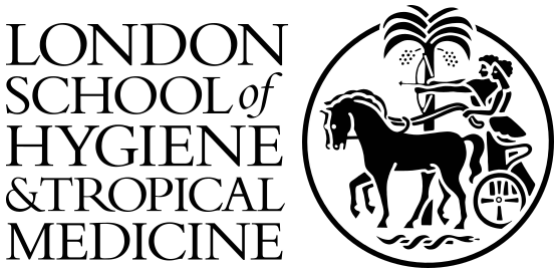

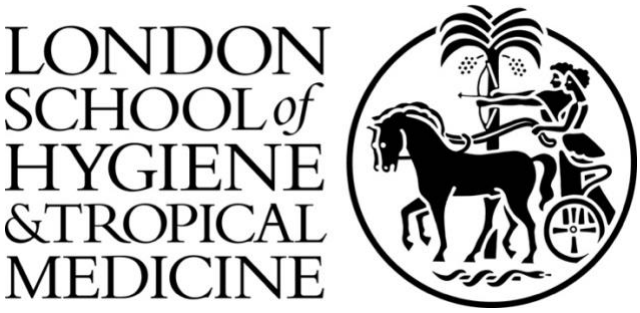

A STUDY OF RISK FACTORS OF MATERNITY OUTCOMES USING LARGE, ROUTINELY-COLLECTED ELECTRONIC DATASETS

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Thesis submitted in accordance with the requirements for the degree of Doctor of Philosophy of the University of London

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Funding: Healthcare Quality Improvement Partnership

Declaration by candidate

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Abstract

Background In the UK, almost all maternity care (>99% of births) is delivered via the National Health Service, which serves a varied population (approximately 22% from ethnic minority groups) according to a set of agreed standards and guidelines with common training pathways for maternity professionals. This makes the UK a useful high-income context in which to investigate maternity care and outcomes. Increasing availability of electronic health record data for women giving birth has made it possible to understand risk factors for adverse outcomes and the impacts of policy change in maternity care more closely. Furthermore, there is growing attention to ethnic and socioeconomic inequalities in outcomes of maternity care. The overall aim of this thesis is to demonstrate how data collected during maternity care can be used to understand determinants of maternity outcomes. In particular, I look at the association between women's socioeconomic and ethnic background and their maternity outcomes.

Methods In this thesis, observational epidemiological studies using national patient-level datasets address four related issues in maternity care in England and Wales. First, the quality of coding of ethnicity is evaluated in a cross-validation study comparing two sources of ethnicity data for women giving birth. Second, risk factors for adverse pregnancy outcomes (postpartum haemorrhage, maternal intensive care admission, and preterm birth) are examined using multivariable logistic regression models adjusting for clinical risk factors and care received. Third, the performance of the risk-classification system used to determine women's choice of birthplace, using the National Institute for Care Excellence guideline for Intrapartum Care, is evaluated by calculating the proportion of women in each risk group who experience a complicated birth requiring obstetric or neonatal assistance. Fourth, the proportion of adverse pregnancy outcomes (stillbirth, preterm birth, and fetal growth restriction) attributable to socioeconomic and ethnic inequality is estimated using population attributable fractions.

Results First, cross-validation of ethnicity data between datasets supports the use of ethnicity collapsed into groups, with caution over results for women with mixed ethnicity, for whom the most inconsistencies are observed. Second, studies examining risk factors for severe

maternal morbidity (maternal intensive care admission and postpartum haemorrhage) demonstrate evidence that these outcomes are more common for Black women than women from other ethnic groups; this association persists following adjustment for clinical characteristics and differences in care given. Furthermore, detailed evaluation of risk factors for preterm birth demonstrates that different groups of women experience iatrogenic (provider-initiated) and spontaneous preterm birth, and these should be measured separately. Third, giving more weight to parity and history of previous caesarean improves the risk assessment of women giving birth at term in comparison to currently used classification methods. Finally, ethnic and socioeconomic inequalities are responsible for a substantial proportion of stillbirths, preterm births and babies born with fetal growth restriction; while socioeconomic inequalities are partially attenuated by adjustment for the modifiable maternal risk factors BMI and smoking, ethnic inequalities are not.

Conclusions Increasing availability of clinical data have made it possible to evaluate maternity care in more depth, demonstrating lessons for clinical risk assessment and care, avenues for further research development, and potential targets for political and public health interventions to improve the health and circumstances of women before and during pregnancy. As electronic records become more widespread and comprehensive, the quantity and sophistication of questions it will be possible to answer will expand, encompassing a wider reach of women's healthcare before, during and after birth. This thesis demonstrates that such data, if handled carefully, can support our understanding of individual risk factors, risk classification, and healthcare systems and policy, and be used to develop recommendations to improve both healthcare policy and clinical care for women and their families.

Acknowledgements

Firstly, I would like to thank my supervision team, Kate Walker, Jan van der Meulen, and Dharmintra Pasupathy, who have been unfailingly supportive and patient through what has been a long journey of iterative understanding, interrupted by maternity leave and the pandemic. They have challenged me to consider my statements, deepen and widen my knowledge and conduct research with methodological rigour and constant self-critique. I count myself lucky to have had the opportunity to work with them and hope to do so again the future.

I am indebted to the colleagues I have worked with throughout the studies in this thesis and particularly to the NMPA Project Team members past and present. I have learnt an enormous amount from working in this multidisciplinary team. I would particularly like to thank Ipek Gurol-Urganci, Hannah Knight and David Cromwell, for methodological advice and providing the foundations on which much of this work is built; Andrea Blotkamp, Fran Carroll, Lindsey Mamza and Natalie Moitt, for company through the seemingly endless weeks of data cleaning and report writing in the early days of the project; and Sophie Relph, Harriet Aughey, Jane Hawdon, Tina Harris and Asma Khalil for providing inspiration and insights and challenging me to knock my thoughts into shape.

The RCOG have provided a unique environment in which to conduct a PhD and I am grateful to have had the opportunity to work at the College and understand the way in which it works to improve women's health.

Finally, I would like to thank my family: my husband Jon, who has provided endless support, advice, sympathy, childcare, and food; and our son Nathaniel, my closest companion for much of this thesis, who in reproducing many aspects of my own personality has taught me how to handle myself with more understanding. I look forward to listening more and typing less in my time with them.

Abbreviations and definitions

Apgar score	A five-component score that is used to summarise the health of a newborn baby, typically at 1, 5 and 10 minutes of age.
BMI	Body mass index, defined as an individual's weight in kilograms divided by their height in metres squared.
CTG	Cardiotocography, a device used to measure fetal heart rate and uterine activity in labour
FGR	Fetal growth restriction, indicated by a baby born with a birthweight below the 3rd centile
HES	Hospital Episode Statistics, an administrative database of hospital admissions in England
IMD	Index of Multiple Deprivation, a measure of neighbourhood socioeconomic deprivation
ICNARC	Intensive Care National Audit and Research Centre
Instrumental birth	Birth with the assistance of either a ventouse cup or forceps.
MBRRACE-UK	Mothers and babies: Reducing Risk through Audits and Confidential Enquiries across the UK; the collaboration which conducts surveillance and investigates the causes of maternal deaths, stillbirths and infant deaths.
Midwife-led unit	A birth setting which is led by midwives with no obstetric presence
MIds	Maternity Indicators dataset, the national maternity dataset for Wales
MIS	Maternity Information System(s), computer systems used to impute data about maternity care
NHS	National Health Service
NMPA	National Maternity and Perinatal Audit
OASI	Obstetric anal sphincter injury. A tear from childbirth that extends into the anal sphincter (third degree tear) or mucosa (fourth degree tear).
Parity	The number of previous registerable births a woman has had.
PEDW	Patient Episode Dataset for Wales, an administrative database of hospital admissions in Wales
Perinatal	Related to events around the time of birth
PPH	Postpartum haemorrhage, excess blood loss after birth
RCOG	Royal College of Obstetricians and Gynaecologists.
Registerable birth	In UK law, a birth is registrable, meaning it will be recorded in national statistics and issued with a certificate of birth or stillbirth, if the baby is born without signs of life after 24 completed weeks of gestation or with signs of life at any gestation.
SGA	Small for gestational age, indicated by a baby born with a birthweight below the 10th centile
Stillbirth	The birth of a baby without signs of life at or after 24 weeks of gestation.
Term gestation	Gestation of 37+0 weeks or more

1. Introduction

This PhD encompasses six observational studies which all use electronic health record data to understand determinants of, and inequalities in, maternity outcomes in England and Wales between 2015-17. In this introduction, I will first explain why studies such as these are of value in maternity care. I will then describe maternity services in England and Wales, the women accessing maternity care, and how quality of maternity care is measured. I will then introduce the background for specific topics of study, including measuring maternity outcomes, and ethnic and socioeconomic inequalities in maternity care. In this way, I will set the stage for the research design presented in Chapter 2.

1.1 Observational research in maternity care

Pregnancy and birth are physiological processes that happen to women who are, for the most part, healthy. The most common outcome is a healthy mother and baby. Many complications of pregnancy and birth are avoidable with good antenatal, intrapartum and postnatal care (1). There remains substantial variation in maternity outcomes across and between nations (2,3). The challenge of providing good and consistent maternity care is multifaceted and encompasses not only the challenges experienced in delivering good healthcare generally, but also the difficulties in defining what constitutes the best possible maternity care and identifying women at 'high risk' of adverse outcomes.

Maternity care has evolved to preserve the life of mothers and infants, much of it prior to the advent of evidence-based medicine (4). Most obstetric interventions were therefore introduced in the absence of an evidence base from clinical trials, through a philosophy of continuous improvement. Many of the most critical interventions continue to lack a robust evidence base for their intended effect or clear indications for their use. For example, continuous electronic fetal monitoring with cardiotocography (CTG) has uncertain benefit for the reduction of neonatal brain injury but is nonetheless widely used (5,6). While most interventions such as the induction of labour, caesarean section and instrumental birth have a definite benefit, they may also cause harm, with possible long-term consequences for both the mother and infant. The 'ideal' rates of these interventions are therefore much-debated.

Observational studies using large datasets offer a useful opportunity to evaluate determinants of adverse outcomes, establish accurate risk assessment, and understand variation in those outcomes, including inequalities. Studies such as these have been described as types of prognosis research, namely "fundamental prognosis research" and "prognostic factor research" (7,8). In fundamental prognosis research, rates of events are described, including variations and inequalities in those rates (7). In prognostic factor research, relationships between prognostic factors ("any measure that among people with a given startpoint is associated with a subsequent endpoint") and outcomes are evaluated (8). Large datasets allow development of prognosis studies to examine rare outcomes and to better understand the drivers behind common complications of pregnancy and birth (9,10).

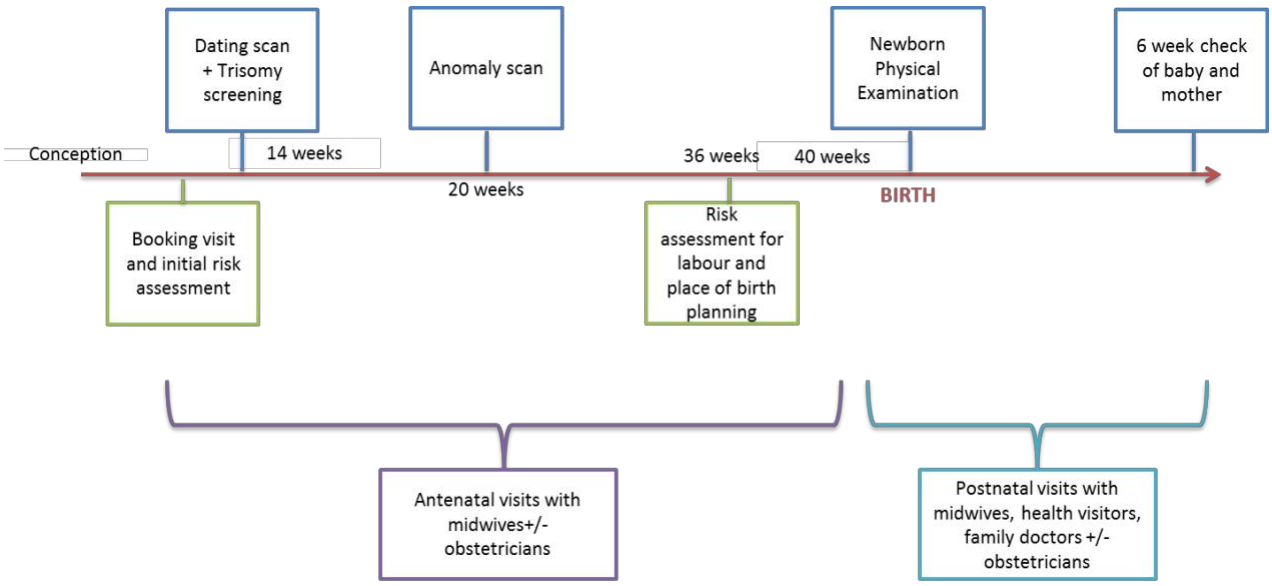
1.2 Maternity services in England and Wales

Almost all women in the UK have their pregnancy and birth care delivered through the National Health Service; only 0.3% of births in England and Wales in 2020 occurred in non-NHS organisations (11). Care provided in the NHS follows a set of agreed standards and guidelines, with common training pathways for maternity professionals. The population served is varied with approximately 22% of women from an ethnic minority group (12).

The primary contact point for most women in the antenatal period is a midwife or midwifery team, who may be based in the community or more commonly in a hospital. For women considered at higher risk of complications, this care is shared with obstetricians, and sometimes with other medical specialists (for example, endocrinologists).

All women are offered a minimum of 7 (in multiparous women) or 10 (in primiparous women) antenatal visits with a health care provider, and at least two scans: a dating scan which also offers screening for some abnormalities at between 11- and 13-weeks' gestation; and a detailed anomaly scan at 18-21 weeks' gestation (13) [Figure 1.1].

Figure 1.1 Schedule of routine antenatal care in England and Wales



During labour, all women are cared for primarily by a midwife, with care shared with a multidisciplinary team as required; this team may include obstetricians, anaesthetists, physicians, nurses, and other clinical and non-clinical staff. While labour is a physiological process, best outcomes are achieved when there is a degree of intervention offered. The most important intervention is the presence of a trained midwife or other skilled birth attendant (14). Other interventions, may provide improved comfort (analgesia, including the provision of epidurals by anaesthetists) or safety in the birth (induction of labour, augmentation of labour, caesarean section, instrumental birth, typically delivered by obstetricians). Over time, the level of intervention typically practiced in obstetrics has risen in the UK and across the world (15), driven by demographic changes but also a shifting culture of practice towards risk avoidance. This has led to harm, particularly for the increasing number of women with repeated caesarean births who are at increased risk of serious complications in future pregnancies. Increasing use of intervention may be associated with poorer experiences and perceived loss of agency for women giving birth (16).

Care during labour can be delivered in one of four settings: the woman's home, a freestanding midwife-led unit (FMU); a midwife-led unit co-located with an obstetric unit (alongside

midwifery unit, AMU); and an obstetric unit (OU). The choice of setting is determined by maternal choice with counselling from the care provider based on the estimated clinical risk at the onset of labour; maternal choice and agency can however be constrained by eligibility criteria for midwifery-led birth settings (17). In an obstetric unit, the full range of care services, including emergency procedures and the provision of anaesthesia, is available. In midwifery-led units, care is limited to that which is provided by midwives. Giving birth in midwifery led settings (midwifery led units or home) has been proven to be associated with a lower rate of interventions, while being safe for women at low risk of complications (18). The configuration of these services in England and Wales is described in Figure 1.2, and the care delivered in each setting and typical eligibility criteria is described in Table 1.1.

of maternity services by country in England and Wales in 2017 (adapted with permission from the NMPA organisational survey 2017 (19))

	ENGLAND	WALES
 TRUST/BOARD	134 trusts	7 boards
 SITE	106 OU+AMU 51 OU only 63 FMU only	12 OU+AMU 14 FMUs (0 OU only)
 MATERNITY UNIT	157 OUs 106 AMUs 63 FMUs	12 OUs 12 AMUs 14 FMUs

KEY	
trust/board	administrative organisation encompassing one or more sites on which maternity (and other health) services are delivered
site	location at which health services are delivered, which may encompass one or more units
maternity unit	setting in which maternity care is delivered
OU	obstetric unit
AMU	alongside midwifery-led unit (collocated with obstetric unit)
FMU	freestanding midwifery-led unit (on separate site from any OU)

Table 1.1. Types of maternity unit and typical eligibility criteria.

Birthplace	Obstetric-led unit	Midwife-led unit	Home birth
Setting	Hospital	Co-located with obstetric unit (alongside midwife-led unit) or freestanding	Woman's own home
Monitoring available	Continuous monitoring with cardiotocography (CTG) or intermittent monitoring	Intermittent monitoring with Pinard or doppler	Intermittent monitoring
Analgesia available	Epidural, injectable opiates, tablets, Entonox	Injectable opiates, tablets, Entonox, water	Injectable opiates, tablets, Entonox, water
Staff available	Midwifery, obstetrics, anaesthetics, neonatal	Midwifery If alongside, easy access to other staff members in emergencies	Midwifery
Typical eligibility	All women	Women considered at low risk of complications†; in some units, women with specific risk factors (e.g. maternal age, or obesity) and no other risk factors	Women considered at low risk of complications†; however, all women can request assistance at a home birth
†Risk of complications is typically evaluated according to National Institute for Health and Care Excellence (NICE) Guideline 190: Intrapartum care for healthy women and babies (17)			

Postnatal care is provided through community midwifery teams, supplemented by health visitors and, if there have been complications at the birth, follow up visits at the hospital with obstetric teams. Routine postnatal screening for fetal abnormalities is performed at the Newborn Physical Examination between 6 and 72 hours of life, and at six weeks of age by general practitioners. All women are offered a postnatal appointment between six to eight weeks postpartum in primary care with a GP.

Much of the process of maternity care, including the number of appointments offered and the choices available to women about their place of birth, is established by a series of clinical risk assessments. While some of these, notably the one for venous thromboembolism (20,21), have an underlying evidence base, most are based on a binary evaluation of the presence or absence of risk factors decided by clinical consensus. There has been no formal evaluation of

how accurately the risk assessment used across England, recommended in the NICE Intrapartum Care Guideline (17) predicts clinical risk of adverse birth outcomes.

1.2.1 Policy and practice changes

Maternity care in England and Wales is currently high on the political and policy agenda, in all four nations. The National Maternity Review published in England in 2015 led to a Maternity Transformation Programme (MTP) to implement the recommendations of its report, "Better Births"; initially commissioned for five years from 2016, it has now been extended to 2025 (22). The aims of this programme are to improve quality of care, safety, continuity of care and maternal choice through funded workstreams which deliver guidance and intervention to maternity units across England. In particular, the MTP seeks to work to deliver the ambition in England to halve the rates of stillbirths, neonatal mortality, brain injury and maternal mortality by 2025.

In Wales, a five-year vision for maternity services was published in 2019 (23); similarly to the plan in England, this focuses on goals for safety, quality, choice, and continuity of carer.

Alongside this drive for higher-quality, safer care with more choice and personalisation, there have also been recent legal changes (Montgomery v. Lanarkshire Health Board) which support the provision of more detailed information about risks of treatment options to women giving birth (24).

1.3 Women receiving maternity care

The fertility rate (the number of children each woman would have if she lived until the end of her childbearing years) has fluctuated between 1.6 and 1.9 since the mid-1970s, following the introduction of the abortion act in 1968 and widespread access to the oral contraceptive pill from the late 1960s (25). However, the population of women receiving maternity care has radically shifted over time. The average age of women giving birth has risen steadily since the 1970s (25) and the prevalence of maternal obesity in the first trimester has increased from 7.6% in 1989 to 15.6% in 2007 and then to 22.1% by 2016/17 (12,26). Furthermore, the population of women giving birth is also influenced by general population trends. The

proportion of the population that is from an ethnic minority group or was born outside the UK has been increasing steadily, and was 14.1% in the 2011 census compared to 8.8% in the 2001 census, with numbers expected to be higher in the published results for the 2021 census (27). Socioeconomic inequality in the UK rose rapidly in the 1980s and has stayed high relative to other European countries (28).

These changes to the population of women giving birth have contributed to increases in the prevalence of comorbidities such as gestational diabetes, and an increase in the caesarean section and induction of labour rate (29,30). There has also been an increase in interventions with the purpose of improving outcomes, for example an increase in the indications for caesarean birth (24), and an increased use of induction to reduce stillbirth rates (31,32). Together, these changes in both the care given and the population of women giving birth have led to an increase in the rates of caesarean section and induction of labour. This means that more women require more complex care, including direct obstetric care and the involvement of other doctors, as well as additional skills from midwifery professionals. Over time, this increase in intervention has also resulted in a shift in the outcomes of pregnancy, with for example changes in birthweight distribution due to intervention for babies suspected of being small for their gestational age (33) and a decrease in rates of stillbirth (11).

1.4 Measuring the quality of maternity care

In England and Wales, several initiatives exist to measure the quality of maternity care. These include: MBRRACE (Mothers and Babies: Reducing Risk through Confidential Enquiries), which investigates maternal and perinatal deaths; UKOSS (the UK Obstetric Surveillance System) which investigates severe obstetric morbidity; and the NMPA (National Maternity and Perinatal Audit), which was established in 2016 and uses electronic health record data to measure processes and outcomes of maternity and newborn care in order to drive quality improvement (12,34,35). This PhD was hosted within the NMPA.

The NMPA is an initiative commissioned by the Healthcare Quality Improvement Partnership (HQIP) and funded by the English, Scottish and Welsh governments. It is led by the RCOG together with the Royal College of Midwives (RCM), the Royal College of Paediatric and Child

Health (RCPCH), and LSHTM. The project is hosted by the RCOG. The NMPA uses quality indicators to measure the care received by women giving birth in Britain.

1.5 Outcomes in maternity care

This thesis considers a number of outcomes of maternity care, chosen for analysis from a list developed in a prioritisation exercise conducted by the National Perinatal Epidemiology Unit in 2014 and refined by the NMPA Project Team (36).

In maternity care, what constitutes an 'outcome' may differ in different situations. The most clinically robust outcomes are maternal death and stillbirth, but these are rare in high-income countries, which can mean that statistical comparisons between groups lack power. In this thesis, I examine determinants of, and inequalities in, maternity outcomes, in particular:

(1) Maternal admission to intensive care
(2) Postpartum haemorrhage of 1500ml or more
(3) Preterm birth
(4) Stillbirth
(5) Fetal growth restriction (birthweight <3rd centile)
(6) Complicated birth, a composite measure of caesarean section, instrumental birth, obstetric anal sphincter injury, postpartum haemorrhage of 1500ml or more, or neonatal Apgar score[1] less than 7 at 5 minutes of age

By examining the determinants of and inequalities in maternity outcomes it is possible to understand drivers of adverse outcomes and identify groups at higher risk, as well as potentially modifiable aspects of care which may enable clinical recommendations to improve maternity outcomes.

Maternal outcomes chosen for examination in this thesis focus on aspects of severe maternal morbidity (37,38), sometimes described as 'near-miss' maternal morbidity. The two specific

[1] Apgar score is a standardised scoring system (out of 10) for infants after birth, typically measured at 1, 5, 10 minutes of age, which combines information about the baby's breathing, heart rate, tone, skin colour and reflexes. It usually signifies the need for short term neonatal assistance, has a correlation with the baby's likelihood of long-term adverse outcomes (45).

outcomes chosen were postpartum haemorrhage (PPH) and intensive care admission. PPH is associated with substantial maternal morbidity and remains a leading cause of maternal mortality in the UK and around the world (35,39). The data in this thesis from electronic maternity records offered a unique opportunity to measure PPH on a national scale and examine different cut offs, as recording of estimated blood loss at birth was highly complete (12). Maternal intensive care admission is a marker of requiring the additional care provided in an intensive care unit and therefore of severe maternal illness.

