly, the shift to understanding the values and attitudes may also prove fruitless with respect to smoking cessation. Most likely a broader approach, tapping into what one of the study participants said in the paper from 2003: that you need to have a “bloody good life” to be able to quit smoking. This is evidenced by studies of smoking relapse that show that the majority of women who quit smoking during pregnancy have relapsed within a year postpartum (CDC 2004, Scheibmeir et al. 1997, Ershoff et al. 1995, Bottorff et al. 2000).

As mentioned in the beginning of the chapter, in “Risk, Fear, Blame, Shame and the Regulation of Public Safety,” Jonathan Wolff proposes that there are more important considerations than simple, objective risk when dealing with risk perception:

“In the current climate people profess to distrust scientists, doctors, the government, . . . In the light of this it is rather hard to see how anyone comes to any beliefs about anything . . . I am not proud of humanity for this, but it may turn out that once we do the sums, the most cost-effective way of reducing public anxiety could be to spend huge amounts of money on almost useless safety devices . . . in fact the practice of symbolic safety measures to reduce fears is much older [than recent terrorism prevention screening]. Has, in recent times, anyone’s life been saved on a standard commercial aircraft by a life-jacket? Or by that little whistle?” (Wolff 2006).

This perspective allows for a broader picture of risk and may help to understand why knowledge about risks alone may not motivate some women to quit smoking during pregnancy: the symbolic aspects of risk may be as important as the objective risks, and so women who live within more socially distinct clusters of friends and family who also smoke during pregnancy and who may rarely or never experience any adverse effects of smoking may decide that the risks do not apply to them in the same way. They also may not feel connected to the better off clusters who care about minimising risks at the population level, even when individual outcomes are somewhat rare.

Shame, blame and fear in the media, UK and USA

The issue of shame is also relevant to the issue of the stigma associated with smoking during pregnancy. The stigma existed in the 1970s (Graham 1976) and still exists; in 2012 a very popular story in the UK media circulated at the forefront of the news and social media for a period of time in March, when a popular UK celebrity was photographed, 7-months pregnant, smoking 4 cigarettes in a 2-hour period by the Daily Mail (Gutfield 2013). She had received a popular motherhood award previously, and this award was taken from her as a result of the scandal.

This popular media story exemplifies the cultural importance of shame, blame and fear, and demonstrates another difference between the USA and UK. The tone of the article and its comments differ from typical US stories in similar popular media. To give an example, a recent story from the Fox news channel in the USA reported that a man would be jailed for 20 days for ‘pulling a gun on a pregnant woman smoking.’ The question posed for discussion was: “Does the punishment fit the crime?” (Gutfeld 2013) so that the discussion was oriented toward the treatment of the man who threatened a pregnant woman with a gun and not on the pregnant woman or her decision to smoke.

This contrast brings into focus the issue of shame, blame and fear when comparing stigma in different national contexts. In the UK shame seems to be used to modify behaviour: one commenter in the UK referred to the celebrity as a ‘chav’ in an attempt to modify what she saw as unacceptable public behaviour (smoking during pregnancy). The comment may seem harsh, until a comparison is made. In the USA shame may also be used, but it is less familiar as a behaviour-modifying strategy. It may be that a direct physical threat is a more commonly understood cultural method of dealing with what is perceived as bad behaviour: a woman is harming her baby, so she should be shot.

This harsher treatment of public behaviour reflects general trends in the USA where both violence and imprisonment are more commonly used strategies in general (Wilkinson and Pickett 2009). Perhaps because the UK population is smaller, more urban, more tightly knit, or because of lower levels of social and economic inequality, the strategies for modifying public behaviour are more gentle: shaming has the same goal as threatening a person with a gun, but it is a symbolic threat: to be called a ‘chav’ could mean that one would be excluded from certain social groups, or labeled as undesirable and therefore cast out. Shooting someone would have the same effect, but in a physical as opposed to symbolic way.

6.7 Chapter conclusions

Hilary Graham's work (2011) on stigma and smoking provides a scientific framework for understanding these differences, proposing that stigma and the 'stigma-inducing potential of policy' must be understood within the context of social class and the history of how smoking behaviour has changed during the past 60 years: from a habit of elites to a habit of the disadvantaged. Further, she argues for policy evaluations that have an equity focus and for a broadening of tobacco control policies so that they 'engage directly with social inequalities.' In other words, a more reasonable approach to tobacco control--instead of focusing on the smoking behaviour of individuals--would focus on the inequalities in 'life chances and living standards' of those most at risk of taking up smoking.

On one side there has been, during the 36-year time period covered by the systematic review of qualitative studies (1976-2012) an increasing emphasis on individualised risk and self-quantification (Lupton), a more general attempt to understand how technology interacts with our perception of the world, and risks more specifically (Beck 1992) and a more recent suggestion that attempts to understand risk perception include not only objective risk as estimated in a population, but also the fear, blame, and shame that accompany any given risk (Wolff 2006), and in particular the risk of smoking during pregnancy.

While shame and blame seem to be intended to bring about a positive outcome (smoking cessation) by the individuals in both countries represented in the popular media stories mentioned above, it may be that these individuals are, in their own ways, simply mimicking the approach of policy in focusing on the behaviour of individuals. Following the analysis about stigma and smoking outlined by Graham (2011), both policy makers and individuals may be better off considering the upstream socio-economic factors that result in highly stacked odds against smoking cessation for disadvantaged groups. In this case it seems that guns, stigma, and shame are not the right tools for the task.

7

Discussion and conclusions

•Aim of this chapter

The aim of this chapter is to discuss the findings of the thesis, to draw conclusions from the studies conducted and to evaluate how they have contributed to the thesis aims. The first of these aims is to assess and augment the epidemiological evidence of a causal link between maternal smoking during pregnancy and child mental health. The second of these aims is to assess whether current policy, guidance and public discourse in the UK and USA accurately reflect the evidence base. The third of these aims is to assess whether women's perceptions of the risks of smoking during pregnancy accurately reflect the evidence base, policy and guidance.

7.1 Summary of findings

7.2 Evaluation and alternative explanations

7.3 Implications for policy

The aim of this thesis was to further understanding of the link between maternal smoking during pregnancy and mental health outcomes among children. The thesis comprises (a) a longitudinal epidemiological analysis of smoking during pregnancy and child mental health outcomes using cohort data for UK children from before birth to 7 years of age (b) an exploration of what policy documents, official guidance and qualitative studies tell us about how the epidemiological risks of smoking in pregnancy are reflected in public policy and discourse.

Existing epidemiological evidence was reviewed prior to the quantitative analyses. The data analysed are from the Millennium Cohort Study. Data for 13,161 mothers and children, analysed longitudinally, were used to link exposure to maternal smoking during pregnancy to child mental health outcomes (hyperactivity and aggressive behaviour) at 3, 5 and 7 years of age. Additionally a review of official and lay health guidance in two countries (United Kingdom and United States) was conducted to ascertain the extent to which the potential link between maternal smoking during pregnancy and increased risk of child mental health problems is reflected in ante-natal care policy and practice in these countries. Similarly, a review of qualitative studies was conducted to ascertain the extent to which the risk of child mental health problems is reflected in women's perceptions of the risks of smoking during pregnancy.

Summary of Findings

During the past 10 years high-quality studies (and studies of lower quality) have consistently observed an association between prenatal smoking exposure and child mental health problems, though a few well designed recent studies have provided conflicting findings, and further disentangling of exposure and potential confounding factors is needed.

Prenatal smoking, socioeconomic position, genetics, family environment, parental mental health and other chemical and environmental exposures, including other endocrine disrupting chemicals, should be explored together, and in more depth, to understand the associations that have been observed between maternal smoking during pregnancy and child mental health during the past 20 years.

The original and significant contribution of this thesis is a confirmation of the link between smoking in pregnancy and the development of disruptive behaviour problems in children in a large population-based sample from the United Kingdom and further confirmation that this

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effect seems to be reversible with improving economic conditions in families of exposed children. In terms of policy and discourse, ante-natal care packets could be modified to include information about these risks for pregnant women.

Given that the evidence is extensive, and weighty, but not definitive about a causal link between maternal smoking during pregnancy as a human brain teratogen, the findings of this thesis are outlined in terms of explanatory models and how they currently interact with policy and perceptions of risk.