Fetal and neonatal outcomes in this thesis include stillbirth, preterm birth and fetal growth restriction. Stillbirth, sometimes described as fetal death, is the death of a fetus in utero after the threshold of viability, defined in the UK as 24+0 weeks gestation (11). Preterm birth is the birth of a live baby before term, or 37+0 weeks gestation (11) and is associated with short- and long-term sequelae for babies including increased infant mortality, healthcare need and poorer school performance (40). In England, there is a national target to reduce stillbirth by 50% and preterm birth by 25% between 2019 and 2025 respectively (41). Fetal growth restriction is the birth of a baby with a birthweight less than the 3rd centile, defined by a growth chart which includes babies at that gestation (in these studies I have used birthweight charts referenced by paediatricians, which apply WHO standards to UK data (42)), and is also associated with adverse short- and long-term health sequelae for babies (43,44).

Outcomes need to be relevant to the question being studied. To examine the effectiveness of a risk classification system for women giving birth, this thesis uses a composite outcome of 'complicated birth' incorporating any of: caesarean section, instrumental delivery, postpartum haemorrhage of 1500ml or more, obstetric anal sphincter injury, or neonatal compromise measured by an Apgar score of less than 7 at 5 minutes. An Apgar score is a measure of the baby's condition commonly evaluated at 1, 5 and 10 minutes of age; a score of less than 7 is associated with subsequent increased risk of infant morbidity and mortality (45). These components of the outcome encompass the most common reasons for needing obstetric or neonatal medical assistance at the time of birth, and therefore are clinically relevant to counselling women regarding their choice of birthplace (34,45–48).

1.6 Ethnic and socioeconomic inequalities in maternity care in England and Wales

1.6.1 Inequalities in health in England and Wales

Inequalities in health are defined by the King's Fund as "*avoidable, unfair and systematic differences in health between different groups of people*" (46). Health inequalities can include differences in life expectancy and health status, access to care, quality of care, experience of care, health behaviours (such as smoking and nutrition) and wider determinants of health, such as safe employment and good-quality housing (46,47). Health inequalities can be determined by many factors, with four commonly cited:

(1) Socioeconomic factors, such as income and employment
(2) Geographical factors, such as urban or rural location, or region
(3) Specific individual characteristics, including ethnicity, sex or gender, sexual orientation, disability
(4) Socially excluded groups, sometimes called 'inclusion health' groups such as homeless people, migrants, sex workers, or prisoners (48)

Inequalities may broadly be attributed to: social and cultural factors, for example, structural racism, access to healthcare, and religious and health beliefs; lifestyle factors, including diet, exercise, and alcohol; economic factors, including insecure employment and income; public health measures, including programmes targeting smoking and obesity; and environmental factors, including housing and pollution (46,47,49).

In the UK, healthcare is universally provided free at the point of access by the NHS as part of a broader system of social insurance and support, the welfare state, established by the Labour government elected after the Second World War and in line with similar initiatives implemented across Europe in the first half of the 20th century (50). The overall aim of these institutions is to promote social and economic well-being, and to enable individuals from all sectors of society to flourish. However, despite the existence of the welfare state, research and policy documents have consistently demonstrated wide-ranging inequalities in health.

The UK, like other developed nations, has a long history of reporting socioeconomic inequalities in health (51–56). The Black report in 1980 (57) demonstrated that the death rate for men in the lowest social class was twice that for men in the highest social class, and that

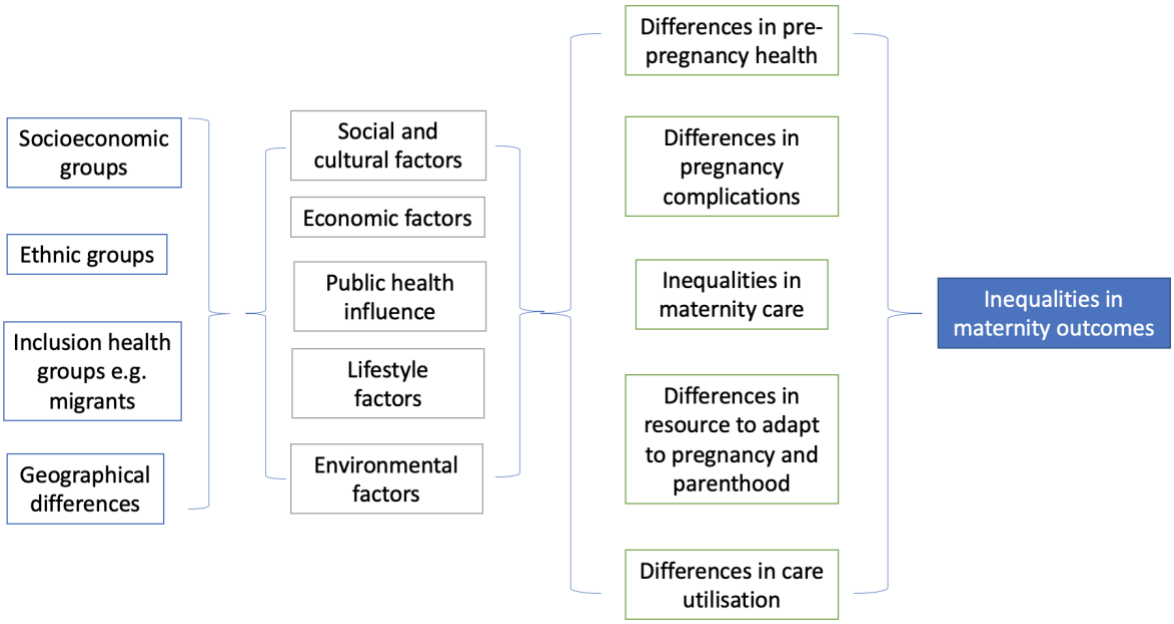
this gap was widening. The Acheson report in 1998 echoed these findings by demonstrating that individuals in higher social classes had disproportionately benefitted from overall trends of prolonged life expectancy between 1970 and 1990 (58). The Marmot review in 2010 demonstrated similarly extensive inequalities (47), and the ten year follow up study in 2020 showed that the situation had deteriorated, and the policies of austerity followed by the UK government since 2010 had led to a decline in life expectancy which was particularly prominent in young socially deprived women living in the North of England (59).

There is also sustained evidence of ethnic inequality in morbidity and mortality in the UK (60–64). Factors underlying this are undoubtedly tied to ethnic differences in socioeconomic deprivation; however, cultural factors, behavioural factors, biological factors, and structural racism are all considered to play a role (62). There also is evidence that care inequality also plays a substantial role, as the NHS provides poorer care to ethnic minority groups: examples exist across the health system, including access to joint replacement (65), cancer diagnosis and care (66,67), and appropriate escalation of diabetes treatment in primary care (68). It is unknown how these factors interact and which is most responsible for observed inequalities between ethnic groups.

1.6.2 Inequalities in maternity care in the UK

While overall inequalities in health are primarily measured in age at disability and death, such inequality also affects women of childbearing age. Women from socioeconomically deprived areas and ethnic minority groups are more likely to enter pregnancy in poorer health or with adverse health behaviours (69), to develop pregnancy related complications such as gestational diabetes (70,71), and experience poorer maternity care during pregnancy and birth (72–74). This leads, together with the pathways discussed above, to inequalities in maternity outcomes. Some of the factors underlying these inequalities are summarised in Figure 1.3; for simplicity, this figure does not attempt to explicate the interconnected relationships between those factors, which are complex and often poorly understood.

Figure 1.3. Summary structure of determinants of inequalities in maternity outcomes.



This is reflected in the evidence: studies of maternal and perinatal morbidity and mortality in the UK have consistently revealed substantial evidence of inequalities in outcomes for women from socioeconomically deprived and/or ethnic minority groups: in maternal morbidity and mortality, and in perinatal mortality (34,35,75–79). In the 2016-18 triennium, rates of maternal mortality in the UK were almost four times higher for women from Black ethnic groups and almost two times higher for women from south Asian ethnic groups when compared to white women (35); in 2018, women living in the most deprived of areas in the UK had a risk of perinatal death 80% higher than those in living in the least deprived areas (34). The causal mechanisms underlying these inequalities, and to what extent these are determined by inequalities in pre-existing health as compared to inequalities in pregnancy care, are however poorly understood.

In this thesis I consider socioeconomic and ethnic inequalities in maternity outcomes. I seek to add to the available information on the size and determinants of socioeconomic and ethnic inequality, and the proportions of each outcome attributable to inequalities, in the following outcomes:

(1) Maternal intensive care admission
(2) Postpartum haemorrhage of 1500ml or more
(3) Stillbirth

(4) Preterm birth

(5) Fetal growth restriction (birthweight <3rd centile)

1.7 Aims and Objectives of this thesis

The overall aim of this thesis is to demonstrate how electronic health record data collected during maternity care can be used to understand determinants of, and inequalities in, maternity outcomes.

To do this, this thesis addresses four related issues in maternity care in the UK. These are:

(1) The quality of coding of ethnicity in electronic health record data

(2) Risk factors for adverse maternity outcomes

   a. Associations between ethnicity and admission to intensive care among women giving birth

   b. Associations between ethnicity and postpartum haemorrhage

   c. Risk factors for preterm birth, split into iatrogenic (provider-initiated) and spontaneous

(3) Risk of complicated birth at term in nulliparous and multiparous women

(4) The proportion of adverse pregnancy outcomes (stillbirth, preterm birth and fetal growth restriction) which are attributable to socioeconomic and ethnic inequality

The first objective is methodological, a validation of the data used in the subsequent studies. The other three objectives address research questions concerning prognosis in maternity care which can be framed according to the PROGRESS (PROGnosis RESearch Strategy) framework (7).[2] Objectives (2) and (4) address questions of prognostic factors: that is, specific characteristics which are associated with the prognosis of the mother or the baby (8). Objective (3) addresses a question of fundamental prognosis: the course of birth "in the context of the nature and quality of current care" (7).

[2] The PROGRESS framework, first proposed in 2009 (7), characterises prognosis research as "the investigation of the relations between future outcomes (endpoints) among people with a given baseline health state (startpoint) in order to improve health". Four types of prognostic questions exist in health research: fundamental prognosis research; prognostic factor research; prognostic model research; and stratified medicine research. This thesis answers questions of the first two types (7).

2 Methods Chapter 1: Research Design Overview

This section describes the overall approach using electronic health record data, the data sources used, study design, statistical methods and ethical approval.

2.1 Overall approach: use of electronic health record data

The studies contained within this thesis all use linked datasets comprising information captured during routine clinical care of women giving birth in England and Wales. Within this programme of work, I have sought to address common concerns about the validity and usefulness of these data while carrying out research to inform clinical care, health policy and future research.

The use of electronic health record data is particularly important for maternity care due to the scale of care provided. In England, over half a million births occur each year: individual-level data collection is impractical. Where detailed individual level data collection is clearly required, such as in maternal death, this is done separately and extremely effectively through dedicated national systems. Some data is collected through the mandatory registration process of births and stillbirths, and this can be used to provide accurate statistics. However, maternal death is fortunately rare, and stillbirth uncommon; for more common outcomes, such as postpartum haemorrhage, it is necessary to use health data.

Prior to the work on this thesis, the use of such data had been established in England for well over 15 years, through secondary analyses of the database Hospital Episode Statistics which had been used to produce maternity indicators including for rates of caesarean section and vaginal birth after previous caesarean (VBAC) (80,81). However, there were also substantial acknowledged limitations within the datasets available, including the under-recording of severe maternal morbidity, including PPH (37).

For this thesis, new maternity datasets were available: in Wales, the Maternity Indicators DataSet (MIDS) and in England, a dataset produced from extracts from hospital Maternity Information Systems (MIS), linked together for the purposes of the NMPA. Datasets

constructed in this way had been shown in a pilot project to provide accurate information that could be used to measure care quality (82).

2.2 Data sources

The primary population data for these studies are obtained from four population level electronic datasets, linked together for the purposes of the NMPA. Access to these data were available to me through my affiliation with the NMPA as a Clinical Fellow. The work detailed within this thesis falls within the programme of work undertaken by the NMPA to understand the scale and determinants of variation in maternity care and outcomes in Britain.

Non-identifiable patient-level data was accessed via a secure server hosted on behalf of the RCOG on the N3 network, which meets security standards necessary to hold patient data.

2.2.1 Data curation

The dataset used in these analyses is unique, comprised of linked datasets curated to form one central dataset. This was created by the NMPA team in a four-step approach, summarised in Figure 2.1:

(1) In England, each individual hospital trust uploaded an annual data extract from their maternity information system to match a provided data specification (83). In Wales and Scotland, national datasets were uploaded.

(2) These files were then individually cleaned by trust (or country) using a pre-created code file, to a specified format, in three phases

   a. Phase 1: cleaning and removal of identifying information, and creation of NMPA study identifiers

   b. Phase 2: cleaning of other data fields, including the reformatting of times and dates, the exclusion of implausible values (defined clinically using record-book data or, where not available, four SDs outside the mean), and the automated and manual inspection of possible duplicates to identify multiple births. This step was important and long as each unit has slightly different clinical practice and thus clinical coding. Each individual hospital extract was individually cleaned by a member of the analysis team (64). In this way it was possible to

evaluate inconsistencies such as, for example, reporting women's parity as that at the end of their birth episode, rather than that at booking. This ensured a relatively uniform dataset prior to Phase 3.

c. Phase 3: merge with other trusts to form a national dataset for each country

(3) These national dataset files were then linked using a national spine supplied by central data agencies (NHS Digital in England, National Welsh Informatics Service in Wales) to allow onward linkage to hospital records (Hospital Episode Statistics (HES) in England, and Patient Episode Statistics for Wales (PEDW) in Wales). In England, this also encompassed all previous HES records for the woman (for all previous hospital admissions) from 1st April 2000.

(4) These national linked maternity-hospital datasets were then appended to form an overall NMPA dataset.

I contributed to the design of this data curation process, which formed a foundation for the later work on my PhD described in this thesis. I led on the development of Phase 2 clinical cleaning, and contributed heavily to the manual process of conducting the cleaning, linkage and appending of datasets. The reason for this laborious process was that there were, at the time, shortcomings in the available central data in England for maternity services. For the past decade, the NHS in England has focused on the production of the Maternity Services DataSet (MSDS). The specification for MSDS is substantial, covering several hundred items encompassing characteristics of women and their babies and details of antenatal, intrapartum and postpartum care using a modular structure (84). The dataset is still working towards maturity with substantial changes to the data specification over its lifetime (85). The process described here was intended to be an interim solution while MSDS reached maturity.

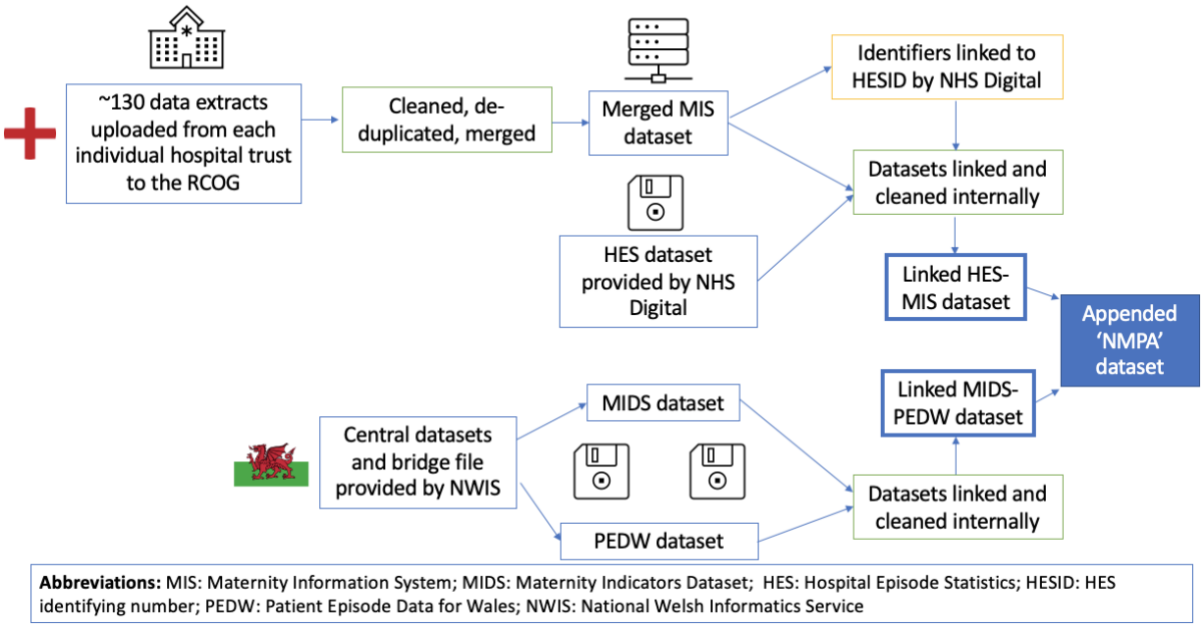
For studies within this thesis, selection of countries and datasets used was based on available information. More data about historical admissions was available in England, and therefore it was possible to develop previous medical history in more detail as described in Chapter 4; where data was not available for a research study, the country was excluded (see Table 2.1 for details).

2.2.2 Data linkage

All of the studies in this thesis use linked datasets, most commonly two: MIS and HES. This allows for a richer data source than using either dataset alone, with some information only available in one of the two datasets (e.g. MIS contains Apgar and BMI; HES contains comorbidity and historical pregnancy data), and cross-validation and reduction of missingness where information is available in more than one dataset. For all analyses, the MIS constitutes the spine, so women are only included in the dataset if they have a MIS record. Linkage was conducted by a trusted third party (NHS Digital) who linked MIS records to HES via a deterministic process, using maternal and neonatal NHS numbers, dates of birth and postcode. This resulted in linkage of records for approximately 92% of all women and babies and thus a very rich dataset for analysis (12).

One of the components of this thesis is a novel linkage to maternal intensive care admission data, providing the opportunity to derive new outcomes and develop new information about the quality of maternity care. The linkage was conducted by the Intensive Care National Audit and Research Centre (ICNARC) using identifiers available within both maternity and external datasets to identify women who are admitted to adult intensive care settings during pregnancy, birth or the year after. Following receipt of the spine, I merged the datasets and evaluated the linked dataset. Further detail is available in the associated NMPA report (86).

Figure 2.1 The formation of the NMPA dataset



2.3 Study design

This section provides a summary of the design of the studies included in this thesis. The thesis consists of six observational studies. The results of these analyses have been presented in the form of six research papers. Four have been published in the peer-reviewed literature; one has been accepted for publication; and one is currently under review.

2.3.1 The quality of coding of ethnicity in electronic health record data.

The first part of the research was methodological, to establish the feasibility of using the linked datasets to describe and explore inequalities by ethnic group. This was a cross-validation using the two linked datasets available in England: MIS and HES. The study sought to establish the agreement on ethnicity coding between datasets; the nature of any inconsistencies; and to what extent the choice of dataset changed the results of any analyses, using as examples rates of a common outcome (emergency caesarean birth) and an uncommon outcome (obstetric anal sphincter injury). The results of this analysis are now published in the peer-reviewed literature as a paper which is included in the methods section of this thesis:

Validation of ethnicity in administrative hospital data in women giving birth in England: cohort study (Chapter 3)

2.3.2 Risk factors for adverse outcomes: maternal intensive care admission, postpartum haemorrhage, and iatrogenic and spontaneous preterm birth.

The second part of this research sought to understand the risk factors underlying three maternity outcomes: maternal intensive care admission during pregnancy and up to six weeks postpartum; postpartum haemorrhage of 1500ml or more; and preterm birth, split into iatrogenic and spontaneous.

The first two outcomes both relate to severe maternal morbidity. For the first study, I linked intensive care data to MIS and HES data to establish whether intensive care admission had occurred in pregnancy, birth or the postpartum period up until six weeks. For the second study, I used blood loss data available in the MIS to examine rates of severe postpartum haemorrhage (≥1500ml of blood loss at birth). For each study, I used a series of multivariable logistic regression models to explore the extent to which the association between ethnicity and maternal morbidity was modified by other factors in the woman's pre-existing health, her health in pregnancy, and/or her care at the time of birth. These analyses produced two research papers, included in the results section of this thesis:

Associations between ethnicity and admission to intensive care among women giving birth: a cohort study (Chapter 4)

*Risk of postpartum haemorrhage is associated with ethnicity: a cohort study of 981 801 births in England (*Chapter 5)

The third outcome examined was preterm birth. Preterm birth may be classified into two sub-groups; iatrogenic and spontaneous preterm birth depending on whether birth is initiated by the provider of maternity care (87). I used MIS data to divide the preterm population into those born following a spontaneous onset of labour and those with a provider-initiated birth. Using electronic health record data, I described the rates and risk factors associated with Iatrogenic and spontaneous preterm birth among singleton births in England. The findings of this analysis are presented in the form of a research paper which has been submitted for publication.

Iatrogenic and spontaneous preterm birth in England: population-based cohort study (Chapter 6)

2.3.3 Risk classification of women in pregnancy and at birth.

The third part of the research was to evaluate the NICE risk classification typically used for recommending place of birth, with two purposes: first, to evaluate its clinical use in predicting risk of complicated birth sufficiently to guide place of birth, and second, to understand whether it could be used as a transparent form of describing clinical risk in both further studies and the NMPA. To evaluate this, I developed and derived a composite outcome, 'complicated birth' which encompassed the complications which would require immediate attention from an obstetric or neonatal team (namely, birth by caesarean or instrument, obstetric anal sphincter injury, postpartum haemorrhage of 1500ml or more, and neonatal Apgar score of less than 7). The study was descriptive in nature, giving figures for the proportions of women in each risk group who had a complicated birth. The output of this part of the research for this thesis has been published as a research paper which is included in the results section of this thesis:

Risk of complicated birth at term in nulliparous and multiparous women using routinely collected maternity data in England: cohort study (Chapter 7)

2.3.4 Ethnic and socioeconomic inequalities in adverse pregnancy outcomes

The next part of the research explored the extent to which adverse pregnancy outcomes are attributable to inequality. This work arose from the observations in Chapter 4 and 5 that much of severe maternal morbidity is governed by ethnic inequality.

I used crude and adjusted population attributable fractions to estimate the proportion of adverse birth outcomes attributable to ethnic and socioeconomic inequality. Three outcomes were considered: stillbirth, preterm birth and babies born with fetal growth restriction (<3rd birthweight centile according to UK-WHO birthweight charts (42)). Population attributable fractions were used to estimate the proportion of these adverse pregnancy outcomes that would not have occurred if all women in England had the same risk as women in the least deprived socioeconomic group or from a White ethnic background (88,89). These were

estimated in their crude form, and also with adjustment (using logistic regression models) for smoking status and body mass index (BMI) at the onset of pregnancy. This was done to explore the extent to which these modifiable risk factors mediate socioeconomic and ethnic inequalities.

I also estimated the proportion of adverse pregnancy outcomes attributable to specific groups, including the combination of socioeconomic and ethnic groups together. For this I used group attributable fractions, which are an estimate of what proportion of adverse outcomes would not have occurred in a specific group, had all women in the group had the same risk as White women in the least deprived socioeconomic group.

The findings of this analysis are presented in the form of a research paper which has been published in the peer-reviewed literature.

> *Adverse pregnancy outcomes attributable to socioeconomic and ethnic inequalities in England: a national cohort study* (Chapter 8)

Table 2.1 Summary of data sources, inclusion criteria, and outcome definitions for included studies

Chapter	Title	Data sources (country)	Inclusion criteria	Outcome(s) being studied
3.Methods Chapter (Research Paper 1)	Validation of ethnicity in administrative hospital data in women giving birth in England: cohort study	MIS/HES 2015-17 (England only)	All birth records within the NMPA dataset were included. For cross-validation, the analysis was restricted to women with a record in both MIS and HES	n/a
4.Results Chapter (Research Paper 3)	Associations between ethnicity and admission to intensive care among women giving birth: a cohort study	MIS/HES/ICNARC (England); Mids/PEDW/ICNARC (Wales) 2015-16	All birth records within the NMPA dataset were included (all registerable* births).	Maternal admission to an intensive care unit in pregnancy and/or during or up to six weeks after birth. Women were defined as having an intensive care admission if they had an ICNARC record.
5.Results Chapter (Research Paper 3)	Risk of postpartum haemorrhage is associated with ethnicity: a cohort study of 981 801 births in England	MIS/HES 2015-17 (England only)	Birth records meeting all of: • occurring in hospital trusts in which 80% of MIS records contained information about blood loss • records of either live or stillbirths that occurred at or after 24+0 weeks gestation • with complete information about blood loss.	Recorded maternal blood loss at birth of 1500ml or more.
6.Results Chapter 3 (Research Paper 4)	Iatrogenic and spontaneous preterm birth in England: population-based cohort study	MIS/HES 2015-17 (England only)	Birth records meeting all of: • occurring in hospital trusts meeting NMPA quality checks (completeness of 70% or more, and distribution) for gestational age, delivery method, and labour onset • records of singleton livebirths at or above 22+0 weeks gestation • with complete information about labour onset and delivery method.	Preterm birth (<37 weeks gestation), split into iatrogenic (initiated by the healthcare provider) and spontaneous

Chapter	Title	Data sources (country)	Inclusion criteria	Outcome(s) being studied
7.Results Chapter 4 (Research Paper 5)	Risk of complicated birth at term in nulliparous and multiparous women using routinely collected maternity data in England: cohort study	MIS/HES 2015-16 (England only)	Birth records meeting all of: • occurring in hospital trusts where 70% or more of records were complete on each of maternal BMI, maternal age, and gestational age • singleton pregnancy in women aged 15-45 with a record in both MIS and HES of a singleton pregnancy with complete information on maternal BMI, maternal age and gestational age The majority of the analysis was further restricted to women who gave birth at term (37+0 to 41+6 weeks gestation).	Complicated birth, a composite outcome including one or more of instrumental birth, caesarean section, postpartum haemorrhage of 1500ml or more, obstetric anal sphincter injury (3^{rd}/4^{th} degree tear) and neonatal Apgar score of 7 or less
8.Results Chapter 5 (Research Paper 6)	Adverse pregnancy outcomes attributable to socioeconomic and ethnic inequalities in England: a national cohort study	MIS/HES 2015-17 (England only)	Birth records meeting all of: • Singleton pregnancy with a recorded gestation between 24+0 and 42+6 completed weeks • Recorded birth outcome of either livebirth or stillbirth (one trust was dropped as no record of this variable).	Stillbirth, preterm birth (birth before 37 weeks gestation) and fetal growth restriction (birthweight below 3^{rd} centile)

2.4 Statistical Methods

The statistical methods for each individual study are described in depth in each chapter. However, there are several common themes to the methods used, which are described in brief here.

2.4.1 Choice, definitions and validation of variables used

2.4.1.1 Choice of outcome variables used

Outcomes covered in this thesis were chosen from a list first identified by a scoping Delphi exercise conducted by the NPEU to inform the development of the NMPA. Outcomes were further refined on discussion with the NMPA Project Team, and with the NMPA Clinical Reference and Women and Families Groups, following review of data availability and quality.

In Chapter 7, I used a composite outcome, complicated birth, to assess the current risk classification used to counsel women giving birth. Composite outcomes incorporate the presence or absence of more than one individual measure. These sub-measures may be incorporated as binary outcomes or differentially weighted, for example to account for severity. Composite outcomes have several potential disadvantages: first, rare components of the outcome (such as stillbirth) can be masked by more common components (such as caesarean birth), leading to unclear conclusions; second, adequate risk-adjustment can be challenging if different components have different sizes and directions of associations with risk factors; and third, multiple choices are required in their design, such as what outcomes should be included and whether components should be weighted. If these choices are not transparently made and reported they can obscure the underlying picture (90–92). Composite outcomes must therefore be carefully defined, with a clear description of the components and the rationale for their inclusion. The study was accompanied by a breakdown of the results by each component of the composite outcome to facilitate interpretation and re-use of the results (90).

2.4.1.2 Choice of independent variables used

Independent variables used in models were chosen using a stepwise approach. For each model, a short pragmatic literature review of previous studies examining the outcome was undertaken, and the variables found to be associated with the outcome identified. For each identified variable, I identified whether it was available in the dataset; and if it was, if it was sufficiently complete and appeared clinically valid. This was assessed by tabulating completeness, cross-validating between datasets where possible (for example, between HES and MIS for ethnic group as described in Chapter 3), evaluating for clinical plausibility (where possible, in comparison to national studies or other data sources such as the Office for National Statistics for prematurity) and producing scatter plots by trust to evaluate consistency of coding. Where it was not possible to clearly identify relevant information in the dataset, appropriate sensitivity analyses were considered: for example, for postpartum haemorrhage, previous PPH is an important risk factor but information was not available in the dataset, therefore a sensitivity analysis restricted to primiparous women (in whom previous PPH could not have occurred) was performed.

2.4.1.3 Definition and validation of variables used

Throughout this thesis, particular attention has been taken to define and validate exposure and outcome variables. This has been done in three steps:

(1) Definition of the variable, using validated definitions or algorithms where available (for example, for parity (93)) and, where not available, using clinical input to select relevant codes
(2) Checking for validity, either by comparison to published rates of the outcome overall where available, by cross checking between multiple sources of data or by clinical sense-checking
(3) For variables with sufficient frequency (approximately >0.2%), production of scatter plots by trust to check for coding abnormalities at trust level, to enable identification of coding abnormalities.

For example, in Chapter 7, I have used the NICE Intrapartum Care Guidance to derive, in the linked dataset, women's risk classification at the onset of labour. This was done by, for each included condition, exploring relevant codes in HES for the relevant diagnosis or procedure,

checking these with a senior clinician, and then comparing the prevalence of the condition using these codes to other published estimates of the frequency of these conditions in pregnancy, where available, and among women of childbearing age, where not available in pregnancy. For the outcome measure, complicated birth, these steps were repeated for each individual part of the composite measure.

For ethnicity, cross-checking between datasets enabled an improved understanding of the quality of ethnicity recording in routine electronic data, the conclusions of which are described in detail in Chapter 3.

2.4.1.4 Limitations of coding variables: considerations

It has been important to be aware of the limitations of coding in electronic health record data.

The first substantial limitation is incomplete data. Despite extensive cleaning processes described above, differences in data completeness exist between hospitals, with a small proportion (<10%) having very poor data quality. Even data items which are considered 'mandatory' (for example, ethnic group) may include categories which can only be regarded in any analysis as missing, such as "not stated". In acknowledgement of this, in each analysis, hospitals with poor-quality data about the outcome of interest or other key variables, or poor linkage to key datasets were excluded. It was not always possible to identify the completeness of the outcome within the dataset, particularly where the outcome was identified by linkage (i.e. for intensive care admission). For all analyses where it was possible to define the completeness of the outcome within the dataset (e.g. blood loss) records with incomplete information about the outcome of interest were excluded. Therefore, to avoid bias due to selective recording, trusts with low levels of completeness (generally 70%, but 80% for PPH following examination of data distributions) were excluded from the analysis. Where this was done, generally, this excluded a relatively small proportion of hospitals (<10%). This has been demonstrated previously to be a valid way of constructing birth cohorts (94,95). Further details are given in Table 2.1.

Furthermore, there are limitations in the quality of coding of some variables. For this thesis, a particularly important consideration is socioeconomic deprivation, measured using quintiles

of the Index of Multiple Deprivation (IMD). IMD is a government-produced neighbourhood-level measure of deprivation covering approximately 1,500 individuals and including information about the income, crime, health, employment, education, and environment including housing within that area (96). The use of IMD, which is not specific to an individual, will have led to a dilution of observed associations, sometimes called non-differential misclassification (97): this has been discussed in the appropriate manuscripts.

2.4.2 Regression models

Throughout this thesis, there has been a focus on binary outcomes and univariate and multivariable logistic regression models (for most analyses) and Poisson models (in the preterm and complicated birth analyses) have been used to describe and unpick associations between characteristics and outcomes. Regression modelling is a flexible method of estimating associations. Logistic regression models report odds ratios (ORs), which represent the ratio between the odds that an outcome would occur given a particular exposure and the odds of the outcome occurring in the absence of that exposure. Poisson models report risk ratios (RRs) which represent the ratio between the risk of an outcome under a particular exposure and the risk of that outcome in the absence of the exposure (98). For rare outcomes, ORs and RRs approximate one another (98). Preterm and complicated birth were relatively common outcomes so Poisson regression was used to provide RRs, whereas the other outcomes in this thesis for which relative measures of effect were reported (ICU admission, PPH) were much more rare so this was not necessary.

Within regression models measuring population effects it was necessary to account for clustering of the outcome within individual units, to account for unmeasured differences in women's characteristics and clinical or coding practices. Clustering of outcomes in individual units was accounted for in regression analyses either by using robust standard errors. With robust standard errors, the parameter estimates are not changed by clustering, but the standard errors are widened to allow for the uncertainty introduced by clustering. An alternative approach would have been to use random effects models, which include a random intercept for each cluster (usually hospital). Random effects may change the parameter estimates, and allow a quantification of the amount of clustering (98).

2.4.3 Attributable fractions

Attributable fractions (AFs) were used in Chapter 8 to estimate the proportions of stillbirth, preterm birth and fetal growth restriction which are attributable to socioeconomic and ethnic inequality. AFs describe the proportion of adverse outcomes that would not have occurred if the rates of the outcome were the same as in those individuals in the reference group (in my study, women from White ethnic group or least deprived socioeconomic quintile). AFs are derived as follows:

$$AF = \frac{\text{Observed number of outcomes} - \text{Expected number of outcomes}}{\text{Observed number of outcomes}}$$

Attributable fractions can either be attributed to populations as a whole or to specific groups. Population attributable fractions (PAF) describe the proportion of all occurrences of the outcome in that population which are attributable to the characteristic being assessed, i.e. the proportion of the outcome which would not have occurred if all members of the population had the same value of the characteristic as the baseline or reference group. Group attributable fractions describe the population of the outcome within a specific group which is attributable to the characteristic(s) being assessed, i.e. the proportion of the outcome *within that group* which would not have occurred if all members of the group had the same value of the characteristic as the baseline or reference group. These group attributable fractions were used to estimate the proportion of adverse pregnancy outcomes attributable to specific groups, including combinations of socioeconomic and ethnic groups together.

A further step within the study was to provide adjusted population attributable fractions. To do this, I used logistic regression models to estimate the expected number of adverse outcomes, adjusting for ethnicity or deprivation, maternal smoking, BMI at the onset of pregnancy and other maternal risk factors defined according to the NICE guideline for intrapartum care. Then, the adjusted attributable fractions were calculated as described above, but using the expected numbers of adverse outcomes predicted by the logistic regression models. Confidence intervals for the attributable fractions were calculated after using logarithmic transformation to normalise the distribution and stabilise the variance.(99)

2.4.4 Approach to missing data

The primary approach to missing data throughout the thesis has been to include the records which have complete information about the outcome being evaluated in hospital trusts with high completeness for key variables, followed by the use of multiple imputation by chained equations to impute missing covariates. The central assumption of multiple imputation (MI) is that missing information is missing at random given the imputation model is correctly specified, that is that there is nothing external to the model that determines whether a value is missing (100,101). If this assumption is met, MI will give unbiased estimates. However, this assumption is impossible to test, as by definition the data to test it is not available. Therefore, in each analysis where MI was used, the analysis was also carried out in a dataset restricted to records with complete information using all covariates ('complete cases'); analyses using complete cases have been found to be robust to a wider range of missingness assumptions (102). This usually substantially reduced the size of the analysis dataset and thus reduced the statistical evidence of the observed associations (widening the confidence interval). It has been generally acknowledged as best practice to assess the sensitivity of the findings to different missing data assumptions, such as carrying out the analyses in imputed datasets as well as in complete cases only (100).

2.5 Ethics

Approval for the programme of study included in this thesis was provided through the LSHTM Ethics Committee, approval number 14544, on 4 April 2018. The approval letter is provided in Appendix A.

Non-identifiable patient-level data from the National Maternity and Perinatal Audit was used to undertake the analyses within this study. In the data available to me, personal identifiers only included the mother's age, ethnicity and IMD, and the date of her admission and on which she had given birth. Data governance and appropriate approvals were established as part of the NMPA audit programme. The research in this PhD is supportive of the Audit and therefore included in the scope of these approvals. The Audit funder, the Healthcare Quality

Improvement Partnership (HQIP) approved the use of audit data for each individual analysis within this thesis.

2.6 Involvement of women and families

The work in thesis is inspired by and often directly influenced by the NMPA Women and Families Involvement Group (WFIG), which I co-led on the initial set up and management of between 2017 and 2019 together with the RCOG's Patient and Public Involvement (PPI) team. This group, which has had between 15 and 20 members, consists of representatives from some charities and stakeholder groups together with lay members who have had direct personal experience of maternity care in the UK since 2014. This group was recruited from existing public involvement initiatives at the RCOG and RCPCH, and a targeted Twitter and Facebook campaign; individual conversations were held with self-nominated lay individuals in order to ensure a balanced group. The intention was to form a group which could, through continuous participation, meaningfully advise the project. The NMPA's PPI and formation of this group was highly commended in HQIP's 2018 Richard Driscoll Memorial Award for PPI.

The WFIG have fed into the work in this thesis in their discussions regarding choice of and risk adjustment for clinical outcomes, inequalities in birth outcomes and experience, and in their own experiences of information sharing regarding clinical risk and how that was used to determine their choices around place of birth and other aspects of their care.

2.7 Other outputs

During my PhD, I worked at the RCOG as a clinical fellow for the National Maternity and Perinatal Audit. As part of this, I also contributed to the following national reports and research papers. These do not form a part of this research thesis; however, they have influenced and draw upon the work undertaken and skills developed in my PhD.

*denotes joint first authorship

National Maternity and Perinatal Audit Project Team. Organisational Report 2017. London, RCOG, 2017. https://maternityaudit.org.uk/FilesUploaded/NMPA%20Organisational%20Report%202017.pdf

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Aughey, H.*, Jardine, J.*, Moitt, N. et al. Waterbirth: a national retrospective cohort study of factors associated with its use among women in England. BMC Pregnancy Childbirth 21, 256 (2021). https://doi.org/10.1186/s12884-021-03724-6

Jardine, J*, Relph, S*, Magee, LA, von Dadelszen, P, Morris, E, Ross-Davie, M, Draycott, T, Khalil, A. Maternity services in the UK during the coronavirus disease 2019 pandemic: a national survey of modifications to standard care. BJOG 2021; 128: 880– 889. https://doi.org/10.1111/1471-0528.16547

Jardine J, Morris E. COVID-19 in Women's health: Epidemiology, Best Practice & Research Clinical Obstetrics and Gynaecology, 2021, https://doi.org/10.1016/j.bpobgyn.2021.03.010

Gurol-Urganci I*, Jardine JE*, Carroll F, et al. Maternal and perinatal outcomes of pregnant women with SARS-CoV-2 infection at the time of birth in England: national cohort study. Am J Obstet Gynecol 2021 https://doi.org/10.1016/j.ajog.2021.05.016

Gurol-Urganci I*, Waite L*, Webster K*, Jardine JE* et al. Obstetric interventions and pregnancy outcomes during the COVID-19 pandemic in England: A nationwide cohort study. PLoS Medicine 2022 https://doi.org/10.1371/journal.pmed.1003884

I have also contributed to policy documents and guidance surrounding COVID-19 in Pregnancy and co-produced a specification of indicators for the National Maternity Dashboard in England.

3. Methods Chapter: Ethnicity Coding

The aim of this part of the thesis was to describe and validate the coding of ethnicity data in women giving birth in England, in order to establish a classification for use later in the thesis. The findings of this analysis have been published as a research paper.

3.1 Research Paper 1

Validation of ethnicity in administrative hospital data in women giving birth in England: cohort study
This article has been accepted for publication in *BMJ Open* following peer review and can also be accessed online at https://bmjopen.bmj.com/content/11/8/e051977.full

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RESEARCH PAPER COVER SHEET

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SECTION A – Student Details

Student ID Number	1511701	**Title**	Dr
First Name(s)	Jennifer		
Surname/Family Name	Jardine		
Thesis Title	A study of risk factors of maternity outcomes using large, routinely collected electronic datasets		
Primary Supervisor	Kate Walker		

If the Research Paper has previously been published please complete Section B, if not please move to Section C.

SECTION B – Paper already published

Where was the work published?	BMJ Open		
When was the work published?	August 2021		
If the work was published prior to registration for your research degree, give a brief rationale for its inclusion	n/a		
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SECTION C – Prepared for publication, but not yet published

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SECTION D – Multi-authored work

For multi-authored work, give full details of your role in the research included in the paper and in the preparation of the paper. (Attach a further sheet if necessary)	Designed study with collaborative input from coauthors, conducted primary analysis with checking from a statistical co-author, wrote first draft of paper, coordinated feedback, implemented revisions from coauthors.

SECTION E

Student Signature	
Date	4/11/2021

Supervisor Signature	
Date	16/11/2021

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Validation of ethnicity in administrative hospital data in women giving birth in England: cohort study

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ABSTRACT

Objective To describe the accuracy of coding of ethnicity in National Health Service (NHS) administrative hospital records compared with self-declared records in maternity booking systems, and to assess the potential impact of misclassification bias.

Design Secondary analysis of data from records of women giving birth in England (2015–2017).

Setting NHS Trusts in England participating in a national audit programme.

Participants 1 237 213 women who gave birth between 1 April 2015 and 31 March 2017.

Primary and secondary outcome measures (1) Proportion of women with complete ethnicity; (2) agreement on coded ethnicity between maternity (maternity information systems (MIS)) and administrative hospital (Hospital Episode Statistics (HES)) records; (3) rates of caesarean section and obstetric anal sphincter injury by ethnic group in MIS and HES.

Results 91.3% of women had complete information regarding ethnicity in HES. Overall agreement between data sets was 90.4% (κ=0.83); 94.4% when collapsed into aggregate groups of white/South Asian/black/mixed/other (κ=0.86). Most disagreement was seen in women coded as mixed in either data set. Rates of obstetrical events and complications by ethnicity were similar regardless of data set used, with the most differences seen in women coded as mixed.

Conclusions Levels of accuracy in ethnicity coding in administrative hospital records support the use of ethnicity collapsed into groups (white/South Asian/black/mixed/other), but findings for mixed and other groups, and more granular classifications, should be treated with caution. Robustness of results of analyses for associations with ethnicity can be improved by using additional primary data sources.

Strengths and limitations of this study

- ► This study uses a large data set of ethnicity as reported to midwives at the time of booking pregnancy to validate ethnicity in administrative hospital data from birth episodes.
- ► The use of routine data for validation ensures the study is large and representative.
- ► The main limitation of this study is that it is restricted to largely healthy women giving birth.

INTRODUCTION

Routinely collected electronic health records offer the opportunity to evaluate care, outcomes and associations among large numbers of service users. There is wide interest in using routinely collected data to explore in more detail inequalities in care/outcomes between ethnic groups.[1] The information about ethnicity in routinely collected data sources needs to be accurately recorded to enable such analyses.[2 3]

Hospital Episode Statistics (HES), an administrative data set which captures admissions at National Health Service (NHS) hospitals in England, records ethnicity at each attendance. Previous validation studies of ethnicity in HES have demonstrated that completeness has improved over time, and that there is overall good agreement between HES and general practice records[4] and patient self-reported ethnic group in patients with cancer.[5] However, these studies have also demonstrated heterogeneity between hospitals and disagreement between data sources in the recording of non-white ethnicity.[4 5] It is unknown to what extent these discrepancies still exist, and whether similar patterns are seen in young, ethnically diverse groups such as women giving birth.

In this study, we make use of linked data on women giving birth to examine the accuracy of ethnicity recording in HES. We compare ethnicity in HES to that in electronic maternity records in maternity information systems (MIS) in England. MIS records reflect self-reported ethnicity reported to midwives at the time of the pregnancy booking appointment, where a woman's social, medical and maternity history are comprehensively reviewed. Recording of ethnicity is mandatory within the Maternity Data Standard in England, and is used to guide care (eg, screening for

gestational diabetes mellitus).[6] Ethnicity data in HES is also self-reported, derived from the hospital's record systems entered at the time of the admission (in this case, for birth).

The aims of this study were (1) to ascertain the completeness of ethnicity data in HES in the records of a young, ethnically diverse population: women giving birth in England; (2) to compare agreement between HES and maternity data sources; (3) to examine how sensitive the findings of statistical analyses are to the ethnicity data source, using rates of emergency caesarean section and obstetric anal sphincter injury as illustrative examples. Based on our findings we develop recommendations for the use of ethnicity coding and the interpretation of results using HES ethnicity data.

METHODS

Data sets

This study used two data sets, linked together for the purpose of the National Maternity and Perinatal Audit (NMPA) in England: administrative data for the hospital admission resulting in the birth episode from HES, and maternity data from MIS. HES was provided via NHS Digital. Individual hospital trusts provided extracts directly from the MIS to the NMPA.[7] Furthermore, for the purposes of comparison to national data on ethnic group, publicly available aggregate data from the Office for National Statistics (ONS) based on the 2011 census was used.[8]

The cohort consisted of 1 165 252 women who gave birth in the NHS in England between 1 April 2015 and 31 March 2017 and who had a linked record available in both MIS and HES (figure 1).

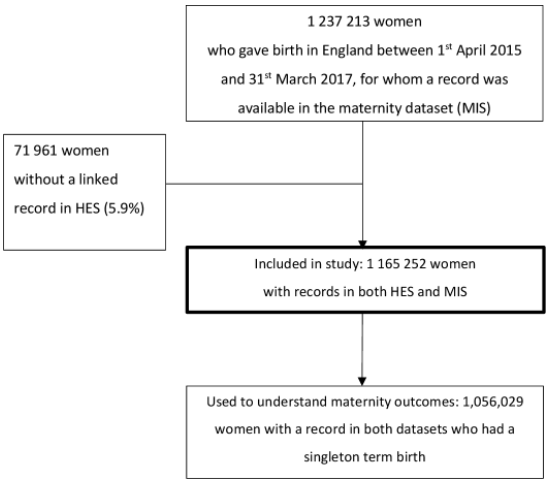

Figure 1 Flow diagram for study cohort. HES, Hospital Episode Statistics; MIS, maternity information systems.

Linkage

Data sets were linked by a trusted third party (NHS Digital) using deterministic methods based on the NHS number, postcode and maternal date of birth.[9]

Coding of ethnicity

All three data sets code ethnicity using the 16+1 ONS categorisation system from the 2001 census.[10] Ethnicity was considered 'complete' if it was not missing and not 'unknown'. For the purposes of understanding varying levels of granularity, ethnicity was considered both as individual codes and collapsed into five aggregated groups used by ONS: white; South Asian or British Asian; black or black British; mixed and other (including Chinese and other (free text, not categorised)).