These are:

1. That components of cigarette smoke such as nicotine, or aspects of cigarette smoking, such as foetal oxygen deprivation, act as **teratogens** on the developing brain, creating vulnerabilities in key functions such as auditory processing, leading to vulnerabilities in healthy mental and social development.
2. That it is simply the **social and economic context** of women who smoke during pregnancy that acts indirectly on the developing brain and leads to vulnerabilities in key functions such as auditory processing, leading to vulnerabilities in healthy mental and social development.
3. That it is both, and that there may be an '**avalanche**' effect, in that difficulties accumulate and result in further challenges to child health, which then further affect family well-being over time.

In the literature review (Chapter 3), consistent evidence was found for both the Teratogen hypothesis and the Social and Economic context hypothesis. The majority of the papers in the literature review (2001-2013) reported positive, unmixed associations between maternal smoking during pregnancy and child mental health.

Still, there are reasons to doubt the association is causal, or purely causal. First, there is a bias of publication toward positive findings, and so there may be null studies that are not captured because of this bias. Second, many of the studies were either not powered to control for extensive social and economic factors, or they were not representative of whole populations and therefore not generalisable. Third, there is the question of why, when smoking during pregnancy is declining, hyperactivity and aggression among children is on the rise.

The highest quality study by Pickett et al (2008) is the strongest previous evidence for this doubt. In a large, nationally representative, population-based longitudinal sample, they found that children whose mothers did smoke during pregnancy but then quit smoking did best in terms of temperament and mental health outcomes. This brings the association squarely into question because these children had the biochemical exposure in utero, but they fared even better than those with no exposure at all.

What can explain this unless there is a plasticity in brain development that essentially means that as conditions improve, so do outcomes related to brain structure and function. Or, it could simply be that it is exposure in the last trimester which is relevant since the children of quitters didn't have this exposure, *and* they have mothers with willpower and desire to do the right thing for the child.

Table 7.1 Summary of Findings from this Thesis

	TERATOGEN	SOCIAL AND ECONOMIC CONTEXT	AVALANCHE	POLICY AND GUIDANCE	RISK PERCEPTION
Chapter 3 Longitudinal Study	<ul style="list-style-type: none"> • Evident in infancy and early childhood • Increased odds of hyperactivity • Increased odds of aggression 	<ul style="list-style-type: none"> • Similar effect to the effect of smoking during pregnancy in later childhood, apparent by age 7 	<ul style="list-style-type: none"> • Over time, effect of smoking is the same as the effect of persistent childhood poverty and is overtaken by age 7 	<ul style="list-style-type: none"> • Teratogen mentioned • Social and economic context not mentioned • Avalanche effect not mentioned 	<ul style="list-style-type: none"> • Risk of effects on child mental health and behaviour not mentioned by women in qualitative studies about smoking during pregnancy
Chapter 4 Policy Review	<ul style="list-style-type: none"> • Clearly mentioned in both UK and USA guidance 	<ul style="list-style-type: none"> • Not mentioned in UK or USA smoking related guidance 	<ul style="list-style-type: none"> • Not mentioned in UK or USA smoking related guidance 	<ul style="list-style-type: none"> • Avalanche effect not mentioned 	<ul style="list-style-type: none"> • Women's perceptions of risk not mentioned in policy and guidance
Chapter 5 Risk Perception Review	<ul style="list-style-type: none"> • Not mentioned by women in qualitative review studies 	<ul style="list-style-type: none"> • Not mentioned by women in qualitative review studies 	<ul style="list-style-type: none"> • Mentioned in terms of having a "good life" to be able to quit smoking 	<ul style="list-style-type: none"> • Women reported uncertain advice about risks from GPs, midwives 	<ul style="list-style-type: none"> • Risks most mentioned: low birthweight and asthma

Explanatory Models: Health and well-being of children whose mothers smoke during pregnancy and how evidence is reflected in to policy, official guidance and public discourse

In Chapter 4 the Avalanche hypothesis was explored, comparing children with smoking exposure to those without who were persistently poor across childhood to see how their trajectories compared. The results, which show that smoking and poverty have similar effects in terms of child mental health, provide evidence for the Avalanche hypothesis. In this model,

advantage can either accumulate or reverse-accumulate, and child mental health outcomes follow accordingly. Smoking, though representing a chemical exposure, is seen as another challenge to development, on equal footing with other exposures such as economic insecurity and equally likely to cause problems. Removing the exposure to smoking removes the mental health risks, but only when other exposures such as economic insecurity are also removed. These exposures are linked and difficult to separate fully in the context of disadvantage and health inequalities in the United Kingdom.

It may be more important to put in place social policies that act as snow nets, or other social safety nets that prevent one disadvantage from accumulating with other to develop into a disaster. Here the quote of one mother from the review of qualitative studies seems relevant: *“to quit smoking you have to have a bloody good life.”*

Individual will or political will?

Considering the question: *“What is the goal of healthy child development?”* brings into focus the idea that maternal smoking during pregnancy is almost entirely treated as an individual problem. After reviewing the scientific evidence, augmenting it in a large, UK-based sample and comparing the evidence to what policy, guidance and public discourse say about maternal smoking during pregnancy, it is almost universal in these sources that the focus is on individual level risks to the child’s health and that the lever is the mother’s individual decision to quit smoking during pregnancy.

There are a few problems with this. First, it is not clear that smoking during pregnancy is the beginning or end of the exposure of concern. It is possible that physical, teratogenic damage is done to gametes by smoking before pregnancy, and it seems equally likely that this damage could be reversed under improved conditions, whether by removing the smoking exposure or by removing larger contextual effects such as living in relative poverty during childhood.

One thing that was noticeably missing from both the research evidence and official policy and guidance was the idea that smoking, currently, is a socially patterned behaviour that is very difficult to quit, but which seems to become easier to quit under better social and economic conditions. So the question is: is maternal smoking during pregnancy the responsibility of individual mothers who smoke at the beginning of pregnancy, who may already be living in disadvantaged circumstances, including as adolescent pregnant women? Or is it the responsibility of wider society, to encourage women to have a healthy pregnancy? If it is this, then this seems to be simply a variation of the first question: encouraging women is the same

thing as expecting them, in a supportive way, to take responsibility for their health-related behaviours. Or it is a problem of political will? Is leaving women to live in poverty, with insecure employment and childcare options, with insecure housing and increasingly expensive education to improve social circumstances the main problem?

Throughout this thesis the implications for child health and healthy development have been discussed. These implications will be re-visited at the end of the chapter, but first the existing evidence and further avenues for improving the evidence base are evaluated.

7.2 Evaluation and weak spots in the research base

During the past 10 years high-quality studies (and studies of lower quality) have consistently observed an association between prenatal smoking exposure and child mental health problems. In spite of extensive work aimed at disentangling, questions remain about the extent of effects attributable to prenatal smoking and other interrelated exposures—and whether effects are permanent. What is clear is that prenatal smoking is consistently and strongly associated with relative disadvantage. Therefore, policies aimed at helping pregnant women out of disadvantage are likely to have positive effects on both the exposure (prenatal smoking) and the outcome (child mental health).

The methods used in this thesis are useful for updating and augmenting the evidence base and for understanding how the scientific evidence reverberates in the public sphere. There is good quality evidence for this risk, and in the longitudinal study described in Chapter 4 it was clear that children whose mothers smoked during pregnancy started off life with more difficulties in terms of hyperactivity and aggression, even if these problems attenuate over the course of childhood and become overtaken by other exposures such as childhood poverty.

This thesis also brings into perspective some further questions. The first of these is: what is the goal of healthy child development? Is it an individual goal (i.e good educational attainment), a community level goal (i.e good adaptation to the social and economic environment and neighbourly behaviour), or a societal goal (i.e creativity and contribution to society), or something in between? Answering these questions in future work could lead to a further tailoring of ante-natal care policy and guidance according to what is intended and what role mothers and the people who surround them play in healthy child development.

7.3 Implications for policy

The findings from this thesis could be useful for understanding the relationship between epidemiological evidence and ante-natal policy and practice, and for identifying where any links in the chain from evidence to policy to practice exist.

In the case of maternal smoking during pregnancy, there is a good base of evidence for a likely causal, but not irreversible link between this exposure and child mental health. The evidence is well translated and up to date in official policy and guidance in both the UK and USA, and the popular pregnancy literature sources have also integrated and translated it, for the most part accurately.