Analysis

For 1 165 252 women where both HES and MIS records were available, ethnicity codes were compared for completeness. Cross-validity was checked for individual ethnicity codes and by the five aggregated ethnic groups. Agreement was assessed using Cohen's kappa (κ) statistic, which measures the level of agreement of a categorical variable between two different sources on a scale from 0 to 1, taking into account the probability of chance agreement.[11]

To evaluate how sensitive statistical analysis of results were to the data source for ethnicity, we examined the relationship between ethnicity and rates of a common outcome of birth (emergency caesarean section) and an uncommon outcome (obstetric anal sphincter injury (OASI)) known to be associated with ethnic group.[12 13] Both outcomes are well coded and are used for national quality comparisons.[7] Women were included in this analysis if they had a singleton birth at term (37^{+0} to 42^{+6} weeks). Definitions of singleton birth at term, emergency caesarean section and OASI were made using the coding framework developed by the NMPA.[14] Poisson regression was used to examine the associations between each outcome and ethnic codes and ethnicity collapsed into groups, using recorded ethnicity in each of HES and MIS.

Two supplementary analyses were carried out. First, the frequency of complete ethnicity codes was tabulated and compared with the published ethnicity of women aged 16–49 from the 2011 census.[8] Second, in order to assess whether there was any bias in linkage to HES, the likelihood of having a linked record was tabulated by ethnic group for all women with a record in HES.

All analyses were performed in Stata V.14.1.

Data access statement

The data are available for further research and service evaluation following approval from the data controllers, which are the Healthcare Quality Improvement Partnership (www.hqip.org.uk) for the data derived from the MIS and NHS Digital for HES.

Table 1 Assessing agreement between ethnicity group recorded in MIS and in HES for 1 165 252 women with records in both data sets

			MIS						
		Total	White	South Asian	Black	Mixed	Other	*Missing*	% agreement*
HES	Total	1 165 252	814 492	126 155	52 201	19 501	44 946	*107 957*	
	White	804 648	**754 312**†	1428	716	2412	6911	*38 869*	98.5
	Row %*		**98.5**	0.2	0.1	0.3	0.9	*4.8*	
	Column %*		**97.0**	1.2	1.4	13.0	16.3	*69.8*	
	South Asian	124 341	1395	**111 863**†	566	760	3844	*5913*	94.5
	Row %*		1.2	**94.5**	0.5	0.6	3.2	*4.8*	
	Column %*		0.2	**93.6**	1.1	4.1	9.1	*10.6*	
	Black	52 572	880	438	**44 909**†	1287	1236	*3822*	92.1
	Row %*		1.8	0.9	**92.1**	2.6	2.5	*7.3*	
	Column %*		0.1	0.4	**90.6**	7.0	2.9	6.9	
	Mixed	42 269	16 273	3141	2525	**13 358**†	2915	*4057*	35.0
	Row %*		42.6	8.2	6.6	**35.0**	7.6	*9.6*	
	Column %*		2.1	2.6	5.1	**72.2**	6.9	7.3	
	Other	39 713	5086	2654	868	680	**27 424**†	*3001*	74.7
	Row %*		13.9	7.2	2.4	1.9	**74.7**	*7.6*	
	Column %*		0.7	2.2	1.8	3.7	**64.8**	*5.4*	
	Incomplete/ missing	*101 709*	*36 546*	*6631*	*2617*	*1004*	*2616*	***52 295***†	*51.4*
	*Row %**		*35.9*	*6.5*	*2.6*	*1.0*	*2.6*	***51.4***	
	*Column %**		*4.5*	*5.3*	*5.0*	*5.1*	*5.8*	***48.4***	
% agreement*			97.0	93.6	90.6	72.2	64.8	*48.4*	

*Percentages in rows, columns and of agreement between ethnic groups are among records with complete, non-missing values for ethnic group.
†Bold values signify where values are in agreement.
HES, Hospital Episode Statistics; MIS, maternity information systems.

Patient and public involvement

The NMPA advisory group for inequalities provided the motivation for investigating this question, and will guide the dissemination of this research.

RESULTS

Data completeness

Complete codes for ethnicity were present in 91.3% of the 1 165 252 HES records linked to MIS. Among the 1 165 252 women, 95.5% had a complete code for ethnicity in at least one of HES and MIS (table 1).

Agreement between ethnicity in HES and MIS

Of the 1 165 252 women with records in both HES and MIS, 1 007 881 (86.5%) had complete ethnic codes in both data sets. The overall agreement between aggregated ethnic groups was 94.4% (κ=0.86) and between individual ethnic codes was lower at 90.5% (κ=0.83) (table 2).

When ethnicity was recorded as white, South Asian or black, there was between 91% and 99% agreement between data sources on aggregated ethnic group, with the highest agreement in women recorded as white (table 1). The largest discrepancy between HES and MIS was in the recording of women with mixed ethnicity (table 1). A larger proportion of women were coded as mixed ethnicity in HES than in MIS (table 1). Of the women coded as mixed ethnicity in HES, only 35% were recorded as mixed ethnicity in MIS, with 43% recorded as white in MIS (table 1 and online

Table 2 Overall agreement between ethnic origin coded in HES and MIS in 1 007 881 women with complete ethnicity in both data sets

		MIS	
		%	κ
HES	All ethnicity codes*	90.5	0.83
	Aggregated groups†	94.4	0.86

*All 16 ethnicity codes defined by the Office for National Statistics.
†Aggregated groups of white/South Asian/black/mixed/other.
HES, Hospital Episode Statistics; MIS, maternity information systems.

supplemental table 1). For women recorded as mixed ethnicity in MIS there was a relatively high agreement in HES (72%).

For women with ethnic group recorded as a mix of two ethnicities in one data set, they were often recorded in the other data set as just one of these two ethnicities. For example, of those women coded as 'White/South Asian' in MIS, 59% were assigned to the same group in HES, 15% were coded in a 'White' group in HES; 10% were coded in a 'South Asian' group, 5% had no ethnicity recorded in HES; and 7% were 'Other Mixed' (online supplemental table 1). None of these codes are fully inconsistent with the 'White/South Asian' group in MIS. Similar patterns were seen for groups within white and black: only 60% of those recorded as 'White Irish' in MIS were assigned to the same group in HES, but a further 31% were assigned to 'White British' or 'Other White' groups; for women coded as 'Other Black' in MIS, only 45% were assigned to the same group in HES (the lowest agreement of all groups) but a further 38% were recorded as 'Black African' or 'Black Caribbean' which again may not be fully inconsistent (online supplemental table 1).

Sensitivity of statistical analyses to ethnicity data source

The overall rates and rate ratios comparing OASI and emergency caesarean section by ethnic group were very similar regardless of whether HES or MIS was used to classify ethnicity (table 3 and online supplemental table 2). However, small differences were seen in the estimates of the rates of caesarean section, and the rates and rate ratios of OASI, in the mixed and other groups, which were the ethnicity groups with the lowest agreement between data sources. For example, the estimated rate of caesarean section in women from mixed ethnic groups was 14.9% (95% CI 14.4% to 15.4%) in MIS and 15.3% (14.9% to 15.6%) in HES (table 3).

Supplementary analyses

The prevalence of white ethnicity was lower in women in this study than in women aged 16–49 in the aggregate census data (82.6% in census data, and 77.1% and 75.7% among complete values in MIS and HES, respectively). Women in HES were twice as likely to have their ethnicity recorded as mixed as women in MIS or the census (4.0% compared with 1.9% and 2.3%, respectively) (online supplemental table 3).

Women whose recorded ethnicity was black or mixed, or who did not have a recorded ethnicity, were less likely to have had complete identifying information in both data sets to enable linkage between the data sets than white women (7.1%, 7.3% and 7.6% unlinked compared with 5.7%); women with ethnicity recorded as South Asian were more likely to have linked data (4.6% unlinked) (online supplemental table 4).

DISCUSSION

Main findings

Ethnicity is complete in administrative hospital records for 91% of women giving birth in England. Overall, administrative and maternity data sets demonstrated very good agreement on aggregated ethnicity group, with κ over 0.85. However, there was poor agreement on the recording of mixed ethnicity, with a substantial proportion of those women coded as mixed ethnicity in HES recorded as white in MIS. In addition, women who had their ethnicity coded as black or mixed in their maternity record were less likely to have their record linked to an administrative record. Estimates of associations between ethnicity and each of a common and uncommon outcome were largely unaffected by the data source for ethnicity.

These results indicate that ethnicity in HES for women giving birth in England is highly complete, with good validity when compared with other data sources, and can be used to draw robust conclusions about associations between aggregated ethnicity groups and outcomes. The exception is with the coding of mixed and other ethnicity, for which there is a coding issue and results are not entirely robust to the choice of data source. Furthermore, for analyses using linked data sets, statistical approaches such as methods of imputation for missing data, are needed to deal with the lower linkage rate for women from black and mixed ethnic backgrounds so that these women are not under-represented in such studies. Studies which are restricted to only those individuals with complete information about ethnic group may exclude a substantial proportion (in our study, 9%) of the population.

Strengths and limitations

This study uses a large data set of self-reported ethnicity in a young, ethnically diverse population to validate ethnicity in HES. MIS have been in widespread use for more than a decade; the recording of this information was mandatory at the time of coding[15] and is known to be used for quality monitoring.[7 16] Primary data collection on self-reported ethnicity would have to be extensive to ensure appropriate representativeness and this is expensive and logistically challenging. Our approach, using two routine data sets to establish validity, ensures the study is robust while maintaining feasibility and cost-effectiveness.

The main limitation of this study is that it is restricted to largely healthy women of childbearing age. However, there is no reason to think that these findings would not be translatable, and that the quality of ethnicity data would not be as good, in other groups of healthcare service users. A further limitation is that the two data sources may not be entirely independent; it is possible that in some hospital settings or in some cases, both sources are derived from the woman's reported ethnic group at the time of booking her pregnancy (eg, if coding in both data sets is derived from a single set of paper medical notes).

Table 3 Rates of emergency caesarean section and obstetric anal sphincter injury by ethnic group using both HES and MIS coding structures, among 1 056 029 women with a record in both data sets who had a singleton term birth between 1 April 2015 and 31 March 2017

	Rate of emergency caesarean section				Rate of obstetric anal sphincter injury			
	Using ethnic group in MIS		Using ethnic group in HES		Using ethnic group in MIS		Using ethnic group in HES	
	Rate per 100* (95% CI‡)	Crude RR† (95% CI‡)	Rate per 100* (95% CI‡)	Crude RR† (95% CI‡)	Rate per 100* (95% CI‡)	Crude RR† (95% CI‡)	Rate per 100* (95% CI‡)	Crude RR† (95% CI‡)
All	14.09 (14.02 to 14.16)		14.09 (14.02 to 14.16)		2.80 (2.77 to 2.83)		2.80 (2.77 to 2.83)	
Ethnic group								
White	13.01 (12.93 to 13.09)	Ref	13.00 (12.93 to 13.08)	Ref	2.63 (2.60 to 2.67)	Ref	2.65 (2.62 to 2.69)	Ref
South Asian	16.88 (16.66 to 17.10)	1.30 (1.28 to 1.32)	16.82 (16.60 to 17.04)	1.29 (1.27 to 1.31)	3.73 (3.62 to 3.84)	1.42 (1.37 to 1.46)	3.78 (3.67 to 3.90)	1.42 (1.38 to 1.47)
Black	19.94 (19.58 to 20.31)	1.53 (1.50 to 1.57)	20.04 (19.68 to 20.40)	1.54 (1.51 to 1.57)	2.00 (1.87 to 2.13)	0.76 (0.71 to 0.81)	2.05 (1.92 to 2.18)	0.77 (0.72 to 0.82)
Mixed	14.88 (14.36 to 15.41)	1.14 (1.10 to 1.19)	15.26 (14.90 to 15.62)	1.17 (1.14 to 1.20)	2.09 (1.88 to 2.31)	0.79 (0.71 to 0.88)	2.19 (2.05 to 2.34)	0.83 (0.77 to 0.89)
Other	15.15 (14.81 to 15.50)	1.16 (1.14 to 1.19)	14.53 (14.17 to 14.90)	1.16 (1.12 to 1.19)	2.94 (2.78 to 3.11)	1.12 (1.05 to 1.18)	3.22 (3.04 to 3.41)	1.21 (1.14 to 1.29)
Not stated/ missing	15.65 (15.42 to 15.89)	1.20 (1.18 to 1.22)	15.49 (15.25 to 15.72)	1.19 (1.17 to 1.21)	3.45 (3.33 to 3.56)	1.31 (1.26 to 1.36)	3.26 (3.15 to 3.38)	1.23 (1.18 to 1.28)

*Rates per 100 (%) are presented to two decimal places for comparison purposes.
†Rate ratio.
‡CI.
HES, Hospital Episode Statistics; MIS, maternity information system.

Comparison with existing literature

In common with previous studies in other areas of health and older populations, we found that recording is more often inconsistent between data sets in mixed ethnic groups.[4 5] Previous studies have demonstrated that the quality of routinely collected ethnicity data in HES has increased over time.[4] We provide up-to-date information about the validity of ethnicity recording in HES, and additionally demonstrate that completeness of information required for linkage to external data sets is lower in minority ethnic groups.

Our cohort has a higher proportion of non-white women than the 2011 census, and particularly of women from South Asian backgrounds. This finding may be partially explained by population changes in the intervening years, but also aligns with previous evidence that women in South Asian groups, particularly Pakistani and Bangladeshi women, have a higher fertility rate than other ethnic groups in the UK.[17]

Our finding that women from minority ethnic groups are less likely to have the relevant information to enable linkage to other data sets including HES has been demonstrated elsewhere.[18] This is an important source of potential bias in analysis.

Implications

COVID-19 has emphasised the extent to which existing ethnic and socioeconomic inequalities continue to govern health outcomes.[1 19] In women giving birth, as across many areas of healthcare, it is well recognised that those from non-white ethnic groups experience poorer outcomes in the UK and across the world.[20–25] Reducing these inequalities requires a multifaceted approach, including access to good-quality data for monitoring care and outcomes stratified by ethnic group.[2] Electronic health records offer the potential to understand the associations between ethnicity and healthcare and outcomes in more detail, using statistical methods to understand to what extent associations are mediated through other factors such as socioeconomic deprivation and comorbidities. The findings of this study demonstrate that such studies could draw robust conclusions.

The potential of these analyses is, however, limited by incompleteness, inconsistencies and selective missingness in records for individuals from ethnic minority groups, including missing identifying information which may inhibit linkage. Reasons for this are likely to be multifactorial. Women from ethnic minorities are more likely to be recent immigrants to the UK and therefore to have no NHS number, which would enable linkage from their maternity records to HES. Women born outside the UK or in ethnic minority groups are also more likely to book late for antenatal care, which may limit the completeness of their data.[21 26 27]

Among individuals from mixed groups, while there is increased discrepancy between data sets the coding is not always fully conflicting, with many women recorded as a mix of two ethnicities in one data set recorded as only one of these in the other data set. This may be due to limitations in either or both of the design of the data collection framework and the input of the data.[2] The design of the current classification system is limited: for many people from mixed ethnic groups, which are heterogeneous, there are not appropriate categories for inclusion. This may directly affect the data input: when faced with a classification which does not adequately reflect their ethnic group, individuals may default to a choice which is consistent with societal expectations and inbuilt structural racism,[2] which may in part explain why in this study 42.6% of women who were coded in HES at birth as mixed reported their ethnicity to their midwife as white. Furthermore, inconsistent input may reflect true variation in self-perceived ethnicity: there is evidence from sibling studies that there may be uncertainty about parental ethnic origin, leading to inconsistent self-reports of ethnic group.[28] Some established minority groups, for example, mixed groups which do not fall into available categories (eg, mixed black/South Asian), are not explicitly included in the current classification system. This lack of inclusion limits appropriate classification, introducing inconsistencies in the data and preventing studies from establishing health outcomes in these minority groups.

For researchers and policymakers using this data, it is important to understand the potential biases introduced by misclassification and missing information. Robustness can be improved by using linked data sets to improve completeness and performing sensitivity analyses to assess bias in recording of ethnicity. The strength of analyses can be further improved by clear approaches to missing data: if, as in this study, other linked data sources exist, these can be used to inform imputation procedures for missing data. Rather than simply infilling values from one data set into another, values of ethnicity in one data set can be included in a model to impute missing values in the other data set using multiple imputation. This approach has the advantage that it takes into account the uncertainty due to missing data while incorporating the (very informative) information in the other data set.

We recommend that those using ethnicity data in HES where possible test their results by repeating their analysis using other available primary sources, and that HES is used primarily to draw conclusions about associations between aggregated ethnic group and outcomes, with use of individual ethnic groups treated more cautiously, particularly in mixed and other ethnic groups.

CONCLUSIONS

Our findings support the validity of the use of ethnicity, collapsed into aggregated groups of white/South Asian/black/mixed/other, in administrative hospital data in England: both for monitoring care by ethnic group and to understand the associations between ethnic group and outcomes. However, while ascertainment of ethnic group can be improved by using multiple data sources, there remains a need to improve the completeness and

accuracy of recording, particularly among people from mixed ethnic groups, where reporting may be limited by a lack of appropriate categories and may be vulnerable to inconsistencies in self-reporting. Researchers and analysts should be aware of the potential for misclassification bias, particularly among mixed and other ethnic groups and when the most granular level of available data are used. Analysts should also be aware of the potential for linkage bias due to lower levels of identifying information, required for linkage, in records of individuals from ethnic minority groups. National efforts are required to improve the quality, completeness and accuracy of coding of ethnic group in administrative hospital data; to ensure equity in the recording of identifying information; and to provide appropriate and up-to-date classification systems for ethnicity.

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Contributors JEJ and KW conceived the study. JEJ and AF performed the analyses. JEJ, AF, MC, IGU, DP and KW evaluated the results. JEJ wrote the first draft. JEJ, AF, MC, IGU, DP and KW revised the paper. KW is senior author.

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Competing interests None declared.

Patient consent for publication Not required.

Ethics approval This study used data collected to evaluate service provision and performance and therefore it was exempt from ethical review by the NHS Health Research Authority. The use of data without patient consent was approved by the Confidentiality Advisory Group of the NHS Health Research Authority for the purpose of national clinical audit and health service evaluation (16/CAG/0058).

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Table S1. Agreement (%) between ethnicity recorded in HES, and ethnicity recorded in MIS datasets, among 1 056 029 women with a record in both datasets

			HES																
			Missing	White			Mixed				South Asian				Black			Other Stated	
				White British	White Irish	Other White	White/ Black Caribbean	White /Black African	White / S Asian	Other Mixed	Indian	Pakistani	Bangladeshi	Other S Asian	Caribbean	African	Other Black	Chinese	Other
MIS	Missing		48%	27%	0%	9%	1%	0%	1%	2%	1%	1%	1%	2%	1%	2%	1%	0%	2%
	White	White British	4%	92%	0%	1%	0%	0%	0%	1%	0%	0%	0%	0%	0%	0%	0%	0%	0%
		White Irish	5%	25%	60%	6%	0%	0%	1%	1%	0%	0%	0%	0%	0%	0%	0%	0%	0%
		Other White	5%	11%	0%	77%	0%	0%	1%	2%	0%	0%	0%	0%	0%	0%	0%	0%	3%
	Mixed	White /Black Caribbean	5%	8%	0%	1%	65%	2%	0%	9%	0%	0%	0%	0%	4%	1%	2%	0%	2%
		White /Black African	7%	4%	0%	2%	6%	53%	0%	7%	0%	0%	0%	1%	1%	14%	3%	0%	2%
		White /S Asian	5%	12%	0%	3%	0%	0%	59%	7%	2%	3%	1%	4%	0%	0%	0%	0%	3%
		Other Mixed	5%	8%	0%	8%	5%	1%	2%	56%	1%	1%	0%	2%	2%	2%	1%	0%	5%
	South Asian	Indian	6%	1%	0%	0%	0%	0%	2%	1%	83%	2%	0%	4%	0%	0%	0%	0%	1%
		Pakistani	6%	1%	0%	0%	0%	0%	0%	0%	1%	88%	0%	2%	0%	0%	0%	0%	1%
		Bangladeshi	4%	0%	0%	0%	0%	0%	0%	1%	1%	2%	88%	2%	0%	0%	0%	0%	1%
		Other S Asian	5%	1%	0%	2%	0%	0%	3%	3%	6%	4%	2%	65%	0%	1%	0%	1%	7%
	Black	Caribbean	5%	1%	0%	0%	6%	1%	0%	3%	0%	0%	0%	0%	72%	5%	5%	0%	1%
		African	5%	1%	0%	0%	0%	2%	0%	1%	0%	0%	0%	1%	1%	84%	3%	0%	2%
		Other Black	5%	1%	0%	1%	2%	2%	0%	3%	0%	0%	0%	1%	8%	30%	45%	0%	2%
	Other Stated	Chinese	5%	1%	0%	1%	0%	0%	5%	5%	0%	0%	0%	6%	0%	0%	0%	73%	3%
		Other	6%	4%	0%	14%	0%	0%	1%	4%	2%	1%	0%	6%	0%	2%	1%	1%	58%

Table S2. Rates of emergency caesarean section and obstetric anal sphincter injury by ethnic group using both HES and MIS coding structures, among 1 056 029 women with a record in both datasets

	Rate of emergency caesarean section				Rate of obstetric anal sphincter injury			
	Using ethnic group in MIS		Using ethnic group in HES		Using ethnic group in MIS		Using ethnic group in HES	
	Rate (95% CI), %	Crude RR (95% CI)	Rate (95% CI), %	Crude RR	Rate (95% CI), %	Crude RR	Rate (95% CI), %	Crude RR
All	14.09 (14.02, 14.16)		14.09 (14.02, 14.16)		2.80 (2.77, 2.83)		2.80 (2.77, 2.83)	
Ethnic group								
White British	12.76 (12.68, 12.85)	Ref	12.76 (12.68, 12.84)	Ref	2.67 (2.63, 2.71)	Ref	2.67 (2.63, 2.71)	Ref
White Irish	15.31 (14.29, 16.36)	1.20 (1.11, 1.29)	13.94 (12.94, 14.99)	1.09 (1.01, 1.18)	2.70 (2.26, 3.20)	1.01 (0.85, 1.21)	3.37 (2.86, 3.94)	1.26 (1.07, 1.48)
White Other	14.24 (14.04, 14.45)	1.12 (1.10, 1.13)	14.33 (14.13, 14.54)	1.12 (1.10, 1.14)	2.46 (2.38, 2.56)	0.92 (0.89, 0.96)	2.53 (2.44, 2.62)	0.95 (0.91, 0.99)
Indian	19.33 (18.90, 19.76)	1.51 (1.48, 1.53)	19.31 (18.87, 19.74)	1.51 (1.47, 1.55)	5.15 (4.91, 5.39)	1.93 (1.84, 2.03)	5.32 (5.08, 5.57)	1.99 (1.89, 2.09)
Pakistani	14.50 (14.17, 14.83)	1.14 (1.11, 1.17)	14.61 (14.28, 14.95)	1.15 (1.12, 1.17)	2.94 (2.79, 3.11)	1.10 (1.04, 1.17)	3.00 (2.84, 3.16)	1.12 (1.06, 1.19)
Bangladeshi	17.28 (16.68, 17.89)	1.36 (1.11, 1.66)	17.14 (16.54, 17.75)	1.34 (1.29, 1.40)	2.76 (2.51, 3.03)	1.04 (0.94, 1.14)	2.84 (2.58, 3.12)	1.06 (0.97, 1.17)
Other Asian	17.68 (17.18, 18.20)	1.39 (1.34, 1.43)	17.34 (16.88, 17.85)	1.36 (1.32, 1.40)	3.84 (3.59, 4.10)	1.44 (1.34, 1.54)	3.77 (3.52, 4.03)	1.41 (1.32, 1.51)
Caribbean	17.45 (16.64, 18.28)	1.37 (1.30, 1.44)	17.62 (16.81, 18.46)	1.38 (1.31, 1.45)	1.47 (1.22, 1.75)	0.55 (0.46, 0.66)	1.38 (1.13, 1.17)	0.52 (0.43, 0.62)
African	20.72 (20.26, 21.17)	1.62 (1.58, 1.67)	20.62 (20.18, 21.06)	1.62 (1.58, 1.66)	2.15 (1.99, 2.32)	0.81 (0.75, 0.87)	2.20 (2.05, 2.37)	0.82 (0.77, 0.89)
Other Black	19.60 (18.73, 20.49)	1.54 (1.46, 1.61)	20.19 (19.20, 21.20)	1.58 (1.50, 1.67)	1.98 (1.68, 2.31)	0.74 (0.63, 0.87)	2.11 (1.77, 2.49)	0.79 (0.66, 0.94)
Chinese	13.81 (13.01, 14.65)	1.08 (1.02, 1.15)	15.26 (14.90, 15.62)	1.01 (0.94, 1.09)	3.98 (3.53, 4.47)	1.49 (1.33, 1.68)	4.38 (3.88, 4.93)	1.64 (1.45, 1.85)
Mixed	14.88 (14.36, 15.41)	1.17 (1.12, 1.21)	15.26 (14.90, 15.62)	1.20 (1.16, 1.23)	2.09 (1.88, 2.31)	0.78 (0.71, 0.87)	2.19 (2,05, 2.34)	0.82 (0.77, 0.88)
Other	15.42 (15.04, 15.81)	1.21 (1.18, 1.24)	15.45 (15.05, 15.89)	1.21 (1.18, 1.25)	2.73 (2.56, 2.91)	1.03 (0.96, 1.10)	2.98 (2.80, 3.19)	1.12 (1.05, 1.20)
Not stated/Missing	15.65 (15.42, 15.89)	1.23 (1.20, 1.25)	15.49 (15.25, 15.72)	1.21 (1.19, 1.24)	3.45 (3.33, 3.56)	1.29 (1.25, 1.34)	3.26 (3.15, 3.38)	1.22 (1.17, 1.27)