The missing link seems to be in ante-natal care packets, where the link is not mentioned. It may be that the reading level of these materials is intended to be lower and more accessible than for the popular pregnancy advice books, but there are two problems with this.

First, if the effect of smoking during pregnancy on child mental health is a solid, albeit subtle neurotoxic effect, then mothers who smoke during pregnancy should know about it, whether it helps them to quit smoking or not. The most direct route for public policy and practice to ensure this communication is through ante-natal care packets.

Second, the women who are most likely to smoke during pregnancy are also the most likely to be disadvantaged in other ways and the least likely to have other good health behaviours. They may not access the leading commercially available pregnancy advice guides. In Chapter 6 there is a suggestion that physicians and midwives may avoid talking about smoking during pregnancy with women, and so there is a gap that emerges. Adding this information in an accessible format to publicly provided ante-natal care packets could fill this gap by ensuring that those most likely to need the information will see it when they attend routine, publicly provided ante-natal care.

It is clear that prenatal smoking is consistently and strongly associated with disadvantage—so policies aimed at helping pregnant women out of disadvantage are likely to have positive effects on both the exposure (prenatal smoking) and the outcome (child mental health).

APPENDIX 1: SMOKING DURING PREGNANCY AND CHILD MENTAL HEALTH OUTCOMES, 2001-2010

STUDY ID	COUNTRY	N	SAMPLE	MEASUREMENT OF PRENATAL SMOKING EXPOSURE	EXPOSED %	PERIOD OF FOLLOW-UP	MEASUREMENT OF OUTCOME	SUPPORT FOR CAUSAL CLAIM (ANY EXTERNALISING BEHAVIOUR OR INFANT DIFFICULT BEHAVIOUR)	ADJUSTED OUTCOMES	STUDY QUALITY	QUALITY SCORE (NEWCASTLE-OTTAWA SCALE FOR COHORT STUDIES)	AGE GROUP ANALYSED
SILBERG 2003	USA	589	Adolescent twins ages 12-17, Virginia	Mother's report 12-17 years after birth	26	0 years	CD using the CAPA scale	No	No effects observed after adjustment	HIGH	5	Adolescents
INDREDAVIK 2007	Norway	84	Adolescent s age 14, Norway	Mother's report during pregnancy	38	14 years	Mother, father and teacher report (ASEBA: YSR; CBCL), Child psychiatrist report (CGAS) Externalising and internalising behaviours	Yes	Externalising, internalising, ADHD and total problems	HIGH	6	Adolescents
NIGG AND BRESLAU 2007	USA	713	Adolescent s age 17 years, Detroit	Mother's report 6 years post pregnancy	31	11 years	Mother and teacher and self (child) reports	Mixed	Effect not significant for ADHD but significant for ODD and subsequently CD.	LOW-MEDIUM	4	Adolescents
WAKSCHLAG 2002	USA	77	African-American children age 10	Mother's report during pregnancy	71	10 years	Study staff diagnosed CD in 10 year olds	Mixed	Effects observed for CD among boys but not girls. Maternal responsiveness accounted for some of this effect.	HIGH	8	Children

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GRAY 2004	USA	869	869 children ages 3, 5 and 8 years	Mother's report during pregnancy	33	8 years	CBCL/2-3, CBCL/4-18	Yes	Effects observed for clinically significant behaviour problems at all time points [OR=1.57 (1.20-2.04)]	LOW-MEDIUM	4	Children
WAKSCHLAG 2006B	USA	93	93 children ages 1, 1.5 and 2 years	Mother's report verified by laboratory assay	47	2 years		Mixed	Effects observed for externalising behaviours only at age 2 years.	HIGH	9	Children
MARKUSSEN LINNET 2006	Denmark	1,355	Children age 3 years	Mother's report during pregnancy	21	3.5 years	Mother's report on Preschool Behaviour Questionnaire	Mixed	Effect of prenatal smoking 10+ cigarettes/day observed for hyperactive-distractibility behaviour [OR=1.6 (1.0-2.3)] but not aggressive or anxious behaviour	HIGH	6	Children

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HÖÖK 2006	Sweden	1,428	Children age 3 and 677 children age 5.5 years	Mother's report during pregnancy and when child age 3 months	16	4-6 years	Mother's report on CBCL for	Yes	Effects observed for externalising behaviour, destructive/delinquent behaviour at both time points. Equally strong for boys and girls. Height and weight also lower among children whose mothers smoked during pregnancy.	HIGH	7	Children
CORNELIUS 2007	USA	357	Children age 6, Pittsburgh	Adolescent mother's self-report during pregnancy and within 3 days of the birth	58	6 years	CBCL, RAS, SNAP. Externalising and internalising behaviours	Yes	Effects observed for hyperactivity but not other outcomes	HIGH	7	Children
CARTER 2007	New Zealand	1,038	Children, South Auckland	Mother's report, 6 weeks post-pregnancy (smoking during 1st trimester)	22	2 years	CBCL Externalising and Internalising behaviours	Yes	OR for total behaviour problems=1.75 (1.12-2.74), Internalising behaviour (by children of lone mothers) OR=3.35 (1.29-8.67), Externalising (by girls) OR=2.37 (1.12-5.04)	HIGH	6	Children

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SEN AND SWAMINANTHAN 2007	USA	8,395	Children ages 4-6 years and 8-10 years, NLSY	Mother's report 4 years post-pregnancy	Not reported	4-10.5 years	BPI scale	No	Found that alcohol but not smoking predicted behaviour problems in children.	LOW-MEDIUM	4	Children
HUIJBREGTS 2008	Canada	1,745	Children age 17-42 months, Quebec	Mother's report, 5 months post-pregnancy	25	3 years	Mother's report on a behavioural scale of physical aggression	Yes	Trajectory model estimation showed 3 distinct developmental patterns for physical aggression (PA) and four for hyperactivity-hyperimpulsivity (HI). Prenatal smoking predicted child likelihood of following PA trajectories	HIGH	6	Children

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JOHANSSON 2008	Sweden	8,850	Children age 3 years	Mother's report during pregnancy	8.5	3 years	Child wellbeing including rhinitis, wheezing, use of cough and broncho-dilating medicines, sleep disturbances, excessive crying and irritability	Mixed	Effects observed for excessive crying OR 1.31 (1.13-1.51) and irritability OR=1.27 (1.09-1.48) in children exposed pre and postnatally. For children only exposed prenatally, only effects observed for use of broncho-dilating drugs OR=1.45 (1.03-2.04) and poor sleep OR=2.06 (1.09-3.87)	HIGH	6	Children
DONOFRIO 2008	USA	8,889	Children ages 4-10	Mother's report, aimed for within 1 year post-pregnancy	29	4-10 years	Selected items from CBCL	Mixed	Effects (CP and ODP) were non-significant after comparing differentially exposed siblings. Effects (ADHD) were attenuated after comparing siblings.	LOW-MEDIUM	4	Children

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THARPAR 2009	Multi-country	815	Children ages 4-11 years	Mother's report 4-11 years post-pregnancy		N/A (not a cohort)	ADHD symptoms	No	Significant differences observed for genetically related vs. unrelated offspring, suggesting inherited effects rather than prenatal smoking effects	LOW-MEDIUM	0	Children
ROZA 2009	Netherlands	4,680	4680 children age 18 months	Mother's (and father's) report during pregnancy	22	1.5 years	Both externalising behaviours and "total problems" on the CBC	No	Associations accounted for by controlling for parental socioeconomic status and psychopathology	HIGH	6	Children
STENE-LARSEN 2009	Norway	22,545	Children age 18 months the Mother and Child Cohort Study	Mother's report, 17th week of pregnancy	3.8	2 years	Externalising behaviours	Yes	Externalising behaviours 1.32 (1.03-1.70), not moderated by child's sex	HIGH	7	Children
BRION 2010B	Brasil	509	Children age 4 years from Pelotas Brasil	Mother's report during perinatal visit)	29	4 years	CBCB	Mixed	Effects observed for conduct/externalising only after adjustment 1.82 (1.19-2.78).	LOW-MEDIUM	4	Children

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BRION 2010A	UK	6,735	Children age 4 years from SW England	Mother's report during pregnancy (ALSPAC: by mail,	16	4 years	SDQ	Mixed	Effects observed for conduct/externalising only after adjustment 1.24 (1.07-1.46)	HIGH	5	Children
HUIJBREGTS 2007	Canada	1,745	Children ages 17-42 months, Quebec	Mother's report 5 months post-pregnancy	25	3 years	Mother's report on a behavioural scale of physical aggression	Yes	Prenatal smoking AND PSE X Maternal anti-social behaviour AND PSE X Family income predicted high-risk trajectory. Critical adversities	HIGH	6	Children
PICKETT 2008	UK	18,263	Children age 9 months	Mother's report 9 months post-pregnancy	23	0 months	Three dimensions from Carey Infant Temperament Scale	Mixed	Effect of heavy smoking OR=1.17 (p=0.09). Prenatal smoking followed by quitting during pregnancy was associated with improved outcomes among offspring at 9 months of age	HIGH	5	Infants

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STROUD 2009	USA	962	Mother-neonate pairs, National Collaborative Perinatal Project, Rhode Island	Mother's report during pregnancy	62	3 days	Graham-Rosenblith Behavioural Examination of the Neonate	Yes	Increased irritability (1 pack/day smoking exposure) and increased muscle tone (less than 1 pack/day and 1 pack/day smoking exposure groups)	HIGH	6	Infants
MAUGHAN 2001	UK	5,770	Children ages 5, 10, 16	Mother's report 1 month post-pregnancy	40	16 years, 3 timepoints	Mother's report on Rutter A2. Conduct and hyperactivity problems	Mixed	OR for conduct problems 1.53.	LOW-MEDIUM	4	Longitudinal
TREMBLAY 2004	Canada	572	Children ages 17, 30 and 42 months	Mother's report 5 months post-pregnancy	not reported separately	3 years	Mother's reports of physical aggression	Yes	Prenatal smoking along with other family factors predicted high-risk trajectory	LOW-MEDIUM	0	Longitudinal

APPENDIX 1: SMOKING DURING PREGNANCY AND CHILD MENTAL HEALTH OUTCOMES, 2001-2010

STUDY ID	COUNTRY	N	SAMPLE	MEASUREMENT OF PRENATAL SMOKING EXPOSURE	EXPOSED %	PERIOD OF FOLLOW-UP	MEASUREMENT OF OUTCOME	SUPPORT FOR CAUSAL CLAIM (ANY EXTERNALISING BEHAVIOUR OR INFANT DIFFICULT BEHAVIOUR)	ADJUSTED OUTCOMES	STUDY QUALITY	QUALITY SCORE (NEWCASTLE-OTTAWA SCALE FOR COHORT STUDIES)	AGE GROUP ANALYSED
BATSTRA 2003	Netherlands	1,186	Children ages 5-11 years	Mother's report at time of birth	47	11 years	Mother's and teacher's report: whether they found the child to be more/ same/less withdrawn or troublesome and attention deficient than average	Yes	Effects observed for externalising (troublesome) behaviour and attention deficit.	HIGH	6	Multiple
THARPAR 2003	UK	2,054	Twin children and adolescents ages 5-16	Mother's report 5-16 years after birth	29		Mother and teacher report on CD and ADHD scales developed from the DSM-III-R, DSM-IV, and ICD10	Mixed	Effects observed for ADHD	LOW-MEDIUM	4	Multiple

APPENDIX 1: SMOKING DURING PREGNANCY AND CHILD MENTAL HEALTH OUTCOMES, 2001-2010

STUDY ID	COUNTRY	N	SAMPLE	MEASUREMENT OF PRENATAL SMOKING EXPOSURE	EXPOSED %	PERIOD OF FOLLOW-UP	MEASUREMENT OF OUTCOME	SUPPORT FOR CAUSAL CLAIM (ANY EXTERNALISING BEHAVIOUR OR INFANT DIFFICULT BEHAVIOUR)	ADJUSTED OUTCOMES	STUDY QUALITY	QUALITY SCORE (NEWCASTLE-OTTAWA SCALE FOR COHORT STUDIES)	AGE GROUP ANALYSED
BROOK 2006	USA	208	Children ages 8-13 years, Puerto Rican and African-American populations, NY	Mother's report 8-13 years post-pregnancy	29	0 years	Adapted scales from previously validated child aggressive behaviour scales	Yes	Maternal unconventionality, maternal warmth and pregnancy smoking associated with child aggressive behaviour	HIGH	5	Multiple
WAKSCHLAG 2006A	USA	448	Children ages 7-19 followed up biannually	Mother's report 7 years post-pregnancy	37	7 years	Developmental pattern of CD in boys	Yes	Effect observed for ODD+ADHD [OR=2.66, p<0.05]	LOW-MEDIUM	4	Multiple
MARTIN 2006	Finland	2,001	Infants age 6 months. Also 676 children ages 5 years and 420 children age 12 years, Helsinki	Mother's report during pregnancy	"Not reported"	12 years	Temperament, behaviour and academic performance	Mixed	Effects observed for temperament, behaviour and academic problems. Contrary to expectation, infants exposed to heavy prenatal smoking had less distress to novelty and less irregularity.	HIGH	5	Multiple


```
gen smresp = amsmus0a

recode smresp -9=0 -8=0 -1=0 1/max=1

label variable smresp "Did subject provide valid response for smoking initiator question"

*coding cigarettes smoked before pregnancy

gen cigbfpre = 0

recode cigbfpre 0=.a if smresp == 0

recode cigbfpre 0=.a if amcipr00 == -8

recode cigbfpre 0=1 if amcipr00 >0 & amcipr00 <10

recode cigbfpre 0=2 if amcipr00 >=10 & amcipr00< 999

label variable cigbfpre "Number of cigarettes smoked before pregnancy"

label define cigbfpre 0 "Zero" 1 "less than 10" 2 "10 or more"

label values cigbfpre cigbfpre

*amount during pregnancy

gen cigdupre = cigbfpre

replace cigdupre =3 if amcich00 == 0

replace cigdupre =2 if amcich00 >=10 & amcich00 <90

replace cigdupre =1 if amcich00 <10 & amcich00 >0

label variable cigdupre "Number of cigarettes smoked during pregnancy"

label define cigdupre 0 "Zero" 1 "less than 10" 2 "10 or more" 3 "quit"

label values cigdupre cigdupre

gen pregsmok=cigdupre
```

APPENDIX 3: DERIVED VARIABLES, MATERNAL SMOKING DURING PREGNANCY AND CHILD MENTAL HEALTH, MILLENNIUM COHORT STUDY, UNITED KINGDOM 2000-2008

*0=female / 1=male

gen sex=dhcsexa0

replace sex=0 if dhcsexa0==2

replace sex=1 if dhcsexa0==1

*teenbirth

gen teenbirth = admagb00

replace teenbirth =1 if admagb00 <20

replace teenbirth =0 if admagb00 >=20 & admagb00 <.

replace teenbirth =. if admagb00==-.2

label define teenbirth 0 ">=20" 1 "<20"

label values teenbirth teenbirth

*gcse a-c

gen gcse = amacqu00

replace gcse=. if amacqu00==-.9 | amacqu00==-.8 | amacqu00==-.1

replace gcse=0 if amacqu00==1 | amacqu00==2 | amacqu00==3 | amacqu00==4 |

amacqu00==6 | amacqu00==7 | amacqu00==95 | amacqu00==96

replace gcse=1 if amacqu00==5

label define gcse 0 "no" 1 "yes"

label values gcse gcse

*ethnicminority

gen ethnicminority = adm06e00

replace ethnicminority =. if adm06e00==-.9 | adm06e00==-.8 | adm06e00==-.1

replace ethnicminority=0 if adm06e00==1

replace ethnicminority=1 if adm06e00==2 | adm06e00==3 | adm06e00==4 |

adm06e00==5 | adm06e00==6

label define ethnicminority 0 "no" 1 "yes"

label values ethnicminority ethnicminority

*lonemother

gen lonemother = amrebo00

replace lonemother=. if amrebo00==-.9 | amrebo00==-.8 | amrebo00==-.1

replace lonemother=0 if amrebo00==1 | amrebo00==2 | amrebo00==5

replace lonemother=1 if amrebo00==3 | amrebo00==4 | amrebo00==6 | amrebo00==7

label define lonemother 0 "no" 1 "yes"

label values lonemother lonemother

APPENDIX 3: DERIVED VARIABLES, MATERNAL SMOKING DURING PREGNANCY AND CHILD MENTAL HEALTH, MILLENNIUM COHORT STUDY, UNITED KINGDOM 2000-2008