Table S3. Comparison of ethnicity recorded in MIS and HES for 1 237 213 women who gave birth in England between 1st April 2015 and 31st March 2017 with that of women age 16-49 from the 2011 Census in England

	2011 Census: Women age 16-49		Maternity Information Systems			Hospital Episode Statistics		
Ethnic group	n	%	n	% (all records)	% (useable records)	n	% (all records)	% (useable records)
All categories	12 393 707		1 237 213			1 165 252		
White	10 236 208	82.6%	863 499	69.8%	77.1%	804 686	69.1%	75.7%
Mixed/multiple ethnic group	280 721	2.3%	21 032	1.7%	1.9%	42 269	3.6%	4.0%
South Asian/Asian British	1 192 839	9.6%	132 178	10.7%	11.8%	124 341	10.7%	11.7%
Black/African/Caribbean/ Black British	541 000	4.4%	56 179	4.5%	5.0%	52 572	4.5%	4.9%
Other ethnic group	142 939	1.2%	47 510	3.8%	4.2%	39 713	3.4%	3.7%
Not stated or not recorded			116 815	9.4%		101 709	8.7%	
Total useable codes			1 120 398	90.6%		1 063 543	91.3%	

Table S4. Linkage between MIS and HES for 1 237 213 women who gave birth in England between 1st April 2015 and 31st March 2017

Recorded ethnic group in MIS	Linked to HES (%)	Unable to be linked to HES (%)
White	863 499 (94.3%)	49 007 (5.7%)
S Asian	132 178 (95.4%)	6 023 (4.6%)
Black	56 179 (92.9%)	3 978 (7.1%)
Mixed	21 032 (92.7%)	1 531 (7.3%)
Other	47 510 (94.6%)	2 564 (5.4%)
Not stated /Missing	116 815 (92.4%)	8 858 (7.6%)
Total	**1 165 252 (94.1%)**	**71 961 (5.9%)**

4. Results Chapter: Associations between ethnicity and admission to intensive care among women giving birth

In this part of my thesis, I linked maternity data to intensive care admission data. In the linked dataset, I explored reasons for admission and used logistic regression models to explore the association between ethnicity and intensive care admission. The findings of this analysis have been published as a research paper.

4.1 Research Paper 2

Associations between ethnicity and admission to intensive care among women giving birth: a cohort study

This article has been accepted for publication in *BJOG* (published online 21 September 2021) following peer review and can also be accessed online at https://doi.org/10.1111/1471-0528.16891

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First Name(s)	Jennifer		
Surname/Family Name	Jardine		
Thesis Title	A study of risk factors of maternity outcomes using large, routinely collected electronic datasets		
Primary Supervisor	Kate Walker		

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Research Article

Associations between ethnicity and admission to intensive care among women giving birth: a cohort study

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Accepted 26 May 2021.

Objective To determine the association between ethnic group and likelihood of admission to intensive care in pregnancy and the postnatal period.

Design Cohort study.

Setting Maternity and intensive care units in England and Wales.

Population or sample A total of 631 851 women who had a record of a registerable birth between 1 April 2015 and 31 March 2016 in a database used for national audit.

Methods Logistic regression analyses of linked maternity and intensive care records, with multiple imputation to account for missing data.

Main outcome measures Admission to intensive care in pregnancy or postnatal period to 6 weeks after birth.

Results In all, 2.24 per 1000 maternities were associated with intensive care admission. Black women were more than twice as likely as women from other ethnic groups to be admitted (odds ratio [OR] 2.21, 95% CI 1.82–2.68). This association was only partially explained by demographic, lifestyle, pregnancy and birth factors (adjusted OR 1.69, 95% CI 1.37–2.09). A higher proportion of intensive care admissions in Black women were for obstetric haemorrhage than in women from other ethnic groups.

Conclusions Black women have an increased risk of intensive care admission that cannot be explained by demographic, health, lifestyle, pregnancy and birth factors. Clinical and policy intervention should focus on the early identification and management of severe illness, particularly obstetric haemorrhage, in Black women, in order to reduce inequalities in intensive care admission.

Keywords ethnicity, obstetric haemorrhage, severe maternal morbidity.

Tweetable abstract Black women are almost twice as likely as White women to be admitted to intensive care during pregnancy and the postpartum period; this risk remains after accounting for demographic, health, lifestyle, pregnancy and birth factors.

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Introduction

Intensive care admission signifies severe illness requiring additional care and monitoring, with a high risk of mortality. In pregnancy and birth, there are additional short-term and long-term consequences: during pregnancy, severe illness is associated with problems with fetal growth and development, and preterm birth; postnatal admissions frequently result in separation of the mother and baby, with associated impacts on breastfeeding rates and maternal mental health.[1] Admission to intensive care is considered a marker of severe maternal morbidity.[2,3]

Women from ethnic minority groups suffer poorer outcomes than women from White ethnic groups during pregnancy and birth in the UK.[4–7] In the triennium 2016–18, Black women were over four times more likely to die in pregnancy and childbirth than White women.[8] This is similar to the inequalities that exist in other high-income

countries.[2,3,9–13] It is unclear to what extent this observed association is explained by differences between ethnic groups in demographic, lifestyle, pregnancy and birth factors, including co-morbidities such as gestational diabetes and hypertension, which are more common in women of ethnic minority backgrounds.[14,15] The extent to which intensive care admissions in pregnancy and birth vary by country of origin has been examined in cohorts from the Netherlands[16] and Canada;[17] in both countries, migrant women were more likely to have admissions to intensive care. Variation by ethnic group has been examined in the USA,[18] where Black women are more likely to be admitted. No study has previously examined ethnic variation in the UK. Investigating variation in intensive care admission may offer useful insights into potential mechanisms for addressing ethnic inequalities in maternal morbidity and mortality.[2,3]

This study uses linked maternity and intensive care data from England and Wales, collected for the purposes of national audits, to evaluate the relationship between maternal ethnicity and admissions to intensive care.[19–21] Routinely collected healthcare data sources offer efficient access to large population samples and the opportunity to examine uncommon outcomes such as admission to intensive care and any associations with maternal demographics or characteristics.

The aims of this study were: (1) to quantify the association between ethnicity and severe morbidity requiring admission to intensive care in pregnancy and the 6 weeks following birth; (2) to understand how this association is explained by adjustment for demographic, lifestyle, pregnancy and birth characteristics and (3) to understand the reasons for maternal admission to critical care among different ethnic groups.

Methods

Data sources

We used a national maternity data set that was linked to hospital admission data for the purposes of a national audit.[21] This included data routinely collected in the course of clinical care, which was extracted from the maternity information systems (MIS) used in National Health Service (NHS) hospitals in England and Wales. In England, MIS data were linked at patient level using the mother's and baby's dates of birth, NHS numbers and postcodes to records from the Hospital Episode Statistics (HES), an administrative database containing records of all admissions to English NHS hospitals. Linkage was performed using a deterministic algorithm by a trusted third party (NHS Digital). In Wales, data from MIS are collated to form the Maternity Indicators data set (known as MIds). This was linked at patient level using NHS numbers and dates of birth to the Patient Episodes Database for Wales (PEDW), an administrative data set by the National Welsh Informatics Service. Details of linkage processes are available elsewhere.[21] The linked data contained information on births between the 1 April 2015 and 31 March 2016 in five of six boards in Wales and 128 of 134 trusts in England with an obstetric unit.[21]

The maternity data set was also linked to the Intensive Care National Audit and Research Centre (ICNARC) Case Mix Programme Data set. ICNARC routinely collects information on all admissions to adult general intensive care units in England, Wales and Northern Ireland, together with some specialist intensive care units. The ICNARC Case Mix Programme data set contains information about the source, type and reason for admission, and observations, diagnoses and procedures that occur within the intensive care unit.[19,22] Maternal identifiers (NHS number, date of birth and postcode) for women who gave birth in England and Wales were used by ICNARC to supply records matching all or some of these identifiers for women admitted to intensive care in England and Wales up to 31 March 2017. Further details about the linkage process are available.[22]

Definition of variables

Ethnicity was primarily derived from the hospital admission record (HES/PEDW) and infilled where not useable (unknown [ethnos codes 9, X, Z] or missing) from the MIS record. Ethnicity was categorised into groups: White, Asian or British Asian, Black or Black British, Mixed, Other and Unknown or missing. Ethnicity is self-reported to midwives at the time of booking pregnancy and is well, and generally consistently, recorded in hospital data in England at the level of these groups; there are inconsistencies between more granular classifications (e.g. Black African, Black Caribbean may be coded interchangeably).[23]

A woman was defined as having an intensive care admission if she had one or more recorded admissions to an intensive care unit in the ICNARC data set within the time frame of estimated date of conception to 6 weeks after birth. The plausible date of conception was calculated as the date of birth plus 14 days minus the gestation in days at birth. A woman was recorded as having a level 3 admission if her admitting or discharging level of care was level 3 (i.e. requiring ventilation support, or with multi-organ failure).

Demographic factors included maternal age and socio-economic status. Maternal age was grouped into six categories (16–24, 25–29, 30–34, 35–39, 40–44, 45 or older). Wider age-bands were used for women under 25 and over 44 years because of the small numbers of women admitted to intensive care at these ages. Socio-economic status was identified using the index of multiple deprivation of the

woman's postcode at the time of birth in England and the postcode of her GP surgery in Wales. The index of multiple deprivation is an area-level ranking of relative deprivation that incorporates information about income, education, employment, crime and the living environment for each of the 32 844 lower super output areas in England and 1909 areas in Wales used for population analysis.[24] Using these rankings, areas were separated into population quintiles of relative deprivation.[25]

Obstetric history included parity (with parity of three or more handled as a single category) and previous caesarean section. Lifestyle factors included maternal body mass index (BMI) and smoking status recorded in MIS at the time of booking the pregnancy. BMI was handled using WHO categories.[26]

Pregnancy and birth factors included: mode of birth (unassisted vaginal, instrumental vaginal or caesarean section); preterm birth (occurring before 37 weeks of gestation), multiple birth (twins or higher-order multiple) and stillbirth.

Maternal health conditions complicating pregnancy were identified using the International Classification of Diseases, tenth revision codes[27] recorded in HES/PEDW in the birth episode. These included diabetes (pre-existing and gestational, handled together because of the low frequency of pre-existing diabetes), pre-eclampsia, pre-existing or gestational hypertension, and placental conditions of morbidly adherent placenta or abruption.

Details of all coding frameworks used are available in Table S1.

Analysis

The primary outcome of interest was admission to an intensive care unit during pregnancy, birth and the postnatal period up to 6 weeks after birth.

To estimate crude odds ratios between ethnic group and intensive care admission, univariate logistic regression models were used. To investigate possible explanations for associations, a series of multivariable logistic regression models with robust estimates of standard errors to account for clustering within hospitals were used to estimate adjusted odds ratios. The first model adjusted for demographic factors: maternal age, ethnic and socio-economic group. The second added the woman's obstetric history (parity and whether she had a previous caesarean section) and lifestyle factors that were present at the onset of pregnancy (BMI and smoking status). The third, 'full' model additionally incorporated health conditions (diabetes, pre-eclampsia, hypertension, cardiac conditions and placental conditions) and pregnancy and birth factors (multiplicity, mode of birth, preterm birth and stillbirth).

Thresholds for admission to intensive care are known to vary with the provision of enhanced care for critically unwell women within maternity services, as some units provide higher-level care within maternity units and only admissions to critical care units are captured in ICNARC.[20,22,28] However, care requiring ventilation and for multi-organ failure (level 3) is provided only in intensive care units. For this reason, a sensitivity analysis was carried out using level 3 admission as the outcome in the fully adjusted model.

Levels of missing data were low (<4%) for the majority of variables included in the analysis. However, 6% of women's records were missing information about postcode, which was used to identify socio-economic status, 12% were missing information about ethnicity in both data sources, and 23% were missing information about each of smoking status and BMI at the time of booking. In the regression analyses, multiple imputation using chained equations was used to handle missing values, with regression coefficients estimated using ten imputed data sets and pooled using Rubin's rules.[29] Variables used in the imputed data sets included all variables in the multivariable regressions, and also the year of birth and the hospital in which the woman gave birth. Multiple imputation requires the assumption that data are missing at random given the variables used in the imputation model, which may not be met, in particular for ethnicity, smoking status or BMI. To test the sensitivity of findings to these assumptions, the fully adjusted analysis was repeated using only those records with complete information; this has been found to be robust to a wider range of missingness assumptions.[30]

Primary reasons for admission were available from the intensive care record and were grouped into those directly related to pregnancy and birth and those indirectly related to pregnancy and birth, following a system used for classifying maternal death.[7,8,22] Details of this classification are available in Table S2. The proportions admitted for each group of reasons were presented by ethnic group.

All analyses were performed in Stata version 14.1 (StataCorp, College Station, TX, USA).

Results

A total of 631 851 women were included in the linked data set, of whom 1414 were recorded as being admitted to intensive care during pregnancy, birth and the postnatal period up to 6 weeks, a rate of 2.24 per 1000 maternities. These women each had at least one and a maximum of three recorded admissions to intensive care, with a total of 1619 admissions overall; 261 women (18.5%) had their first admission to intensive care before birth. Of the women admitted to intensive care, 22.3% were recorded as being from ethnic minority groups. (Table 1, Figure S1).

Women were more than twice as likely to be admitted to intensive care if their recorded ethnicity was Black (4.7

Table 1. Characteristics of 631 851 women who gave birth in England and Wales in 2015/16, and 1414 of those women with recorded admissions to intensive care in pregnancy or the postpartum period up to 6 weeks

	All women		Women admitted to intensive care	Rate (per 1000 maternities) admitted		All women		Women admitted to intensive care	Rate (per 1000 maternities) admitted
Risk factor	***n***	**%**			**Risk factor**	***n***	**%**	***n***	
All	631 851		1 414	2.24					
Ethnic origin					Smoking status				
White	434 297	77.7	931	2.14	Non-smoker	417 542	85.6	923	2.21
Asian	63 795	11.4	147	2.30	Smoker	70 078	14.4	182	2.60
Black	26 900	4.8	125	4.65	Missing	144 231	22.8	309	2.14
Mixed	10 078	1.8	19	1.89					
Other	23 763	4.3	54	2.27	Previous caesarean section	87 501	14.3	347	3.97
Missing	73 018	11.6	138	1.89	Missing	20 149	3.2	40	1.99
Age group (years)					Recorded diagnoses				
Under 25	115 669	18.9	270	2.33	Hypertension	3208	0.5	28	8.73
25–29	174 440	28.6	297	1.70	Placental factors	5917	0.9	143	24.17
30–34	190 075	31.1	413	2.17	Pre-eclampsia	11 484	1.8	188	16.37
35–39	105 849	17.3	298	2.82	Cardiac conditions	2036	0.3	67	32.91
40–44	23 340	3.8	92	3.94	Diabetes	32 706	5.2	143	4.37
45 or older	1667	0.3	15	9.00					
Missing	20 811	3.3	29	1.39	Gestation				
					Term	565 436	92.9	865	1.53
Socio-economic deprivation (quintile)					Preterm	42 889	7.1	492	11.47
Least deprived (1)	99 438	16.8	210	2.11	Missing	23 526	3.7	57	2.42
2	84 112	14.2	173	2.06					
3	112 183	18.9	236	2.10	Multiplicity				
4	134 759	22.8	294	2.18	Singleton birth	613 669	97.1	1 317	2.15
Most deprived (5)	161 850	27.3	396	2.45	Multiple birth	18 182	2.9	97	5.33
Missing	39 509	6.3	105	2.66					
					Fetal outcome				
Body Mass Index (kg/m^2)					Livebirth	628 818	99.5	1 345	2.14
<18.5	14 347	2.9	32	2.23	Stillbirth	3 033	0.5	69	22.75
18.5–24.9	236 456	48.4	457	1.93					
25.0–29.9	131 161	26.8	295	2.25	Mode of birth				
30.0–34.9	67 672	13.8	163	2.41	Unassisted vaginal	380 772	61.6	328	0.86
35.0–39.9	25 832	5.2	81	3.14	Instrumental	75 280	12.2	115	1.52
≥40.0	13 447	2.8	62	4.61	Caesarean section	161 665	26.2	951	5.88
Missing	142936	22.6	324	2.27	Missing	14 134	2.2	20	1.42
Parity									
0	264 133	42.7	621	2.35					
1	214 572	34.7	396	1.85					
2	86 037	13.9	189	2.20					
3 or more	53 208	8.6	175	3.29					
Missing	13 901	2.2	33	2.37					

per 1000 maternities) than White (2.1 per 1000 maternities; crude odds ratio [OR] for Black women compared with White women, 2.21, 95% CI 1.82–2.68) but no difference was observed if the recorded ethnicity was Asian (2.3 per 1000), Mixed (1.9 per 1000) or Other (2.3 per 1000) (Tables 1 and 2).

We sought to understand the extent to which adjustment for various characteristics and risk factors could explain the higher intensive care admissions for Black women compared with White women. This was explored using three different models: the first of which adjusted for demographic factors, the second additionally for obstetric history

Table 2. Maternal and pregnancy characteristics associated with admission to intensive care during pregnancy and the early postpartum period up to 6 weeks among women who gave birth in England and Wales in 2015/16

Characteristic	Crude OR	Model 1* (Demographic)		Model 2* (Lifestyle, history)		Model 3* (Pregnancy and birth)	
		Adjusted OR (95% CI)	*P* value**	Adjusted OR (95% CI)	*P* value**	Adjusted OR (95% CI)	*P* value**
Ethnic origin							
White	Ref	Ref	<0.001	Ref	<0.001	Ref	<0.001
Asian	1.08 (0.91–1.28)	1.06 (0.89–1.27)		1.12 (0.94–1.34)		0.98 (0.81–1.19)	
Black	2.21 (1.82–2.68)	2.02 (1.65–2.48)		1.94 (1.57–2.41)		1.69 (1.37–2.09)	
Mixed	0.85 (0.54–1.35)	0.83 (0.52–1.32)		0.84 (0.53–1.33)		0.83 (0.52–1.33)	
Other	1.04 (0.79–1.36)	1.00 (0.76–1.32)		1.06 (0.80–1.40)		1.07 (0.79–1.43)	
Age group (years)							
Under 25	1.37 (1.16–1.62)	1.38 (1.17–1.63)	<0.001	1.35 (1.14–1.60)	<0.001	1.52 (1.27–1.82)	<0.001
25–29	Ref	Ref		Ref		Ref	
30–34	1.27 (1.09–1.47)	1.29 (1.11–1.50)		1.28 (1.10–1.49)		1.15 (0.99–1.34)	
35–39	1.64 (1.40–1.93)	1.66 (1.41–1.95)		1.61 (1.36–1.90)		1.28 (1.08–1.51)	
40–44	2.31 (1.82–2.92)	2.26 (1.78–2.86)		2.07 (1.62–2.64)		1.31 (1.01–1.70)	
45 or older	5.35 (3.17–9.04)	4.89 (2.89–8.27)		4.39 (2.59–7.47)		2.10 (1.23–3.58)	
Socio-economic deprivation (quintile)							
Least deprived (1)	Ref	Ref	0.44	Ref	0.93	Ref	0.93
2	0.96 (0.79–1.18)	0.98 (0.80–1.20)		0.95 (0.78–1.17)		0.95 (0.77–1.17)	
3	0.99 (0.82–1.20)	1.01 (0.84–1.22)		0.96 (0.79–1.17)		0.93 (0.77–1.13)	
4	1.03 (0.86–1.23)	1.03 (0.85–1.24)		0.95 (0.79–1.15)		0.92 (0.76–1.12)	
Most deprived (5)	1.15 (0.98–1.36)	1.14 (0.95–1.37)		1.01 (0.83–1.22)		0.93 (0.77–1.12)	
BMI (kg/m^2)							
<18.5	1.21 (0.87–1.69)			1.22 (0.88–1.69)	<0.001	1.22 (0.84–1.65)	0.006
18.5–24.9	Ref			Ref		Ref	
25.0–29.9	1.16 (1.01–1.33)			1.11 (0.96–1.28)		0.99 (0.85–1.15)	
30.0–34.9	1.26 (1.05–1.52)			1.15 (0.96–1.38)		0.96 (0.79–1.16)	
35.0–39.9	1.71 (1.33–2.19)			1.46 (1.17–1.83)		1.17 (0.90–1.52)	
≥40.0	2.50 (1.91–3.29)			2.10 (1.61–2.75)		1.64 (1.23–2.17)	
Parity							
0	Ref			Ref	<0.001	Ref	0.008
1	0.79 (0.70–0.90)			0.58 (0.51–0.67)		0.95 (0.82–1.19)	
2	0.94 (0.80–1.11)			0.62 (0.52–0.73)		1.05 (0.86–1.26)	
3 or more	1.40 (1.18–1.66)			0.81 (0.68–0.98)		1.33 (1.09–1.61)	
Smoker	1.20 (1.02–1.42)			1.33 (1.13–1.58)	0.001	1.15 (0.95–1.39)	0.14
Previous caesarean section	2.23 (1.98–2.51)			2.41 (2.10–2.76)	<0.001	0.99 (0.85–1.16)	0.92
Maternal conditions							
Diabetes	2.07 (1.74–2.46)					1.26 (1.04–1.53)	0.02
Pre-eclampsia/eclampsia	8.40 (7.20–9.81)					3.11 (2.59–3.74)	<0.001
Hypertension	3.98 (2.74–5.80)					1.59 (1.04–2.42)	0.03
Placental conditions	12.17 (10.22–14.50)					3.46 (2.84–4.22)	<0.001
Cardiac conditions	15.88 (12.37–20.37)					11.28 (8.62–14.77)	<0.001
Mode of birth							
Unassisted vaginal	Ref					Ref	<0.001
Instrumental	1.78 (1.43–2.20)					2.06 (1.65–2.59)	
Caesarean section	6.81 (6.00–7.73)					5.04 (4.31–5.90)	
Fetal complications							
Preterm birth	7.57 (6.78–8.46)					3.53 (3.06–4.06)	<0.001
Multiple birth	4.11 (3.29–5.14)					1.11 (0.86–1.43)	0.41
Stillbirth	10.86 (8.50–13.87)					6.50 (4.86–8.68)	<0.001

*All models are adjusted for variables shown as complete.
**_P_ values for categorical variables are derived using the Wald test.

and lifestyle factors, and the third for these together with pregnancy and birth factors. The increased risk of intensive care admission for Black women was partially explained by adjustment for demographic factors: maternal age and socio-economic status (adjusted OR [aOR] 2.02, 95% CI 1.65–2.48). Lifestyle factors and obstetric history present at the start of pregnancy explained very little of the association (aOR 1.94, 95% CI 1.57–2.41). More of the association was explained by pregnancy and birth characteristics, including presence of co-morbidities, mode of birth, preterm birth and stillbirth (Table 2). Taking all these factors into account, Black women were 1.7 times more likely to be admitted to intensive care than White women (aOR 1.69, 95% CI 1.37–2.09).