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**familystability*

gen familystable=amfcin00

replace familystable=888 if amfcin00==dmfcin00

replace familystable=. if familystable==9 | familystable==8

replace familystable=0 if familystable==1 | familystable==2 | familystable==3 |

familystable==4 | familystable==5 |familystable==6

replace familystable=1 if familystable==888

**oecdpoor*

gen oecdpoor = advoecdpoor

replace oecdpoor=. if advoecdpoor==1

replace oecdpoor=1 if advoecdpoor==1

replace oecdpoor=0 if advoecdpoor==0

label define oecdpoor 0 "no" 1 "yes"

label values oecdpoor oecdpoor

**did mother leave home before the age of 17?*

gen lefthome=amliaw00

replace lefthome=. if amliaw00==9 | amliaw00==8 | amliaw00==1

replace lefthome=0 if amliaw00==2

replace lefthome=1 if amliaw00==1

**taking out boarding school as reason for living away from home*

replace lefthome=0 if amwhli00==5

**did she spend any time in care?*

gen livedincare=amliaw00

replace livedincare=. if amliaw00==9 | amliaw00==8 | amliaw00==1

replace livedincare=0 if amliaw00==2

replace livedincare=0 if amliaw00==1

**now coding: of those who reported they lived in a residential care home*

replace livedincare=1 if (amwhli00==1 | amwhli00==2 | amwhli00==3 | amwhli00==4 | amwhli00==7 | amwhli00==8 | amwhli00==9 | amwhli00==14)

**did her own parents ever separate?*

gen matparentssepar=ampasd00

replace matparentssepar=. if ampasd00==9 | ampasd00==8 | ampasd00==1

replace matparentssepar=0 if ampasd00==2 | ampasd00==3 | ampasd00==4

**how frequently does mother see own mother?*

gen seesmother=amsemo00

APPENDIX 3: DERIVED VARIABLES, MATERNAL SMOKING DURING PREGNANCY AND CHILD MENTAL HEALTH, MILLENNIUM COHORT STUDY, UNITED KINGDOM 2000-2008

```
replace seesmother=. if amsemo00==9 | amsemo00==8 | amsemo00==1
replace seesmother=0 if amsemo00==8
replace seesmother=1 if amsemo00==2 | amsemo00==3 | amsemo00==4 |
amsemo00==5 | amsemo00==6 | amsemo00==7 | amsemo00==9
```

*Mother has no time with friends

```
gen nofriendtime=amfrti00
replace nofriendtime=. if amfrti00==9 | amfrti00==8 | amfrti00==1
replace nofriendtime=0 if amfrti00==1 | amfrti00==2 | amfrti00==3
replace nofriendtime=1 if amfrti00==4 | amfrti00==5
```

*Mother has no-one to share feelings with

```
*ampesh00 (1 and 2 are strongly agree / agree)
gen noonefeeling=ampesh00
replace noonefeeling=. if ampesh00==9 | ampesh00==8 | ampesh00==1
replace noonefeeling=0 if ampesh00==3 | ampesh00==4 | ampesh00==5 |
ampesh00==6
replace noonefeeling=1 if ampesh00==1 | ampesh00==2
```

*No visits to/by other parents

```
*ampeta00 (4 and 5 are disagree / strongly disagree: main other parents can talk to
gen novisits=ampeta00
replace novisits=. if ampesh00==9 | ampeta00==8 | ampeta00==1
replace novisits=0 if ampesh00==4 | ampesh00==5
replace novisits=1 if novisits~=0
```

*Partner perpetrated violence

```
*amforc00 (-9, -8, -1, 1=yes, 2=no, 3=don't want to answer)
gen partperp=amforc00
replace partperp=. if amforc00==9 | amforc00==8 | amforc00==1
replace partperp=0 if amforc00~=1
```

*Mother ever lived with more than one partner

```
*amlico00 (1 is yes / 2 is no)
gen plusone=amlico00
replace plusone=. if amlico00==9 | amlico00==8 | amlico00==1
replace plusone=0 if amlico00==2
```

APPENDIX 3: DERIVED VARIABLES, MATERNAL SMOKING DURING PREGNANCY AND CHILD MENTAL HEALTH, MILLENNIUM COHORT STUDY, UNITED KINGDOM 2000-2008

```

*Mother reported lacking parenting competence
*dmpacr00 (1 not very good at parent / 2 a person who has trouble being a parent)
gen lackcompetence=dmpacr00
replace lackcompetence=. if dmpacr00==8 | dmpacr00==1
replace lackcompetence=1 if dmpacr00==1 | dmpacr00==2
replace lackcompetence=0 if lackcompetence~=1

*Mother smacks child daily or weekly
*dmdisma0 (4 once a week / 5 daily)
gen smack=dmdisma0
replace smack=. if dmdisma0==9 |dmdisma0==8 |dmdisma0==1
replace smack=888 if dmdisma0==4 | dmdisma0==5
replace smack=0 if smack~=888
replace smack=1 if smack==888

*Low sense of control
*control over life
*amcont00 (1 yes / 2 no)
gen lowcont=amcont00
replace lowcont=. if amcont00==9 | amcont00==8 | amcont00==1
replace lowcont=0 if lowcont~=2
replace lowcont=1 if lowcont==2

*(gets what wants out of life)
*amwant00 (1=I never really seem to get what I want)
gen getswant=amwant00
replace getswant=. if amwant00==9 | amwant00==8 | amwant00==1
replace getswant=0 if amwant00==1 | amwant00==3
replace getswant=1 if amwant00==2

*Low satisfaction with life
*satislife
gen satislife = amwali00
replace satislife=. if amwali00==9 | amwali00==8 | amwali00==1
replace satislife=1 if amwali00 >=6 & amwali00<.
replace satislife=0 if amwali00 <6
label define satislife 0 "no" 1 "yes"
label values satislife satislife

```

APPENDIX 3: DERIVED VARIABLES, MATERNAL SMOKING DURING PREGNANCY AND CHILD MENTAL HEALTH, MILLENNIUM COHORT STUDY, UNITED KINGDOM 2000-2008

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*satisfaction with life wave 4

*dmwali00

gen satslife4=dmwali00

replace satslife4=. if dmwali00==9 | dmwali00==8 | dmwali00==1

replace satslife4=1 if dmwali00>=6 & dmwali00<.

replace satslife4=0 if dmwali00<6

label define satslife4 0 "no" 1 "yes"

label values satslife4 satslife4

*Low self esteem

*satisfiedself

gen satisfiedself = amsati00

replace satisfiedself=. if amsati00==9 | amsati00==8 | amsati00==1 | amsati00==5

replace satisfiedself=0 if amsati00==3 | amsati00==4

replace satisfiedself=1 if amsati00==1 | amsati00==2

label define satisfiedself 0 "no" 1 "yes"

label values satisfiedself satisfiedself

*Ever homeless (since birth of CM)

*amhoms00 (-9, -8, -1, 1=yes, 2=no)

gen homeless=amhoms00

replace homeless=. if amhoms00==9 | amhoms00==8

replace homeless=0 if amhoms00==2 | amhoms00==1

*No phone to make calls

*amphon00 (-9, -8, -1, 1=yes, 2=yes incoming, 3=no)

gen nophone=amphon00

replace nophone=. if amphon00==9 | amphon00==8 | amphon00==1

replace nophone=0 if amphon00==1

replace nophone=1 if amphon00==2 | amphon00==3

*Difficulty managing finances

*No bank account

*Very disorganised household

*dmhodi00 (-9, -8, -1, 1=strongly agree, 2=agree, 3=neither, 4=disagree, 5=strongly disagree)

gen vdishouse=dmhodi00

replace vdishouse=. if dmhodi00==9 | dmhodi00==8 | dmhodi00==1

replace vdishouse=0 if dmhodi00~1

APPENDIX 3: DERIVED VARIABLES, MATERNAL SMOKING DURING PREGNANCY AND CHILD MENTAL HEALTH, MILLENNIUM COHORT STUDY, UNITED KINGDOM 2000-2008

*Depression tx W1

```
gen txdepress1=amtrde00
replace txdepress1=. if amtrde00==8
replace txdepress1=0 if amtrde00==1 | amtrde00==2
replace txdepress1=1 if amtrde00==1
```

*Depression tx W4

```
*dmtrde00
gen txdepress4=dmtrde00
replace txdepress4=. if dmtrde00==8 | dmtrde00==9
replace txdepress4=0 if dmtrde00==1 | dmtrde00==2
replace txdepress4=1 if dmtrde00==1
```

*Drink problem

```
gen drinkheavy=amunda00
replace drinkheavy=. if amunda00==9|amunda00==8
replace drinkheavy=0 if amunda00==1 | amunda00==0 | amunda00==1
replace drinkheavy=1 if amunda00>=2 & amunda00<.
```

*Limiting long-term illness

```
*amlolm00 (-1, -8, -9, 1=yes, 2=no)
gen limlongill=amlolm00
replace limlongill=. if amlolm00==9 | amlolm00==8
replace limlongill=0 if amlolm00==1 | amlolm00==2
replace limlongill=1 if amlolm00==1
```

*Unplanned pregnancy

```
*amprpl00 (-9, -8, -1, 1=planned, 2=not)
gen unplan=amprpl00
replace unplan=. if amprpl00==9 | amprpl00==8 | amprpl00==1
replace unplan=0 if amprpl00==1
replace unplan=1 if amprpl00==2
```

*pregfeel2

```
gen pregfeel2 = amprfe00
replace pregfeel2 =. if amprfe00==8 | amprfe00==1
```

APPENDIX 3: DERIVED VARIABLES, MATERNAL SMOKING DURING PREGNANCY AND CHILD MENTAL HEALTH, MILLENNIUM COHORT STUDY, UNITED KINGDOM 2000-2008

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```
replace pregfeel2 =0 if amprfe00==1 | amprfe00==2
replace pregfeel2 =1 if amprfe00==3 | amprfe00==4 | amprfe00==5
label define pregfeel2 0 "happy/very happy" 1 "not bothered/unhappy/very unhappy"
label values pregfeel2 pregfeel2
```

*Late entry into antenatal care

*amanca00 (-9, -8, -1, 1=yes, 2=no)

gen latecare=amanca00

replace latecare=. if amanca00==-9 | amanca00==-8 | amanca00==-1

replace latecare=0 if amanca00==1

replace latecare=1 if amanca00==2

*incomplete immunisations

*amimmua0

gen incomimmune=amimmua0

replace incomimmune=. if amimmua0==-9 | amimmua0==-8 | amimmua0==-1

replace incomimmune=0 if amimmua0==1

replace incomimmune=1 if amimmua0==2

*Not attempted breastfeeding

*ambfeva0 (-9, -8, -1, 1=yes, 2=no)

gen nonip=ambfeva0

replace nonip=. if ambfeva0==-9 | ambfeva0==-8 | ambfeva0==-1

replace nonip=0 if ambfeva0==1

replace nonip=1 if ambfeva0==2

*Postnatal smoking near the child

*amsmkr00 (1 is yes, 2 is no)

gen smokenear=amsmkr00

replace smokenear=. if amsmkr00==-8 | amsmkr00==-1

replace smokenear=0 if amsmkr00==2

replace smokenear=1 if amsmkr00==1

*LBW

gen LBW = adbwgta0

replace LBW =. if adbwgta0==-8

*APPENDIX 3: DERIVED VARIABLES, MATERNAL SMOKING
DURING PREGNANCY AND CHILD MENTAL HEALTH,
MILLENNIUM COHORT STUDY, UNITED KINGDOM 2000-2008*

```
replace LBW=1 if adbwgta0 <=2.5
replace LBW =0 if adbwgta0 >2.5 & adbwgta0 <.
label define LBW 0 ">2.5 kg" 1 "<=2.5 kg"
label values LBW LBW

*preterm delivery
gen preterm=adgest00
replace preterm=. if adgest00==-.1
replace preterm=1 if adgest00 <=258
replace preterm=0 if adgest00 >258 & adgest00 <.
label define preterm 0 "no" 1 "yes"
label values preterm preterm
```

APPENDIX 4: EXPOSURE AND POTENTIAL CO-VARIATES, MILLENNIUM COHORT STUDY, UNITED KINGDOM 2000-2008

N=13,161	No.	%*
Mother heavy smoker (10+ cigarettes per day) during pregnancy	1,882	10.32
Mother light smoker (1-9 cigarettes per day) during pregnancy	2,333	12.80
Mother quit smoking during pregnancy	2,319	12.72
Mother's age at cohort member's (CM) birth <20 years	1,580	8.67
Mother completed GCSE qualification grades A-C at time of CM's birth	6,092	33.40
Mother ethnic minority	2,924	16.06
Mother was had no partner at time of CM's birth	1,747	9.60
Family stable since CM's birth	10,098	55.37
Below 60% median poverty at wave 1	6,429	35.25
Mother lived away from home/school before the age of 17**	2,515	13.81
Mother spent any time in care as a child	262	1.44
Maternal parents separated	5,216	28.60
Mother never sees own mother if alive	556	3.29
Mother never sees own father if alive	1,435	7.87
Mother has no time with friends (or reported having no friends)	5472	30.01
Mother has no-one to share feelings with	1590	9.02
Mother doesn't have other parents to talk to	4254	23.32
Life satisfaction	2,438	18.52
Partner perpetrated violence	344	2.61
Mother ever lived with more than one partner	4,885	28.30
Mother reports lacking parenting competence	385	2.11
Mother smacks child daily or weekly	119	0.90
Low sense of control	1,856	10.18
Usually gets what she wants out of life	12,947	73.50
Ever homeless (since the birth of the CM)	162	0.89
No phone	821	4.51
Very disorganised household	559	3.06
Mother depressed at first data collection wave, when CM was 9 months	1637	8.98
Currently depressed	1234	9.38
Currently treated for depression	1637	8.98
Regular heavy alcohol use (2+ per day)	5,635	30.92
Limiting long-term illness	1,803	9.89
Unplanned pregnancy	8,396	46.11
Late entry to antenatal care	695	3.81
Not attempted breast feeding	6,003	32.92
Incomplete immunisations	702	3.90
Postnatal smoking near the child	2,479	13.60
Low birth weight	1,231	6.75
Preterm delivery	1,468	8.05

*WEIGHTED PERCENTAGES

APPENDIX 5: MULTIVARIATE LOGISTIC REGRESSION MODELS, 7 YEAR OLDS, MILLENNIUM COHORT STUDY, UNITED KINGDOM, 2000-2008

```
. *final model conduct at 7

. xi:logistic sevrconduct i.pregsmok familystable sex oecdpoor matparent nofriend novisits lack
smack lowc
> ont getswant satisfife4 nophone vdishouse txdepress4 nonip smokenear
i.pregsmok      _Ipregsmok_0-3      (naturally coded; _Ipregsmok_0 omitted)

Logistic regression                                Number of obs   =    11181
                                                    LR chi2(19)    =    755.70
                                                    Prob > chi2    =    0.0000
Log likelihood = -3031.8429                        Pseudo R2      =    0.1108
```

sevrconduct	Odds Ratio	Std. Err.	z	P> z	[95% Conf. Interval]
_Ipregsmok_1	1.472986	.1473013	3.87	0.000	1.210813 1.791927
_Ipregsmok_2	1.7451	.1843928	5.27	0.000	1.418665 2.146649
_Ipregsmok_3	1.14179	.1226635	1.23	0.217	.9249985 1.409391
familystable	.7990732	.0617328	-2.90	0.004	.6867941 .929708
sex	1.621036	.1144022	6.84	0.000	1.411628 1.861508
oecdpoor	1.347318	.1057305	3.80	0.000	1.15524 1.571332
matparentsse-r	1.259055	.0924543	3.14	0.002	1.090284 1.45395
nofriendtime	1.171978	.0876775	2.12	0.034	1.012138 1.35706
novisits	1.370494	.1127178	3.83	0.000	1.166458 1.61022
lackcompetence	3.066001	.4218286	8.14	0.000	2.341325 4.014975
smack	7.488199	1.639091	9.20	0.000	4.875935 11.49997
lowcont	1.428115	.1404749	3.62	0.000	1.177703 1.731772
getswant	.8108123	.0646669	-2.63	0.009	.6934772 .9480003
satisfife4	.604873	.049865	-6.10	0.000	.5146264 .7109454
nophone	1.385119	.2021768	2.23	0.026	1.040501 1.843875
vdishouse	1.638451	.2157494	3.75	0.000	1.265751 2.120893
txdepress4	1.490887	.1453351	4.10	0.000	1.231594 1.80477
nonip	1.20309	.0901274	2.47	0.014	1.0388 1.393363
smokenear	1.419052	.12969	3.83	0.000	1.18633 1.697428
_cons	.068113	.009219	-19.85	0.000	.0522421 .0888054