Some complications were associated with particularly high rates of intensive care admission. Following adjustment for demographic, lifestyle, pregnancy and birth factors, women who had pre-eclampsia or placental conditions such as abruption or accreta were three times as likely to be admitted to intensive care (for pre-eclampsia: aOR 3.11, 95% CI 2.59–3.74; for placental conditions: aOR 3.46, 95% CI 2.84–4.22). Women with cardiac conditions were 11 times more likely than women without to be admitted to intensive care (aOR 11.28, 95% CI 8.62–14.77). Women who had a caesarean section were five times as likely (aOR 5.04, 95% CI 4.31–5.90) to be admitted. Women who had a preterm birth were more than three times as likely to be admitted (aOR 3.53, 95% CI 3.06–4.06) and women who had a stillbirth were more than six times as likely (aOR 6.50, 95% CI 4.86–8.68).

These results were robust to a sensitivity analysis restricted to level 3 admissions, although a small increase in risk of intensive care admission in women with diabetes was not apparent in the tighter definition of the outcome. Associations with caesarean birth, placental conditions and stillbirth were stronger with level 3 admission (Table S3). In sensitivity analyses restricted to those women with complete data available (Table S4), the associations with ethnicity were attenuated; this was most evident in the fully adjusted model (Wald *P* value for ethnicity overall 0.09). In these complete case analyses there was much greater uncertainty in the estimates because of the smaller sample size; the adjusted odds ratios for Black ethnicity (in the fully adjusted model, aOR 1.43, 95% CI 95% CI 1.08–1.90) were within the confidence intervals for the results using imputed data (full model aOR 1.69, 95% CI 1.37–2.09).

Two-thirds (67.1%) of admissions were for a reason directly related to pregnancy, such as obstetric haemorrhage, infection, pre-eclampsia and HELLP syndrome (haemolysis, elevated liver enzymes, low platelets) (Figure 1, Table S5). The proportion of admissions that were due to direct, rather than indirect, reasons, and particularly due to obstetric haemorrhage, was higher among women from Black ethnic origin. Forty-two percent of admissions in Black women were for obstetric haemorrhage compared with 34% in White women. Women with no record of

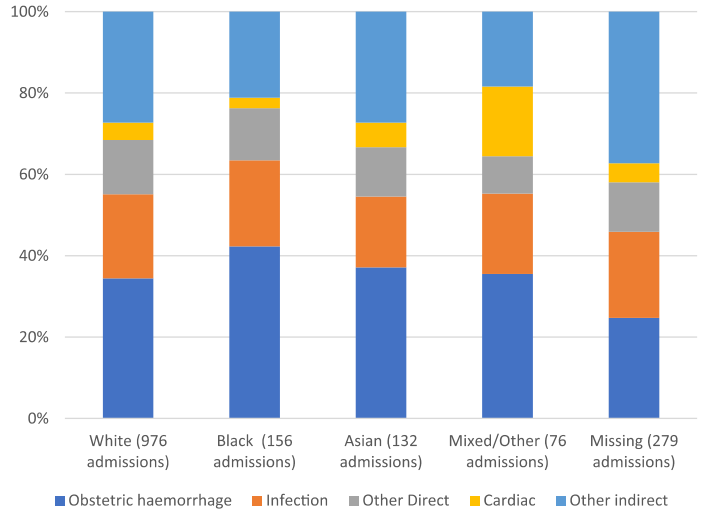

Figure 1. Reasons for admission by ethnic group, for 1340 admissions with complete ethnic group that occurred in pregnancy or the postpartum period for women who gave birth between 1 April 2015 and 31 March 2016.

ethnic origin were more likely to have an admission for an indirect reason.

Discussion

Main findings

Of women who gave birth in England and Wales in 2015/16, 2.24 per 1000 were admitted to intensive care in pregnancy and the 6 weeks after birth. Black women were more than twice as likely as White women to be admitted. This association was only partially explained by adjustment for demographic, lifestyle, pregnancy and birth characteristics. Women with complications, such as placental factors, pre-eclampsia and stillbirth, were much more likely to be admitted to intensive care. These findings were robust to sensitivity analyses using different definitions of the outcome and methods of handling missing data.

Obstetric haemorrhage accounted for a higher proportion of admissions for Black women than for women from other ethnic group.

Strengths and limitations

The main strengths of this study are its size and design. This is a large cohort study using routinely collected data with a high rate of coverage of births in England and Wales (approximately 92%). The use of electronic patient records, collected for payment purposes, reduces the risk of systematic bias: almost all births and intensive care admissions in the UK occur in the NHS. The ICNARC Case Mix Programme data set for evaluating admissions to intensive care is well established and of high quality.[19] Linkage using identifiers such as NHS numbers ensures that matched records are very likely to be true matches, with women identified as having an intensive care admission being highly likely to have been admitted.

Although the linkage method using NHS number, date of birth and postcode is highly specific, the first limitation is in the potential for missed matches.[19,20] Although completeness of identifiers is high in both data sets[19,21] there is no reference standard[22] data set to enable evaluation of the linkage quality. This has the potential to cause bias if ethnicity is associated with the likelihood of complete identifiers. In this data set, any bias would be to an underestimation of effect, as women from ethnic minority groups were less likely to have an NHS number present in the MIS.

Further limitations to this study arise from the missing data within the data set, in particular for ethnicity (12% of records). To account for this, in our primary analyses we use multiple imputation, a methodology that, provided the information about ethnicity is missing at random given all of the other variables in the model, will give unbiased estimates. However, it is possible that this assumption is not met. It is reassuring that our findings are similar in a complete case analysis, where only those records with complete information about all covariates are included, but in this supplementary analysis the association is substantially attenuated; this may be because the sample size is reduced, or because the true association between Black ethnicity and intensive care admission is smaller than in our primary analysis.

The third limitation is the chosen outcome. Admission to intensive care is considered when a woman is too unwell to be cared for in a maternity unit. The capability of maternity units to provide enhanced or high dependency maternity care varies,[31,32] therefore the threshold to consider admission may vary between units. It is possible that our findings could be due to systematically lower admission thresholds in hospitals with higher proportions of Black women. However, similar associations were found when the analysis was limited to women requiring care for multi-organ failure or ventilation (Table S3), therapies not provided outside intensive care settings.[33]

In our analyses we adjust for factors related to the woman's demographics, lifestyle, pregnancy and birth. In women admitted before the day of birth (18.5% of our population) it is possible that the gestation at birth, mode of birth and stillbirth are causally linked to both ethnic group and the antenatal episode of severe illness indicated by intensive care admission. This can introduce a form of bias where the association is inappropriately attenuated.[34] This may partially account for the attenuation of the association between Black ethnicity and likelihood of intensive care admission seen between Model 3 and Model 2.

It may also be that women who were admitted to intensive care differed from those who were not admitted but instead unfortunately died, as the result of a lack of care or escalation as is commonly reported in maternal death.[7,8,35] Data were not available to us for maternal death that occurred outside the hospital admission in which the woman gave birth, limiting the use of death as an alternative outcome in this study. Any change would be small as maternal death is rare, and any bias would be towards an under-estimation of the effect of ethnicity: Black and Asian women are more likely to die during pregnancy and birth in the UK than White women, with the estimated association larger than that seen in our study.[7,8]

Interpretation (in light of other evidence)

The overall rate of admission to intensive care during pregnancy and the postnatal period was similar to that reported in other international studies (2–4:1000).[16,36] Studies from the Netherlands,[16] Canada,[17] and the USA,[18] conducted in local populations, similarly show an association between Black ethnicity or African or Caribbean origin and

admissions to intensive care in pregnancy and the postpartum period. In common with other studies examining severe maternal morbidity in the UK we found no association with socio-economic grouping, reflective of the universal healthcare system.[37]

Studies from the UK Obstetric Surveillance System[4,5,37] have demonstrated that women from Black African and Caribbean ethnic groups are more likely to experience severe morbidity, with a similar reported magnitude of effect. The UK Obstetric Surveillance System also found that women from some Asian ethnic groups (Pakistani and Bengali) were more likely to experience severe maternal morbidity, which we did not find.[4] It is possible that this is masked in our data where we have treated ethnicity in larger groupings to deal with potential coding issues.

The reasons for the association between ethnicity and admission to intensive care or other markers of severe maternal morbidity have been widely hypothesised. Postulated reasons for this association include health at the start of pregnancy, reduced socio-economic status, increased propensity to develop pregnancy-related conditions such as eclampsia, differences in health behaviours, and differences in the way women are treated and listened to during maternity care.[4,5,38–41] In our study, some of the association between ethnicity and intensive care admission was explained by maternal age and co-morbidity, and by pregnancy and birth factors including caesarean birth, preterm birth, placental conditions and stillbirth. However, even following this adjustment, a substantial association remained. We were unable to account for health behaviours, stress, home environment, experiences of maternal care and aspects of structural inequality that may account for the observed associations.[42–44]

In this cohort, intensive care admissions for Black women were more commonly due to obstetric haemorrhage than those for women from other ethnic groups. There is a possible biological explanation: Black women are more likely to have leiomyomata or fibroids, benign tumours of the uterine myometrium that prevent the uterus from contracting, which are associated with an increased risk of postpartum haemorrhage.[45,46] For Black women with increased risk of haemorrhage, appropriate recognition and rapid escalation may avoid the need for additional support and intensive care admission.[47]

A secondary finding of our study was that stillbirth is strongly associated with admission to intensive care. This finding has also been demonstrated in a large study of over 6 million births in California;[48] which found an increased risk of severe maternal morbidity in women with stillbirth (relative risk 4.77, 95% CI 4.53–5.02). There may be common primary causes leading both to stillbirth and maternal admission to intensive care, such as placental abruption. This requires further study, which was not feasible in this analysis because information on timing of stillbirth and other events within labour was limited.

Conclusion

Women of Black ethnicity are more than twice as likely as women of other ethnic backgrounds to be admitted to intensive care during pregnancy and birth. Even when demographic, lifestyle, pregnancy and birth characteristics are taken into account, these women are still 1.7 times more likely to be admitted to intensive care.

Further investigation is needed to understand the unexplained increase in risk. Clinical and policy action should focus on the prediction, early identification and management of severe illness and obstetric haemorrhage in Black women to reduce these inequalities. Particular action is also needed to improve monitoring of women with complications including stillbirth, cardiac and placental conditions, given the high risk of intensive care admission in these groups, and to prevent and treat maternal conditions such as hypertension, diabetes and pre-eclampsia. Established procedures, such as the use of early warning scores at regular intervals, should be attentively used in Black women.[49] If targeted, this has the potential to reduce maternal admissions to intensive care significantly, with an associated reduction in clinical costs and trauma to women and their families.[1]

Disclosure of interests

All authors have previously or currently received funding from the Healthcare Quality Improvement Partnership (HQIP) who commissioned the linkage between ICNARC and maternity data for the National Maternity and Perinatal Audit. HQIP had no involvement in the design, analysis or writing of this study. DP additionally is a member of the Ockenden review and the New South Wales Maternal and Perinatal Review Committee.

Contribution to authorship

JJ and KW conceived the study. All authors planned the analysis. JJ conducted the analysis and wrote the first draft of the paper. All authors reviewed and redrafted the study. KW supervised the study.

Details of ethics approval

This study used data routinely collected in clinical care to evaluate service provision and performance and therefore individual consent was not sought. Institutional consent to access the data was provided by the NHS Health Research Authority Confidentiality Advisory Group, approval number 16/CAG/0058. This study was approved by the LSHTM Ethics Committee, approval number 14544, on 4 April 2018.

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Patient and public involvement
There was no patient and public involvement in this study.

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Data availability statement
The data that support the findings of this study are available from ICNARC, NHS Digital, the National Welsh Informatics Service and HQIP. Restrictions apply to the availability of these data, which were used under license for this study. Data are available from the authors with the permission of ICNARC, NHS Digital, the National Welsh Informatics Service and HQIP.

Supporting Information

Additional supporting information may be found online in the Supporting Information section at the end of the article.

Figure S1. Flow diagram.

Table S1. Data sources for key variables, together with ICD-10 codes used to define co-morbidities.

Table S2. List of indications for admission and classification system.

Table S3. Sensitivity analysis examining admission to level 3 intensive care among 631 851 women who gave birth in England between 1 April 2015 and 31 March 2016.

Table S4. Sensitivity analysis: complete case analysis.

Table S5. Primary reasons for admission by ethnicity in 1619 admissions among 1414 women who gave birth in England and Wales in 2015/16 and were admitted to intensive care in England during pregnancy and the postpartum period up to 6 weeks (data for Fig 1).

Table S6. Summary characteristics of 631 851 women who gave birth in England and Wales in 2015/16, by ethnic group. ■

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Supplementary Files for:

Associations between ethnicity and admission to intensive care among women giving birth in England and Wales: a cohort study

Contents

Supplementary Table S1. Data sources for key variables, together with ICD-10 codes used to define comorbidities

Variable	Data Source	Details
Ethnic group	Primary: HES/PEDW Secondary: MIS	Categorised into White, S Asian, Black, Mixed, Other
Intensive care admission	ICNARC	
Level of intensive care admission	ICNARC	Highest level recorded at either admission or discharge
Primary reason for admission	ICNARC	
Maternal age	Primary: MIS Secondary: HES/PEDW	Maternal age at time of birth. Grouped into six categories 16-24, 25-29, 30-34, 35-39, 40-44, 45 or older
Socioeconomic group	Primary: MIS Secondary: HES	In England, IMD associated with women's recorded postcode at time of birth; in Wales, with postcode of GP practice as individual postcode not available
Body mass index	MIS	
Parity	Primary: MIS Secondary: HES/PEDW	Grouped into four categories: 0, 1, 2, 3 or more
Multiplicity	MIS	
Stillbirth	MIS	
Preterm birth	MIS	Preterm birth if gestational age at birth less than 37 weeks
Mode of birth	Primary: MIS Secondary: HES/PEDW	Grouped into three categories: unassisted vaginal, instrumental birth, caesarean birth
Recorded co-morbidity	HES	Codes recorded in HES episode for maternal admission for birth
Hypertensive disease		
Pre existing		O10, O11, I10, I11, I12, I13, I15
New onset hypertensive disease in pregnancy		O12, O13, O16
Diabetes		
Pre-existing diabetes		O24.0, E10, E11
Gestational diabetes		O24.1
Unspecified		O24.9
Pre-eclampsia/eclampsia		O10, O14, O15
Placental conditions		O43,O44,O45,O46,O69.4
Cardiac conditions		I01, I05-09, I20-28, I30-I52, I97-98

Supplementary Table S2. List of indications for admission and classification system

Diagnosis	Category
Obstetric haemorrhage	Obstetric
Pneumonia	Infection
Pre-eclampsia, eclampsia, and HELLP	Other direct
Other[1]	Other indirect
Cardiac	Cardiac
Malignancy	Other indirect
Genital tract infection	Infection
Non-infectious pulmonary disease (including asthma)	Other indirect
Urinary tract infection	Infection
Other infection	Infection
Diabetes	Other indirect
Bowel complications (e.g. adhesions, perforation)	Other indirect
Seizure disorder (non-eclamptic)	Other indirect
Self harm	Other indirect
Gastroenterology	Other indirect
Venous thromboembolism	Other direct
Non-seizure neurology	Other indirect
Anaphylaxis or drug reaction	Other indirect
Operative injury	Other direct
Renal failure	Other indirect
Non-obstetric haemorrhage	Other indirect
Endocrine	Other indirect
Acute pancreatitis	Other indirect
Pulmonary oedema	Cardiac
Other trauma	Other indirect
Complications of early pregnancy (including OHSS and ectopic pregnancy)	Other direct
Coma or encephalopathy	Other indirect
Stroke	Other indirect
Acute fatty liver of pregnancy	Other direct
Uterine rupture	Other direct
Sickle cell crisis	Other indirect
Hypertensive disease	Other indirect
Vascular (including dissection)	Other indirect
Water intoxication	Other indirect
Amniotic fluid embolism	Other direct

[1] This category contains all indications with frequency of less than 5 that cannot be grouped, for example liver transplant donor/recipient, as well as all admissions without a valid code for admission type.

Supplementary Table S3. Sensitivity analysis examining admission to level 3 intensive care among 631 851 women who gave birth in England between 1st April 2015 and 31st March 2016

Risk factor	Rate per 1000	Crude OR	Adjusted OR	P value*
All	0.9			
Ethnic origin				<0.001
White	0.8	Ref	Ref	
Asian	1.2	1.44 (1.12, 1.85)	1.30 (0.99, 1.72)	
Black	2.2	2.78 (2.10, 3.67)	1.89 (1.38, 2.60)	
Mixed	0.5	0.58 (0.24, 1.40)	0.60 (0.24, 1.48)	
Other	0.9	1.12 (0.73, 1.73)	1.19 (0.78, 1.82)	
Age group				<0.001
Under 25	0.7	1.31 (0.98, 1.75)	1.52 (1.11, 2.07)	
25-29	0.6	Ref	Ref	
30-34	1.0	1.68 (1.31, 2.14)	1.50 (1.17, 1.93)	
35-39	1.2	2.03 (1.56, 2.65)	1.53 (1.16, 2.03)	
40-44	2.5	4.41 (3.20, 6.09)	2.47 (1.74, 3.51)	
45 or older	5.4	9.49 (4.79, 18.81)	3.60 (1.77, 7.35)	
Socioeconomic group				0.29
Least deprived 1- 20%	0.8	Ref	Ref	
Less deprived 21-40%	0.8	1.02 (0.74, 1.44)	1.04 (0.74, 1.47)	
Median deprived 41-60%	0.9	1.20 (0.90, 1.60)	1.10 (0.83, 1.55)	
More deprived 61-80%	0.9	1.10 (0.82, 1.47)	1.00 (0.72, 1.35)	
Most deprived 81-100%	1.0	1.26 (0.96, 1.65)	1.03 (0.75, 1.40)	
BMI (kg/m2)				0.07
<18.5	0.8	1.20 (0.71, 2.02)	1.37 (0.73, 2.59)	
18.5-24.9	0.7	Ref	Ref	
25.0-29.9	1.0	1.37 (1.10, 1.71)	1.18 (0.94, 1.49)	
30.0-34.9	1.0	1.52 (1.16, 1.98)	1.14 (0.86, 1.50)	
35.0-39.9	1.3	1.95 (1.37, 2.77)	1.43 (0.96, 2.14)	
>=40.0	1.8	2.62 (1.74, 2.94)	1.79 (1.15, 2.80)	
Parity				0.06
0	0.9	Ref	Ref	
1	0.7	0.85 (0.69, 1.04)	0.99 (0.78, 1.26)	
2	0.9	0.99 (0.76, 1.28)	1.04 (0.76, 1.43)	
3 or more	1.5	1.75 (1.36, 2.25)	1.45 (1.06, 1.97)	
Smoker	1.0	1.15 (0.89, 1.47)	1.22 (0.91, 1.64)	0.18
Previous CS	1.9	2.64 (2.20, 3.16)	1.01 (0.79, 1.29)	0.93
Maternal conditions				
Diabetes	1.3	1.44 (1.05, 1.97)	0.76 (0.55, 1.06)	0.11
Pre-eclampsia/eclampsia	6.2	7.82 (6.09, 10.04)	2.80 (2.09, 3.75)	<0.001
Hypertension	4.1	4.64 (2.67, 8.05)	1.59 (0.84, 2.98)	0.15
Placental conditions	12.5	16.17 (12.64, 20.67)	4.34 (3.26, 5.77)	<0.001
Cardiac conditions	17.2	20.81 (14.74, 29.38)	13.90 (9.56, 20.21)	<0.001
Mode of birth				<0.001
Unassisted vaginal	0.2		Ref	
Instrumental	0.6	2.58 (1.82, 3.65)	3.12 (2.15, 4.53)	
Caesarean section	2.5	10.42 (8.32, 13.05)	7.24 (5.49, 9.57)	
Fetal complications				
Preterm birth	4.5	7.28 (6.10, 8.69)	2.91 (2.31, 3.66)	<0.001
Multiple birth	4.2	5.02 (3.64, 6.93)	1.37 (0.95, 1.99)	0.09
Stillbirth	11.9	14.29 (10.18, 20.07)	9.27 (6.12, 14.06)	<0.001
***Wald test**				