```
. *final model hyper at 7

. xi:logistic sevrhyper i.pregsmok teenbirth lefthome sex oecdpoor noonefeeling lackcompetence smack
satis
> life4 satisfiedself vdishouse smokenear LBW
i.pregsmok      _Ipregsmok_0-3      (naturally coded; _Ipregsmok_0 omitted)

Logistic regression                                Number of obs   =    10829
                                                    LR chi2(15)    =    597.67
                                                    Prob > chi2    =    0.0000
Log likelihood = -3707.392                        Pseudo R2      =    0.0746
```

sevrhyper	Odds Ratio	Std. Err.	z	P> z	[95% Conf. Interval]
_Ipregsmok_1	1.271694	.1154136	2.65	0.008	1.064464 1.519267
_Ipregsmok_2	1.394338	.1394851	3.32	0.001	1.146084 1.696366
_Ipregsmok_3	1.155188	.1067953	1.56	0.119	.9637412 1.384666
teenbirth	1.44327	.1457619	3.63	0.000	1.18408 1.759195
lefthome	1.306031	.1074464	3.25	0.001	1.111541 1.534551
sex	2.117373	.1343746	11.82	0.000	1.869725 2.397823
oecdpoor	1.334633	.0934762	4.12	0.000	1.163442 1.531013
noonefeeling	1.554938	.1517753	4.52	0.000	1.284188 1.882772
lackcompetence	1.828801	.2547619	4.33	0.000	1.39184 2.402942
smack	3.007658	.6973078	4.75	0.000	1.909336 4.737776
satisfife4	.6617357	.0505976	-5.40	0.000	.5696394 .7687218
satisfiedself	.6631823	.0534746	-5.09	0.000	.5662363 .7767266
vdishouse	1.727294	.2088115	4.52	0.000	1.362904 2.18911
smokenear	1.401209	.1201336	3.93	0.000	1.184471 1.657605
LBW	1.695401	.1911914	4.68	0.000	1.359195 2.114769
_cons	.1106736	.0118243	-20.60	0.000	.089764 .1364538

APPENDIX 5: MULTIVARIATE LOGISTIC REGRESSION MODELS, 7 YEAR OLDS, MILLENNIUM COHORT STUDY, UNITED KINGDOM, 2000-2008

By sex, conduct problems, 7 year olds

```
. xi:logistic sevrconduct i.pregsmok familystable oecdpoor matparent nofriend novisits lack smack
lowcont getswant satisfife4 nophone vdishouse txdepress
> 4 nonip smokenear if sex==1
i.pregsmok      _Ipregsmok_0-3      (naturally coded; _Ipregsmok_0 omitted)

Logistic regression              Number of obs   =    18261
                                LR chi2(18)     =    1261.30
                                Prob > chi2      =    0.0000
Log likelihood = -5743.5293      Pseudo R2      =    0.0989
```

sevrconduct	Odds Ratio	Std. Err.	z	P> z	[95% Conf. Interval]
_Ipregsmok_1	1.617784	.1140024	6.83	0.000	1.409087 1.857391
_Ipregsmok_2	1.776051	.1362995	7.48	0.000	1.528029 2.06433
_Ipregsmok_3	1.067869	.0843646	0.83	0.406	.9146834 1.24671
familystable	.794462	.0442462	-4.13	0.000	.7123065 .886093
oecdpoor	1.293333	.0730489	4.55	0.000	1.1578 1.444731
matparentssepar	1.193368	.0634306	3.33	0.001	1.075303 1.324397
nofriendtime	1.170965	.0624925	2.96	0.003	1.05467 1.300083
novisits	1.2511	.0751592	3.73	0.000	1.112132 1.407432
lackcompetence	3.342209	.3359493	12.00	0.000	2.744563 4.069996
smack	8.009554	1.192286	13.98	0.000	5.98274 10.723
lowcont	1.209617	.0896378	2.57	0.010	1.046093 1.398703
getswant	.8171328	.0475646	-3.47	0.001	.7290293 .9158837
satisfife4	.5807102	.0346074	-9.12	0.000	.5166924 .6526597
nophone	1.316709	.1411231	2.57	0.010	1.067232 1.624502
vdishouse	1.384354	.1360956	3.31	0.001	1.141736 1.678528
txdepress4	1.384351	.100687	4.47	0.000	1.200429 1.596453
nonip	1.237284	.0663432	3.97	0.000	1.113853 1.374393
smokenear	1.408094	.0944284	5.10	0.000	1.234665 1.605884
_cons	.125962	.0117782	-22.16	0.000	.104869 .1512976

```
. xi:logistic sevrconduct i.pregsmok familystable oecdpoor matparent nofriend novisits lack smack
lowcont getswant satisfife4 nophone vdishouse txdepress
> 4 nonip smokenear if sex==0
i.pregsmok      _Ipregsmok_0-3      (naturally coded; _Ipregsmok_0 omitted)

Logistic regression              Number of obs   =    17841
                                LR chi2(18)     =    1037.88
                                Prob > chi2      =    0.0000
Log likelihood = -4058.129      Pseudo R2      =    0.1134
```

sevrconduct	Odds Ratio	Std. Err.	z	P> z	[95% Conf. Interval]
_Ipregsmok_1	1.1783	.1090847	1.77	0.076	.9827736 1.412728
_Ipregsmok_2	1.675633	.1535998	5.63	0.000	1.400077 2.005422
_Ipregsmok_3	1.209012	.1115028	2.06	0.040	1.009084 1.448551
familystable	.8423748	.0575942	-2.51	0.012	.7367288 .9631704
oecdpoor	1.295123	.088107	3.80	0.000	1.133454 1.479851
matparentssepar	1.401114	.0903079	5.23	0.000	1.234837 1.58978
nofriendtime	1.191228	.0782948	2.66	0.008	1.047246 1.355006
novisits	1.519366	.1069226	5.94	0.000	1.323612 1.744071
lackcompetence	2.495572	.3027286	7.54	0.000	1.967497 3.165383
smack	7.089205	1.528281	9.09	0.000	4.646187 10.81679
lowcont	1.655289	.1350719	6.18	0.000	1.410638 1.94237
getswant	.7203997	.0489671	-4.82	0.000	.6305443 .8230599
satisfife4	.610211	.043597	-6.91	0.000	.5304754 .7019317
nophone	1.454571	.1794319	3.04	0.002	1.142176 1.852408
vdishouse	1.857376	.2107019	5.46	0.000	1.487096 2.319854
txdepress4	1.556333	.1300303	5.29	0.000	1.321251 1.833241
nonip	1.27226	.0836923	3.66	0.000	1.11836 1.447338
smokenear	1.550793	.1198458	5.68	0.000	1.332824 1.804409
_cons	.0638083	.0070296	-24.98	0.000	.0514165 .0791865

APPENDIX 5: MULTIVARIATE LOGISTIC REGRESSION MODELS, 7 YEAR OLDS, MILLENNIUM COHORT STUDY, UNITED KINGDOM, 2000-2008

By sex, hyperactivity, 7 year olds

```
. xi:logistic sevyrhyper i.pregsmok teenbirth lefthome sex oecdpoor noonefeeling lackcompetence smack
satislife4 satisfiedself vdishouse smokenear LBW if s
> ex==1
i.pregsmok      _Ipregsmok_0-3      (naturally coded; _Ipregsmok_0 omitted)
note: sex omitted because of collinearity
```

```
Logistic regression      Number of obs      =      17586
                        LR chi2(14)      =      879.30
                        Prob > chi2      =      0.0000
                        Pseudo R2       =      0.0569