Supplementary Table S4. Sensitivity analysis: complete case analyses

		Model 1† (Demographic) n = 509 689		**Model 2† (Lifestyle, history) n = 345 682**		**Model 3† (Pregnancy and birth) n= 341, 411**	
Risk factor	Crude OR	Adjusted OR	p value*	Adjusted OR	p value*	Adjusted OR	p value*
All							
Ethnic origin			<0.001		0.04		0.10
White	Ref	Ref		Ref		Ref	
Asian	1.08 (0.90, 1.28)	1.06 (0.88, 1.28)		1.15 (0.92, 1.45)		1.01 (0.80, 1.29)	
Black	2.17 (1.80, 2.62)	1.88 (1.53, 2.32)		1.64 (1.25, 2.16)		1.43 (1.08, 1.90)	
Mixed	0.88 (0.56, 1.39)	0.80 (0.49, 1.32)		0.98 (0.56, 1.70)		0.95 (0.54, 1.67)	
Other	1.06 (0.81, 1.40)	1.04 (0.78, 1.38)		1.28 (0.92, 1.77)		1.25 (0.89, 1.75)	
Age group			<0.001		<0.001		0.04
Under 25	1.37 (1.16, 1.62)	1.43 (1.20, 1.72)		1.31 (1.04, 1.64)		1.45 (1.15, 1.82)	
25-29	Ref	Ref		Ref		Ref	
30-34	1.28 (1.10, 1.48)	1.31 (1.11, 1.54)		1.27 (1.04, 1.54)		1.12 (0.92, 1.37)	
35-39	1.66 (1.41, 1.94)	1.74 (1.46, 2.07)		1.57 (1.27, 1.94)		1.26 (1.01, 1.56)	
40-44	2.32 (1.84, 2.93)	2.18 (1.68, 2.84)		1.81 (1.31, 2.50)		1.15 (0.82, 1.62)	
45 or older	5.32 (3.16, 8.96)	4.44 (2.42, 8.12)		2.92 (1.29, 6.66)		1.37 (0.59, 3.15)	
Socioeconomic group			0.65		0.98		0.84
Least deprived 1- 20%	Ref	Ref		Ref		Ref	
Less deprived 21-40%	0.97 (0.80, 1.19)	1.03 (0.83, 1.27)		1.03 (0.81, 1.33)		1.03 (0.80, 1.33)	
Median deprived 41-60%	1.00 (0.83, 1.20)	1.03 (0.85, 1.26)		0.97 (0.76, 1.23)		0.95 (0.75, 1.22)	
More deprived 61-80%	1.03 (0.87, 1.23)	1.04 (0.86, 1.26)		1.02 (0.81, 1.29)		0.99 (0.78, 1.25)	
Most deprived 81-100%	1.16 (0.98, 1.37)	1.14 (0.94, 1.38)		0.99 (0.79, 1.26)		0.92 (0.72, 1.16)	
BMI (kg/m2)					<0.001		0.05
<18.5	1.15 (0.81, 1.65)			1.23 (0.82, 1.86)		1.20 (0.79, 1.82)	
18.5-24.9	Ref			Ref		Ref	
25.0-29.9	1.16 (1.01, 1.35)			1.10 (0.93, 1.31)		0.98 (0.82, 1.17)	
30.0-34.9	1.25 (1.04, 1.49)			1.13 (0.91, 1.40)		0.93 (0.75, 1.16)	
35.0-39.9	1.62 (1.28, 2.06)			1.48 (1.12, 1.96)		1.11 (0.82, 1.49)	
>=40.0	2.39 (1.83, 3.12)			2.23 (1.64, 3.03)		1.59 (1.15, 2.20)	
Parity					<0.001		<0.001
0	Ref			Ref		Ref	
1	0.78 (0.69, 0.89)			0.62 (0.52, 0.74)		1.03 (0.85, 1.25)	
2	0.93 (0.79, 1.10)			0.56 (0.44, 0.71)		0.98 (0.76, 1.27)	
3 or more	1.40 (1.18, 1.66)			0.91 (0.72, 1.15)		1.57 (1.23, 2.00)	
Smoker	1.18 (1.00, 1.38)			1.15 (0.94, 1.41)	0.18	1.04 (0.84, 1.28)	0.73
Previous CS	2.20 (1.96, 2.48)			2.39 (2.01, 2.84)	<0.001	0.96 (0.78, 1.17)	0.67
Maternal conditions							
Diabetes	2.07 (1.74, 2.46)					1.39 (1.09, 1.78)	0.008
Pre-eclampsia/eclampsia	8.40 (7.20, 9.81)					3.62 (2.87, 4.58)	<0.001
Hypertension	3.98 (2.74, 5.80)					1.41 (0.79, 2.51)	0.25
Placental problems	12.2 (10.2, 14.5)					3.37 (2.59, 4.37)	<0.001
Cardiac conditions	13.7 (10.8, 17.5)					9.80 (6.74,14.26)	<0.001
Mode of birth							<0.001
Unassisted vaginal	Ref					Ref	
Instrumental	1.77 (1.43, 2.19)					2.10 (1.56, 2.82)	
Caesarean section	6.86 (6.05, 7.78)					5.09 (4.14, 6.26)	
Fetal complications							
Preterm birth	7.57 (6.78, 8.46)					3.39 (2.82, 4.08)	<0.001
Multiple birth	4.11 (3.29, 5.14)					1.26 (0.91, 1.73)	0.16
Stillbirth	10.9 (8.50, 13.9)					5.23 (3.47, 7.88)	<0.001
***Wald test**							

Supplementary Table S5. Primary reasons for admission by ethnicity in 1,619 admissions among 1,414 women who gave birth in England and Wales in 2015-16 and were admitted to intensive care in England during pregnancy and the postpartum period up to six weeks (Data for Fig 1).

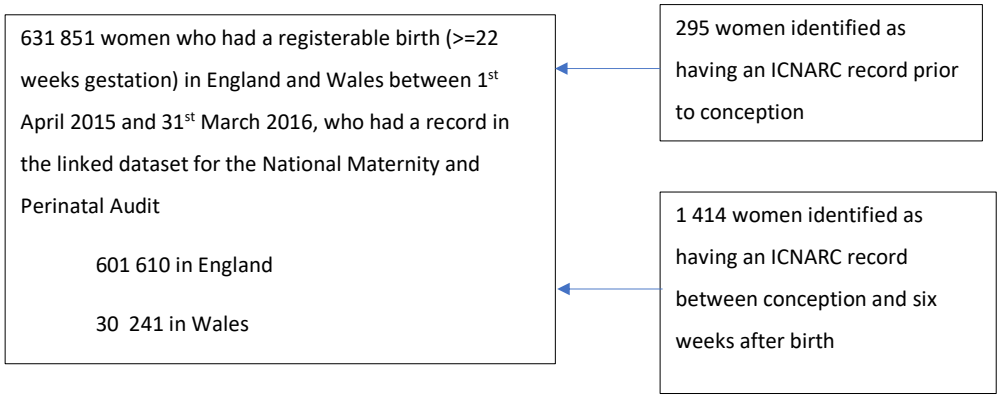
	Direct				**Indirect**			**Total**
	Obstetric haemorrhage	Infection	Other Direct	Total	Cardiac	Other indirect	Total	
White	336 (34.4%)	202 (20.7%)	130 (13.3%)	668 (68.4%)	42 (4.3%)	266 (27.3%)	308 (31.6%)	976
Black	66 (42.3%)	33 (21.2%)	20 (12.8%)	119 (76.3%)	4 (2.6%)	33 (21.2%)	37 (23.7%)	156
Asian	49 (37.1%)	23 (17.4%)	16 (12.1%)	88 (66.7%)	8 (6.1%)	36 (27.3%)	44 (33.3%)	132
Mixed/Other	27 (35.5%)	15 (19.7%)	7 (9.2%)	49 (64.5%)	13 (17.1%)	14 (18.4%)	27 (35.5%)	76
Missing	69 (24.7%)	59 (21.1%)	34 (12.2%)	162 (58.1%)	13 (4.7%)	104 (37.3%)	117 (41.9%)	279
Total	547 (33.8%)	332 (20.5%)	207 (12.8%)	1086 (67.1%)	80 (4.9%)	453 (28.0%)	533 (32.9%)	1619

Supplementary Table S6. Summary characteristics of 631 851 women who gave birth in England and Wales in 2015-16, by ethnic group

Ethnic group		**White**		**S Asian**		**Black**		**Mixed**		**Other**		**Missing**	
		n		**n**		**n**		**n**		**n**		**n**	
		434,297		63,795		26,900		10,078		23,763		73,018	
Age group													
Under 25		87,731	20.9%	6,439	10.2%	3,425	12.9%	2,120	21.9%	3,164	13.5%	12,790	18.6%
25-29		118,496	28.3%	20,371	32.2%	7,035	26.5%	2,775	28.7%	6,321	26.9%	19,442	28.2%
30-34		126,503	30.2%	22,562	35.6%	8,325	31.3%	2,743	28.3%	7,795	33.2%	22,147	32.1%
35-39		70,131	16.7%	11,481	18.1%	5,771	21.7%	1,653	17.1%	4,925	21.0%	11,888	17.2%
40-44		15,253	3.6%	2,293	3.6%	1,776	6.7%	358	3.7%	1,192	5.1%	2,468	3.6%
45 or older		939	0.2%	170	0.3%	232	0.9%	27	0.3%	91	0.4%	208	0.3%
Missing		*15,244*	*3.5%*	*479*	*0.8%*	*336*	*1.2%*	*402*	*4.0%*	*275*	*1.2%*	*4,075*	*5.6%*
Socioeconomic deprivation													
Least deprived 1-20%		78,592	19.1%	5,118	8.7%	1,027	4.2%	1,088	11.6%	2,676	12.3%	10,937	16.4%
Less deprived 21-40%		63,650	15.5%	4,959	8.4%	1,300	5.3%	1,001	10.7%	2,489	11.5%	10,713	16.1%
Median deprived 41-60%		81,357	19.8%	9,065	15.4%	2,853	11.7%	1,522	16.2%	3,708	17.1%	13,678	20.5%
More deprived 61-80%		88,015	21.4%	16,508	28.0%	6,879	28.2%	2,257	24.0%	5,583	25.7%	15,517	23.3%
Most deprived 81-100%		99,775	24.3%	23,261	39.5%	12,300	50.5%	3,519	37.5%	7,264	33.4%	15,731	23.6%
Missing		*22,908*	*5.3%*	*4,884*	*7.7%*	*2,541*	*9.4%*	*691*	*6.9%*	*2,043*	*8.6%*	*6,442*	*8.8%*
Body mass index													
<18.5		9,490	2.8%	2,077	4.4%	340	1.7%	254	3.3%	675	3.8%	1,511	2.8%
18.5-24.9		167,575	48.9%	22,230	46.9%	6,118	30.3%	3,638	46.6%	9,553	54.3%	27,342	51.2%
25.0-29.9		89,602	26.2%	14,318	30.2%	6,645	32.9%	2,112	27.1%	4,504	25.6%	13,980	26.2%
30.0-34.9		46,637	13.6%	6,503	13.7%	4,656	23.1%	1,161	14.9%	2,053	11.7%	6,662	12.5%
35.0-39.9		18,978	5.5%	1,706	3.6%	1,604	7.9%	422	5.4%	601	3.4%	2,521	4.7%
40 or more		10,278	3.0%	590	1.2%	827	4.1%	215	2.8%	197	1.1%	1,340	2.5%
Missing		*91,737*	*21.1%*	*16,371*	*25.7%*	*6,710*	*24.9%*	*2,276*	*22.6%*	*6,180*	*26.0%*	*19,662*	*26.9%*
Parity													
	0	181,588	42.7%	21,615	34.4%	8,161	30.9%	3,889	39.7%	10,505	45.1%	38,375	54.7%
	1	152,074	35.7%	20,959	33.4%	7,927	30.0%	3,332	34.0%	7,517	32.3%	22,763	32.4%
	2	57,532	13.5%	11,562	18.4%	5,544	21.0%	1,512	15.4%	3,213	13.8%	6,674	9.5%
3 or more		34,244	8.0%	8,646	13.8%	4,800	18.2%	1,071	10.9%	2,041	8.8%	2,406	3.4%
Missing		*8,859*	*2.0%*	*1,013*	*1.6%*	*468*	*1.7%*	*274*	*2.7%*	*487*	*2.0%*	*2,800*	*3.8%*
Previous CS		57,375	13.6%	11,502	18.6%	5,962	22.8%	1,446	14.9%	3,310	14.3%	7,906	11.3%
Missing		*13,284*	*3.1%*	*1,817*	*2.8%*	*779*	*2.9%*	*390*	*3.9%*	*652*	*2.7%*	*3,227*	*4.4%*
Smoking status													
non-smoker		279,918	82.5%	44,826	98.0%	18,546	96.2%	6,393	84.9%	16,884	93.8%	50,975	88.2%
smoker		59,339	17.5%	938	2.0%	737	3.8%	1,140	15.1%	1,115	6.2%	6,809	11.8%
Missing		*95,040*	*21.9%*	*18,031*	*28.3%*	*7,617*	*28.3%*	*2,545*	*25.3%*	*5,764*	*24.3%*	*15,234*	*20.9%*
Recorded diagnoses													
Hypertension		17,328	4.0%	8,007	12.6%	1,968	7.3%	522	5.2%	1,729	7.3%	3,152	4.3%
Placental factors		3,980	0.9%	710	1.1%	286	1.1%	89	0.9%	247	1.0%	605	0.8%
Pre-eclampsia/eclampsia		7,610	1.8%	1,135	1.8%	797	3.0%	167	1.7%	406	1.7%	1,369	1.9%
Cardiac conditions		1,485	0.34%	169	0.26%	90	0.33%	34	0.34%	78	0.33%	180	0.25%
Gestation													
Term		390,504	93.0%	56,887	92.6%	23,963	92.1%	8,985	92.3%	21,315	93.7%	63,782	93.2%
Preterm		29,438	7.0%	4,567	7.4%	2,063	7.9%	752	7.7%	1,424	6.3%	4,645	6.8%
Missing		*14,355*	*3.3%*	*2,341*	*3.7%*	*874*	*3.2%*	*341*	*3.4%*	*1,024*	*4.3%*	*4,591*	*6.3%*
Multiplicity													
Singleton birth		427,392	98.4%	62,987	98.7%	26,464	98.4%	9,928	98.5%	23,466	98.8%	72,117	98.8%
Multiple birth		6,905	1.6%	808	1.3%	436	1.6%	150	1.5%	297	1.2%	901	1.2%
Fetal outcome													
Livebirth		432,301	99.5%	63,449	99.5%	26,715	99.3%	10,027	99.5%	23,653	99.5%	72,673	99.5%
Stillbirth		1,996	0.5%	346	0.5%	185	0.7%	51	0.5%	110	0.5%	345	0.5%
Mode of birth													
Unassisted vaginal		264,386	62.5%	37,194	58.9%	15,867	59.8%	6,056	62.9%	14,029	59.7%	43,240	60.1%
Instrumental		51,415	12.2%	8,085	12.8%	1,718	6.5%	952	9.9%	3,153	13.4%	9,957	13.8%
Caesarean section		107,223	25.3%	17,828	28.3%	8,946	33.7%	2,620	27.2%	6,311	26.9%	18,737	26.0%
Missing		*11,273*	*2.6%*	*688*	*1.1%*	*369*	*1.4%*	*450*	*4.5%*	*270*	*1.1%*	*1,084*	*1.5%*

***percentages exclude missing values**

Supplementary Figure S1. Flow diagram



4.2 Further exploration of robustness of findings to different assumptions regarding missing data

During the viva examination, it was discussed whether further work could be done to evaluate the robustness of the findings to different assumptions regarding missing ethnicity data, including the possibility that all missing values of ethnicity could be attributed to a single group. In the dataset, 4% of women have their ethnicity recorded as Black and 12% recorded as missing. In the main analysis, this is dealt with using multiple imputation by chained equations, with a sensitivity analysis looking at complete cases (Supplementary Table S4).

This sensitivity analysis repeated the analysis in the 'full' model (adjusted for demographic, lifestyle, previous obstetric history, pregnancy and birth factors) for admission to intensive care during pregnancy, birth and the postnatal period.

Table 4.2.1 Sensitivity analyses in complete cases with all missing values of ethnic group (1) assumed to be white (2) assumed to be Black and (3) treated as a separate category.

	All missing values of ethnic group changed to White		All missing values of ethnic group changed to Black		Missing ethnic group treated as a separate category	
	Adjusted OR†	p value*	Adjusted OR†	p value*	Adjusted OR†	p value*
White	Ref	0.08	Ref	0.75	Ref	0.03
South Asian	1.05 (0.83, 1.32)		1.00 (0.79, 1.26)		1.01 (0.80, 1.28)	
Black	1.45 (1.09, 1.92)		0.96 (0.79, 1.17)		1.40 (1.06, 1.86)	
Mixed	0.98 (0.56, 1.71)		0.94 (0.53, 1.64)		0.95 (0.54, 1.66)	
Other	1.29 (0.92, 1.81)		1.24 (0.88, 1.73)		1.25 (0.89, 1.75)	
Missing	-		-		0.75 (0.58, 0.98)	
†adjusted for demographic, lifestyle, previous obstetric history, pregnancy and birth factors *Wald test						

In this analysis, there is weak evidence that the group with no recorded ethnic group are at slightly lower risk than the reference, White, group. When they are added to the Black group, as the missing group is approximately three times the size of the Black group, this dilutes the association sufficiently that it disappears. When it is assumed that all missing records are from white women, the associations are not substantially changed. Records with missing ethnic group resemble the white group more than any other (Supplementary Table S6).

5. Results Chapter: Associations between ethnicity and postpartum haemorrhage

In this part of the research, I used logistic regression models to explore maternal characteristics associated with postpartum haemorrhage of 1500ml or more. The findings of this analysis are presented in the form of a research paper which has been accepted for publication.

5.1 Research Paper 3

Risk of postpartum haemorrhage is associated with ethnicity: a cohort study of 981 801 births in England

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RESEARCH PAPER COVER SHEET

Please note that a cover sheet must be completed for each research paper included within a thesis.

SECTION A – Student Details

Student ID Number	1511701	**Title**	Dr
First Name(s)	Jennifer		
Surname/Family Name	Jardine		
Thesis Title	A study of risk factors of maternity outcomes using large, routinely collected electronic datasets		
Primary Supervisor	Kate Walker		

If the Research Paper has previously been published please complete Section B, if not please move to Section C.

SECTION B – Paper already published

Where was the work published?			
When was the work published?			
If the work was published prior to registration for your research degree, give a brief rationale for its inclusion			
Have you retained the copyright for the work?*	Choose an item.	Was the work subject to academic peer review?	Choose an item.

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SECTION C – Prepared for publication, but not yet published

Where is the work intended to be published?	BJOG
Please list the paper's authors in the intended authorship order:	Jennifer Jardine, Ipek Gurol-Urganci, Tina Harris, Jane Hawdon, Dharmintra Pasupathy, Jan van der Meulen, Kate Walker on behalf of the NMPA Project Team
Stage of publication	**Accepted**

SECTION D – Multi-authored work

For multi-authored work, give full details of your role in the research included in the paper and in the preparation of the paper. (Attach a further sheet if necessary)	Designed study with collaborative input from coauthors, conducted primary analysis, wrote first draft of paper, co-ordinated feedback, implemented revisions from co-authors.

SECTION E

Student Signature	[redacted]
Date	4/11/2021

Supervisor Signature	[redacted]
Date	

Title: Risk of postpartum haemorrhage is associated with ethnicity: a cohort study of 981 801 births in England

Authors: Jennifer Jardine (1,2), Ipek Gurol-Urganci (1,2), Tina Harris (3), Jane Hawdon (4), Dharmintra Pasupathy (5,6), Jan van der Meulen (1), Kate Walker (1,7) on behalf of the NMPA Project Team

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Word count (excluding abstract, tables, figures, references): 3139 words

Running title: Ethnicity and postpartum haemorrhage

Keywords: postpartum haemorrhage, PPH, ethnicity

Abstract

Objective: To determine the association between ethnic group and risk of postpartum haemorrhage in women giving birth.

Design: Cohort study.

Setting: Maternity units in England.

Population or Sample: 981 801 records of births between 1st April 2015 and 31st March 2017 in a national clinical database.

Methods: Multivariable logistic regression analyses with multiple imputation to account for missing data and robust standard errors to account for clustering within hospitals.

Main Outcome Measures: Postpartum haemorrhage of 1500ml or more (PPH).

Results: 28 268 (2.9%) of births were complicated by PPH. Risks were higher in women from black (3.9%) and other (3.5%) ethnic backgrounds. Following adjustment for maternal and fetal characteristics, and care at birth, there was evidence of an increased risk of PPH in women from all ethnic minority groups, with the largest increase seen in black women (adjusted odds ratio 1.54 (1.45 to 1.63)). The increase in risk was robust to sensitivity analyses which included changing the outcome to PPH of 3000ml or more.

Conclusions: In England, women from ethnic minority backgrounds have an increased risk of PPH, when maternal, fetal and birth characteristics are taken into account. Factors contributing to this increased risk need further investigation. Perinatal care for women from ethnic minority backgrounds should focus on preventative measures to optimise maternal outcomes.

Funding: HQIP.

Tweetable abstract

Women with an ethnic minority background giving birth in England have an increased risk of postpartum haemorrhage, even when characteristics of the mother, the baby, and the care received are taken into account.

Introduction

Postpartum haemorrhage (PPH), an increased loss of blood at the time of or after birth, is associated with significant morbidity and is a leading cause of maternal death in all settings.[1,2] The experience of PPH is traumatic,[3] and recovery is associated with secondary consequences including an increased risk of postpartum depression and lower rates of breastfeeding.[4,5]

PPH is the result of an interplay of pre-existing risk factors, and events which occur during the labour and birth, and immediate management. It is generally considered that initiatives to reduce the risks related to PPH require a three-step process of prevention, treatment, and rescue.[6] The risk of PPH can be reduced, at least partially, by the use of interventions such as the administration of oxytocin and tranexamic acid.[7,8]

Ethnic background is known to be a determinant of variation in the outcomes of women receiving maternity care across the world.[1] Women from black and south Asian ethnic groups are more likely to experience severe morbidity at the time of birth.[1,9] We have previously demonstrated that black women in the UK have an increased risk of maternal admission to intensive care (ICU) and that haemorrhage is the leading cause of an ICU admission among black women.[10] However, not all women with PPH require intensive care, and significant morbidity is not confined to those with ICU admission. In the US, it has been shown that women from Hispanic and Pacific Islander ethnic backgrounds have an increased risk of PPH,[11] and among non-Hispanic black women, there is an increased risk of severe sequelae of PPH.[12] A national study in Sweden demonstrated that women born outside Sweden were at higher risk of haemorrhage requiring a large transfusion.[13] However, current clinical guidelines do not consider the differential experience of severe morbidity, including postpartum haemorrhage, according to a woman's ethnic background.[8,14–16]

The aim of this study was to understand the association between ethnic background and the risk of PPH using routinely collected data available in England, whether this association differs by level of socioeconomic deprivation, and to what extent the association between ethnic background and PPH is explained by maternal, fetal and birth characteristics.

Methods

Data source

We used a national maternity dataset that was created for the purpose of the National Maternity and Perinatal Audit, a national programme to evaluate care for women giving birth and their babies in Britain (www.maternityaudit.org.uk). This included data routinely collected in the course of clinical care, which was extracted from the maternity information systems (MIS) used in National Health Service (NHS) hospitals in England. These were cleaned, collated and linked to the Hospital Episode Statistics (HES), an administrative dataset which contains information about all hospital admissions within NHS hospital trusts. Trusts are administrative organisations which provide hospital and hospital-associated community care, including home births, in a particular area in England. In England, all women are eligible to give birth in the NHS and almost all do; in 2015-17, only 0.4% of births occurred in non-NHS settings (these are most commonly private hospitals).[17] The dataset collated for the NMPA includes approximately 94% of births which occurred in England in the time period.[18,19]

Definition of cohort

The eligible population was all births between 1st April 2015 and 31st March 2017 in the NHS in England. We restricted the cohort to births in NHS hospital trusts in which over 80% of MIS records contained information about blood loss. Records were included if they recorded either a live or stillbirth that occurred at or after 24 completed gestational weeks and if the delivery record contained complete information about blood loss. Characteristics of included and excluded records are described in Table S1 and the data flow is summarised in Figure 1.

Definition of variables

The primary outcome of this study was maternal blood loss at birth of 1500ml or more. Blood loss is typically estimated using a combination of visual estimates, physiological assessment, and the results of weighing drapes and pads.[20,21] Clinical guidelines in the UK suggest that blood loss of 1500ml or more should be treated as severe PPH with the mobilisation of appropriate staff.[14] In other countries, clinical guidelines include thresholds of 500 and 1000ml.[22,23] Estimated blood loss has been identified as a core outcome for studies related to prevention and treatment of PPH.[24] In our study, we defined PPH as blood loss of 1500ml or more in line with the UK definition of severe PPH, but also examined risk of PPH at 500, 1000, 1500, 2000 and 3000ml.

Ethnicity was primarily derived from the hospital admission record (Hospital Episode Statistics (HES)) and infilled where not useable (unknown (ethnos codes 9, X, Z) or missing) from the MIS record. Ethnic background was classified using the ethnic groups defined for the 2001 UK Census. For the purposes of this analysis, these ethnic groups were collapsed into five groups: 'white', 'south Asian', 'black', 'mixed' and 'other'.[25] This was done because there is evidence that in routinely collected records, more granular analyses can lead to misclassification bias,[26] and to avoid small numbers for some of the ethnic groups.