Log likelihood = -7292.7829
```

sevyrhyper	Odds Ratio	Std. Err.	z	P> z	[95% Conf. Interval]
_Ipregsmok_1	1.401496	.0864003	5.48	0.000	1.241986 1.581493
_Ipregsmok_2	1.257392	.090194	3.19	0.001	1.092479 1.447199
_Ipregsmok_3	1.039856	.0692535	0.59	0.557	.9126068 1.184847
teenbirth	1.282943	.0932375	3.43	0.001	1.112619 1.47934
lefthome	1.595304	.0897089	8.31	0.000	1.428821 1.781186
sex	1	(omitted)			
oecdpoor	1.308513	.0647422	5.43	0.000	1.187579 1.441762
noonefeeling	1.404819	.0972314	4.91	0.000	1.226609 1.608919
lackcompetence	1.977919	.1959541	6.88	0.000	1.628844 2.401806
smack	3.528504	.5321804	8.36	0.000	2.625486 4.74211
satislife4	.6486466	.0349794	-8.03	0.000	.583587 .7209593
satisfiedself	.7283401	.0427231	-5.40	0.000	.6492386 .8170792
vdishouse	1.647267	.1413626	5.82	0.000	1.392249 1.948997
smokenear	1.345755	.0830395	4.81	0.000	1.192457 1.51876
LBW	1.567554	.1308004	5.39	0.000	1.331056 1.846073
_cons	.2268415	.0160783	-20.93	0.000	.1974196 .2606482

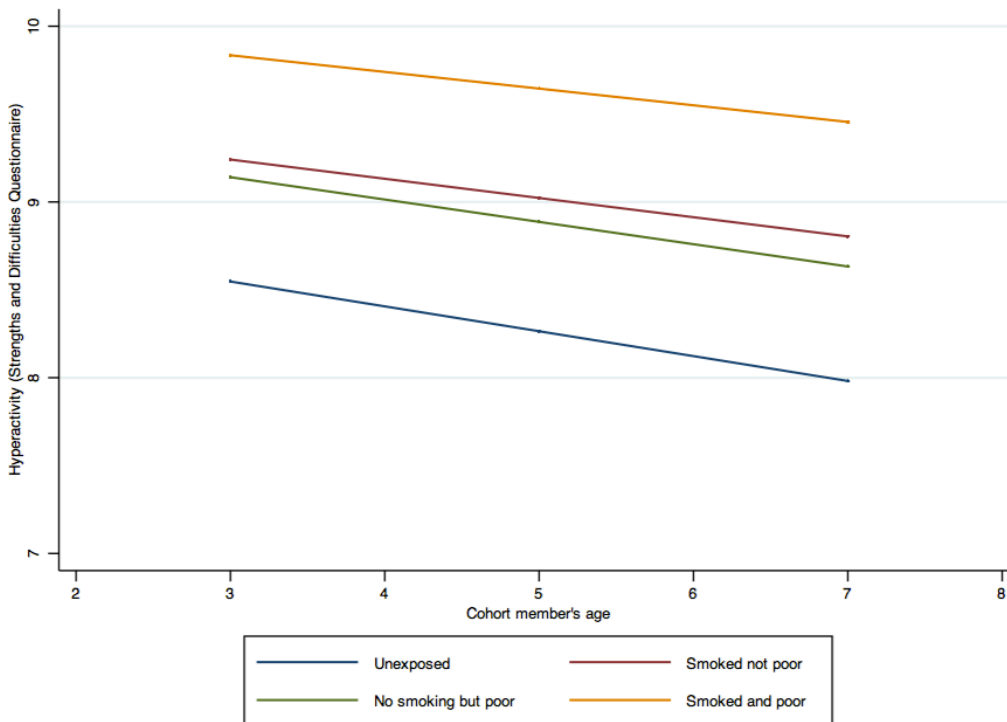
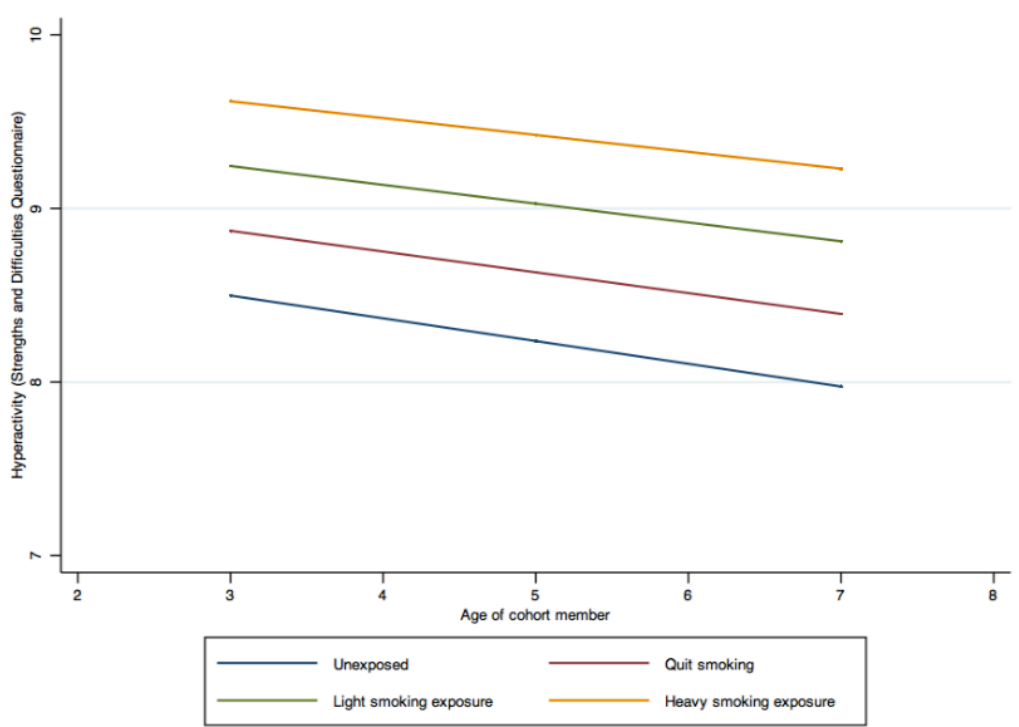
```
. xi:logistic sevyrhyper i.pregsmok teenbirth lefthome sex oecdpoor noonefeeling lackcompetence smack
satislife4 satisfiedself vdishouse smokenear LBW if s
> ex==0
i.pregsmok      _Ipregsmok_0-3      (naturally coded; _Ipregsmok_0 omitted)
note: sex omitted because of collinearity
```

```
Logistic regression      Number of obs      =      17292
                        LR chi2(14)      =      572.43
                        Prob > chi2      =      0.0000
                        Pseudo R2       =      0.0579

Log likelihood = -4656.9496
```

sevyrhyper	Odds Ratio	Std. Err.	z	P> z	[95% Conf. Interval]
_Ipregsmok_1	1.212655	.1062003	2.20	0.028	1.02139 1.439735
_Ipregsmok_2	1.656265	.1483195	5.63	0.000	1.389646 1.974037
_Ipregsmok_3	1.483075	.1195419	4.89	0.000	1.266347 1.736894
teenbirth	1.556724	.1417774	4.86	0.000	1.302234 1.860947
lefthome	.9068699	.0741115	-1.20	0.232	.7726501 1.064405
sex	1	(omitted)			
oecdpoor	1.329307	.0851065	4.45	0.000	1.172543 1.507031
noonefeeling	1.695518	.1492401	6.00	0.000	1.426853 2.01477
lackcompetence	1.778541	.2218933	4.62	0.000	1.392729 2.271229
smack	2.085349	.5653385	2.71	0.007	1.225795 3.547641
satislife4	.6543812	.0448979	-6.18	0.000	.5720433 .7485705
satisfiedself	.6477287	.046689	-6.02	0.000	.5623901 .7460168
vdishouse	1.709861	.1917905	4.78	0.000	1.37241 2.130286
smokenear	1.561649	.117846	5.91	0.000	1.346944 1.810578
LBW	1.782013	.1684572	6.11	0.000	1.480626 2.14475
_cons	.1099367	.0098699	-24.59	0.000	.0921985 .1310876

APPENDIX 6: TRAJECTORIES OF CHILD HYPERACTIVITY, DIFFERENTIALLY EXPOSED TO MATERNAL SMOKING DURING PREGNANCY AND FAMILY POVERTY, MILLENNIUM COHORT STUDY, UNITED KINGDOM, 2000-2008



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