From the MIS, Information was available about maternal characteristics including age, body mass index (BMI), parity, and whether the woman had previously had a caesarean section; and about fetal characteristics including live or stillbirth, multiple birth, and birthweight. Information was also available about the birth: the onset of labour, mode of birth (unassisted vertex, breech vaginal, instrumental vaginal, emergency caesarean or elective caesarean), and whether there was an episiotomy or manual removal of the placenta. Where this information was missing in the MIS record, it was infilled if available from the HES record, with information about parity and previous caesarean section derived from historical records in HES as described elsewhere.[19] Maternal health conditions complicating pregnancy (grouped into hypertensive disorders including pre-existing or gestational; diabetes pre-existing or gestational; conditions which make bleeding more likely; or placental abnormalities including placenta praevia or accreta) were identified using ICD-10 codes[27] recorded in HES in the birth episode.[23] Information about socioeconomic group was available from the Index of Multiple Deprivation (IMD), an area-level measure that encompasses information about social deprivation, economic status, employment and health deprivation of each local area of approximately surrounding a woman's postcode at the time of birth as recorded in the MIS.[28]

Statistical analyses

Descriptive statistics, including the presence of risk factors, were tabulated according to ethnic background, with continuous risk factors dichotomised for brevity. Chi squared statistics were used to compare distributions of characteristics between groups. Logistic regression was used to estimate odds ratios between each included characteristic and risk of PPH.

Multivariable logistic regression models, with robust standard errors to account for clustering within hospital trusts (the Huber/White/sandwich estimator of variance, affecting the standard errors of

the estimates but not the estimated coefficients)[29], were used to estimate odds ratios for PPH by ethnic group, with sequential adjustment for characteristics related to the mother, the baby, and the care received. Within the models, we categorised continuous variables (7 categories for maternal age, 6 categories for BMI, 3 categories for gestational age and 4 categories for birthweight). We also recategorised parity of 3 or more into the same group to account for smaller numbers with parity above 3. Details of all coding frameworks used are available in Table S1.

Crude odds ratios for PPH by ethnic group were estimated by logistic regression. The first multivariable model adjusted for maternal characteristics: the mother's age, socioeconomic group, parity, BMI, previous caesarean, and maternal health conditions complicating pregnancy. The second model included these maternal characteristics, as well as fetal characteristics at birth: multiple birth, stillbirth and birthweight. The third, 'full' model additionally included factors relating to the woman's maternity care: induction of labour, mode of birth, episiotomy, and manual removal of placenta. All models also adjusted for the financial year of birth.

For multiple births, the highest birthweight was used, and the birth was treated as a stillbirth if one baby was stillborn.

Interactions between ethnic and socioeconomic background and between parity and previous caesarean were considered plausible a priori. We evaluated whether there was evidence for these interactions by including an additional interaction term in the full model and using a global Wald test to compare this to the model without the interaction term. For both tests $p>0.1$, so neither interaction was included in the full model.

Missing values were imputed using multiple imputation by chained equations with statistical coefficients obtained in 40 imputed data sets, with the number of datasets chosen to mirror the proportion of cases with any missing data, and pooled using Rubin's rules.[30] Multiple imputation requires the assumption that data is missing at random given the variables used in the imputation model. To test the sensitivity of findings to this assumption, we conducted a sensitivity analysis in which the fully adjusted analysis was repeated in cases with complete information about all covariates; analyses using complete cases have been found to be robust to a wider range of missingness assumptions.[31]

We conducted two further sensitivity analyses to address concerns regarding incomplete information about known risk factors for PPH. In the second sensitivity analysis, to address the lack of information about previous PPH, we restricted the cohort to primiparous women. In the third, to address incomplete information about augmentation of labour, we included additional adjustment for whether the labour was augmented (as a binary variable) in 650 941 women where this was available. This variable was not included in the primary analysis due to concerns about its quality and the high proportion of missing data.[19]

In two further sensitivity analyses, we changed the outcome to PPH of 500ml or more and to 3000ml or more to assess whether the same relationship was observed. These thresholds was chosen to, first, represent the WHO definition of PPH;[16] and second, to represent a cohort of women who were likely to require additional care, such as in an intensive care unit.

All analyses were performed in Stata v16.

Results

The records of 981 801 births between 1st April 2015 and 31st March 2017 were included in the analysis. Of these, 906 961 (92.4%) had complete information about ethnic background.(Figure 1, Table 1) 705 948 of those with complete ethnicity information (77.8%) were white, 107 382 (11.8%) were south Asian, 42 170 (4.6%) were black, 16 456 (1.8%) were mixed and 35 005 (3.9%) were from other ethnic backgrounds.(Table 1)

28 268 (2.9%) of 981 801 births had a recorded blood loss of 1500ml or more (Table 2). When different thresholds were examined, 322 606 (32.9%) of births had a recorded blood loss of 500ml or more; 75 674 (7.7%) had a recorded blood loss of 1000ml or more; 28 268 births (1.2%) had a blood loss of 2000ml or more; and 249 (0.3%) births 3000ml or more. Regardless of definition, the risk of PPH was higher in black women and in women from other ethnic backgrounds. Women with no recorded information about ethnic group had elevated risk of PPH at all thresholds compared to the population average (Table 2).

Compared to white women, the unadjusted risk of PPH of 1500ml or more was increased in black women (crude odds ratio 1.42, 95% CI: 1.35 to 1.50), and in women from other ethnic backgrounds (crude odds ratio 1.27, 95% CI: 1.20 to 1.35) (Table 3). These associations were not substantially altered by adjustment for maternal characteristics, fetal characteristics, or information about the woman's maternity care (aOR for black women including all available information 1.54, 95% CI 1.45 to 1.63; aOR for women from other groups 1.37, 95% CI 1.29 to 1.46).

There was evidence of an increase in the risk of PPH in women from mixed and south Asian ethnic groups only following risk adjustment. For women from south Asian groups, the unadjusted odds of PPH was lower than in white women (crude OR 0.94. 95% CI 0.90 to 0.97); however following adjustment for maternal and fetal characteristics, the direction changed. Following adjustment for all maternal, fetal and birth characteristics, women from south Asian groups had increased odds of PPH compared to white women (aOR 1.14, 95% CI 1.09 to 1.19). For women from mixed groups, however, a stronger effect emerged after adjustment for maternal and fetal characteristics at the time of birth (aOR 1.17, 95% CI 1.07 to 1.28) and persisted following adjustment for birth characteristics (aOR 1.20, 95% CI 1.09 to 1.32) (Table 3). When fetal characteristics were compared between ethnic groups, women in south Asian groups had smaller babies than women from other ethnic groups; women from mixed ethnic groups were also more likely to have a smaller baby than white women (Table S3).

Many of the maternal, fetal and birth characteristics were strongly associated with an increased risk of PPH. We found evidence of a substantially elevated risk of PPH in older women, women with higher BMI and placental abnormalities; in women with stillbirth, preterm birth, multiple birth and increased fetal weight, as well as with assisted or caesarean birth and births with episiotomy (Table S4). While increasing socioeconomic deprivation was associated with a reduction in the risk of PPH (Table S4), we found no evidence of any effect modification of the observed association with ethnicity by socioeconomic deprivation (Table S5).

In sensitivity analyses restricting the cohort to primiparous women, including augmentation as an additional covariate in the model and changing the outcome to PPH of 500ml or more and to 3000ml or more, very similar patterns of association with ethnic group were seen (Table S6). In a further analysis examining whether the observed association of more deprived socioeconomic groups with

a lower rate of PPH was modified by adding smoking to the model, there was no change to the direction of association (adjOR of PPH for women in the most deprived quintile compared to the least deprived quintile in the full model with smoking added, 0.93 (95% CI 0.88 to 0.98); Wald test p=0.03).

Discussion

Summary of findings

Women from black and other ethnic groups are more likely to experience postpartum haemorrhage at the time of birth, regardless of the volume of blood loss used to define PPH. Following adjustment for maternal and fetal characteristics, particularly birthweight, women from all ethnic minority groups have an increased risk of PPH. This association remains following adjustment for characteristics of the woman's birth.

Strengths and Limitations

This study uses data routinely collected in the course of clinical care, with a diverse population that covers approximately 85% of births that occurred in England between 1st April 2015 and 31st March 2017. Strengths of this study include its large size of nearly one million births, and the detailed information available about the woman, her baby and her care, including maternal BMI, comorbidities occurring prior to and during pregnancy, and care at the time of birth. These characteristics were not available to other research groups evaluating association between ethnic group and PPH. [12,32]

Our dataset contains limited information regarding some risk factors for PPH, including the administration of oxytocin for augmentation, previous PPH, maternal anaemia, and length of labour. Although there is a diagnosis code in ICD for PPH, which may be considered to enable 'look-back' it gives substantially lower ascertainment of PPH than in our data, as found previously, and so was not used (Table S7).[33] Our analyses were, however, robust to sensitivity analyses for inclusion of a binary variable for augmentation, and restriction to primiparous women in whom historical PPH is not a factor.

Our central limitation is that, like many observational studies in maternity care, this study lacks information about the measures taken to mitigate the risk of PPH such as the administration of prophylactic synthetic oxytocin or tranexamic acid.[7,8] As a consequence, the observed associations

are likely to be influenced by the risk mitigation measures and the initial treatment which may have weakened the association that we report in this paper between the women's ethnic background and the occurrence of post-partum haemorrhage.[34]

A further limitation in this study is the lack of information about the methods used to estimate blood loss at the time of birth. Measurement of blood loss through visual, or other, estimation is heterogenous; more robust methods of estimation include the weighing of drapes or swabs.[35] Method of estimating blood loss is, however, unlikely to vary by ethnic group.

Interpretation

In the UK, although maternity care is free at the point of access, ethnic and socioeconomic inequalities are still observed in maternal and perinatal mortality.[1,36] This association between maternal ethnic group and risk of PPH, while observed by others, has not been recently evaluated in a setting where healthcare availability is not associated with ethnic group and ability to pay.[12]

It is unlikely that the observed increased risk of PPH is mediated through a woman's socioeconomic background: in our study, we observed no evidence of an increase in postpartum haemorrhage associated with increased socioeconomic deprivation. This concurs with findings of a previous study using registry data from the UK Obstetric Surveillance System, which demonstrated no statistically significant relationship between maternal socioeconomic group and severe maternal morbidity,[37] and with a previous study in our dataset which demonstrated no association between maternal intensive care admission and socioeconomic deprivation. Postpartum haemorrhage is an emergency which occurs when women are usually already in a healthcare setting: more widely, it has been shown that differences in outcome by socioeconomic group are largely driven by richer individuals presenting earlier in their illness and utilising their ability to exercise choice to improve their waiting periods, with little evidence of differential quality of care based on socioeconomic group within the NHS once that care is accessed.[38,39]

Our finding that women from an ethnic minority background are more likely to experience PPH has two possible explanations. First, there may be additional confounding factors not accounted for in our analysis that are associated with both PPH and ethnic minority group. Second, that women from

ethnic minority groups are not given the same level of intra- and postpartum observation and prophylactic treatment to prevent PPH.

With respect to the first potential explanation, we were in our dataset unable to adjust for, or examine through sensitivity analysis, the potential association with prolonged labour or previous PPH. However, this is unlikely to have accounted for our results. There is some limited observational evidence that women from black ethnic groups have shorter, rather than longer second stages of labour.[40] In a sensitivity analysis restricting to primiparous women, who have no previous history of PPH, similar results were seen. We were also unable to adjust for maternal anaemia, levels of which may be higher in women from some ethnic groups[41]. Furthermore, while we were able to adjust for the presence of fibroids where they were coded as a diagnosis, it is possible that this does not capture all fibroids present as not all will be identified on antenatal scans, or considered clinically significant enough to modify care recommendations and thus warrant coding.[42] Further investigation is required to understand whether there are biological considerations regarding effectiveness of medications commonly used to control PPH. [42]

It is also possible that prophylactic treatment and observational measures are not equally considered and offered between ethnic groups. Women from ethnic minority groups in the UK report poorer experiences of antenatal and intrapartum care which may be reflected in less attention to risk factors, antenatal symptoms of anaemia or concerns and symptoms indicative of PPH.[43,44] Investigating this hypothesis requires further detail regarding care pathways, which is not possible in this analysis of routinely collected electronic health data. A case-control study could be used to assess treatment differences by ethnic group.

However, while further investigations are ongoing, it would be prudent for healthcare professionals to be aware of the increased observed risk in women from ethnic minority groups, with the aim of being particularly attentive in monitoring for early identification and treatment of PPH.

Conclusion

Women from an ethnic minority background, and particularly women from a black ethnic group, are at increased risk of PPH. This association persists following adjustment for maternal, fetal and birth characteristics. Further investigation is needed to understand the unexplained increase in risk,

including possible mechanisms and the effectiveness of medications to control bleeding in women from different ethnic groups. While the results of further investigations are awaited, clinical and policy action should focus on the prediction, early identification and management of severe illness and postpartum haemorrhage in women from ethnic minority groups, in order to reduce observed inequalities. Healthcare professionals should be aware of this increased observed risk of postpartum haemorrhage in ethnic minority groups, and, as with all women, be enabled to identify and treat PPH rapidly, to mitigate risk of maternal morbidity and mortality.

Supporting statements

Disclosure of interests (Conflict of interest statement): All authors have received funding from the Healthcare Quality Improvement Partnership (HQIP). HQIP had no involvement in the design, analysis or writing of this study, or in approval of the study for publication.

Author contribution: JJ, JvdM, DP and KW conceived the study. All authors planned the analysis. JJ conducted the analysis and wrote the first draft of the paper. All authors reviewed and redrafted the study. KW supervised the study.

Ethical approval: This study used data routinely collected in clinical care to evaluate service provision and performance and therefore individual consent was not sought. Institutional consent to access the data was provided by the NHS Health Research Authority Confidentiality Advisory Group, approval number 16/CAG/0058. This study was approved by the LSHTM Ethics Committee, approval number 14544, on 4th April 2018.

Patient and Public Involvement: The questions addressed by this study were informed by discussions from the NMPA's Inequalities Sprint Audit reference group, which includes women with lived experience of pregnancy and birth in the UK from diverse ethnic and socioeconomic groups.

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Table 1. Summary characteristics of 906 961 births in England with complete recorded information about maternal ethnic group between 1st April 2015 and 31st March 2017

	*Births with complete information about each characteristic (%)***	*White*	*S Asian*	*Black*	*Mixed*	*Other*
Number of women	906 961	705 948	107 382	42 170	16 456	35 005
Postpartum haemorrhage >=1500ml	28 268 (2.9%)	19 633 (2.8%)	2 806 (2.6%)	1 652 (3.9%)	479 (2.9%)	1 225 (3.5%)
*Maternal characteristics (n, %)**						
Most deprived socioeconomic quintile†	800 047 (88.2%)	160 437 (23.9%)	38 290 (38.5%)	18 641 (48.5%)	5 418 (35.2%)	10 652(33.3%)
Maternal age at birth 35 or over†	900 440 (99.3%)	146 832 (21.0%)	23 928 (22.3%)	12 510 (29.7%)	3 505 (21.4%)	9 423 (27.0%)
Maternal BMI 30 or over (obesity) †	762 767 (84.1%)	130 197 (21.8%)	16 000 (18.2%)	11 571 (33.7%)	3 141 (22.7%)	4 557 (15.6%)
Fibroids	880 534 (97.1%)	893 (0.1%)	271 (0.3%)	455 (1.1%)	60 (0.4%)	90 (0.3%)
Bleeding disorders	880 534 (97.1%)	3 795 (0.6%)	307 (0.3%)	100 (0.3%)	50 (0.3%)	117 (0.4%)
Diabetes	880 534 (97.1%)	32 096 (4.7%)	15 012 (14.3%)	3 492 (8.6%)	1 027 (6.5%)	2 802 (8.3%)
Hypertensive disease	880 534 (97.1%)	39 701 (5.8%)	5 683 (5.4%)	3 847 (9.5%)	875 (5.5%)	1 683 (5.0%)
Placental conditions	880 534 (97.1%)	8 451 (1.2%)	1 330 (1.3%)	545 (1.3%)	191 (1.2%)	451 (1.3%)
Nulliparous	902 245 (99.5%)	292 232 (41.6%)	36 285 (34.0%)	12 647 (30.2%)	6 496 (39.7%)	14 952(43.0%)
Previous caesarean section	902 474 (99.5%)	93 792 (13.4%)	20 161 (18.8%)	9 448 (22.5%)	2 411 (14.7%)	5 039 (14.5%)
*Fetal characteristics (n, %)**						
Multiple birth	906 961 (100%)	11 267 (1.6%)	1 288 (1.2%)	807 (1.9%)	252 (1.5%)	501 (1.4%)
Stillbirth	906 961 (100%)	2 416 (0.3%)	587 (0.5%)	307 (0.7%)	82 (0.5%)	151 (0.4%)
Preterm birth†	906 961 (100%)	49 183 (7.0%)	8 046 (7.5%)	3 360 (8.0%)	1 189 (7.2%)	2 187 (6.2%)
Birthweight of 4500g or more†	904 377 (99.7%)	12 427 (1.8%)	603 (0.6%)	495 (1.2%)	198 (1.2%)	418 (1.2%)
*Birth characteristics (n, %)**						
Induction	896 024 (98.8%)	206 201 (29.6%)	28 091 (26.3%)	10 556 (25.2%)	4 398 (26.9%)	8 417 (24.2%)
Birth assisted by instrument	904 603 (99.7%)	85 370 (12.1%)	13 366 (12.5%)	2 678 (6.4%)	1 624 (9.9%)	4 675 (13.4%)
Birth by caesarean section	904 603 (99.7%)	181 101 (25.7%)	30 775 (28.7%)	14 398 (34.2%)	4 449 (27.1%)	9 455 (27.1%)
Episiotomy	893 819 (98.6%)	106 252 (15.3%)	17 923 (16.9%)	3 655 (8.8%)	1 990 (12.3%)	5 858 (17.0%)
Manual removal of placenta	880 534 (97.1%)	13 061 (1.9%)	1 320 (1.3%)	484 (1.2%)	231 (1.5%)	502 (1.5%)

**percentages of women of each ethnicity with each characteristic are given among records with complete data for that characteristic only*
***percentages of all births with complete data about the characteristic. †these variables are split into more categories for analysis; details in Suppl. Tables 1, 3*
$p<0.001$ for all characteristics using the χ^2 test to evaluate distribution between ethnic groups.

Table 2. Risks of postpartum haemorrhage of 500, 1000, 1500 and 2000ml by ethnic group among 981 801 women who gave birth in England between 1st April 2015 and 31st March 2017

		Recorded blood loss in millilitres*				
		500ml or more	1000ml or more	1500ml or more	2000ml or more	3000ml or more
Number of women	981 801	322 606	75 674	28 268	11 964	2 469
Risk of PPH		32.9%	7.7%	2.9%	1.2%	0.3%
Risk by ethnic group (n, %)						
White	705 948	223 641 (31.7%)	52 427 (7.4%)	19 633 (2.8%)	8 347 (1.2%)	1 723 (0.2%)
South Asian	107 382	37 123 (34.6%)	7 896 (7.4%)	2 806 (2.6%)	1 165 (1.1%)	258 (0.2%)
Black	42 170	16 331 (38.7%)	4 322 (10.2%)	1 652 (3.9%)	737 (1.7%)	165 (0.4%)
Mixed	16 456	5 241 (31.8%)	1 258 (7.6%)	479 (2.9%)	200 (1.2%)	38 (0.2%)
Other	35 005	13 027 (37.2%)	3 205 (9.2%)	1 225 (3.5%)	548 (1.6%)	122 (0.3%)
Missing	74 840	27 243 (36.4%)	6 566 (8.8%)	2 473 (3.3%)	967 (1.3%)	163 (0.2%)

*$p<0.001$ in Chi squared tests comparing distributions by ethnic group for all levels of blood loss

Table 3. Associations between postpartum haemorrhage of 1500ml or more and characteristics available at booking and at birth among 981 801 women who gave birth in England between 1st April 2015 and 31st March 2017

Characteristics	Risk	Crude OR (95% CI)	p value*	Model 1 (maternal characteristics)†	p value*	Model 2 (maternal and fetal characteristics)‡	p value*	Model 3 (maternal, fetal and birth characteristics)§	p value*
Maternal ethnic group**									
White	2.8%	Ref	<0.001	Ref	<0.001	Ref	<0.001	Ref	<0.001
South Asian /Asian British	2.6%	0.94 (0.90, 0.97)		0.98 (0.94, 1.02)		1.18 (1.13, 1.26)		1.14 (1.09, 1.19)	
Black / Black British	3.9%	1.42 (1.35, 1.50)		1.36 (1.29, 1.44)		1.49 (1.41, 1.58)		1.54 (1.45, 1.63)	
Mixed	2.9%	1.06 (0.97, 1.16)		1.09 (0.99, 1.19)		1.17 (1.07, 1.28)		1.20 (1.09, 1.32)	
Other	3.5%	1.27 (1.20, 1.35)		1.27 (1.19, 1.35)		1.34 (1.26, 1.43)		1.37 (1.29, 1.46)	

*Wald test **ethnic group was imputed where it was missing

†maternal characteristics: maternal age, BMI, socioeconomic status, parity, previous caesarean section, medical conditions (diabetes, hypertension, bleeding disorders, fibroids, placental disorders)

‡maternal characteristics and additional fetal characteristics: gestational age, birthweight, livebirth/stillbirth, multiplicity

§maternal characteristics, fetal characteristics and additional birth characteristics: induction of labour, mode of birth, episiotomy, manual removal of placenta

Supplementary Tables for

Risk of postpartum haemorrhage is associated with ethnicity: a cohort study of 981 801 births in England

Table S1. Variable specifications, sources and categories used

Variable	Data Source	Details
Blood loss	MIS	Treated as binary variable (under 1500ml, or 1500ml or more)
Ethnic group	Primary: HES/PEDW Secondary: MIS	Categorised into White, S Asian, Black, Mixed, Other
Maternal age	Primary: MIS Secondary: HES/PEDW	Maternal age at time of birth. Grouped into under 20, 20-24, 25-29 (reference), 30-34, 35-39, 40-44, 45 or older
Socioeconomic group	Primary: MIS Secondary: HES	In England, IMD associated with women's recorded postcode at time of birth
Body mass index	MIS	Grouped using WHO categories (<18.5kg/m2, 18.5-24.9, 25.0-29.9, 30-34.9, 35.0-39.9, 40 or over)
Birthweight	MIS	Grouped into four categories: <2500g, 2500-3499g, 3500g-4499g, 4500g or more
Parity	Primary: MIS Secondary: HES/PEDW	Grouped into four categories: 0, 1, 2, 3 or more
Multiplicity	MIS	
Stillbirth	MIS	
Gestational age	MIS	Categorised into <32 weeks, 32-36 weeks and Term
Mode of birth	Primary: MIS Secondary: HES/PEDW	Grouped into unassisted vaginal, instrumental (forceps/ventouse), breech, emergency caesarean and elective caesarean
Manual removal of placenta	HES	OPCS code in birth episode R29.1
Augmentation	MIS	Binary
Episiotomy	MIS	Binary
Recorded co-morbidity	HES	ICD-10 codes in birth episode
Hypertensive disease		
Pre existing hypertension		O10, O11, I10, I11, I12, I13, I15
New onset hypertensive disease in pregnancy		O12, O13, O16
Pre-eclampsia/eclampsia		O10, O14, O15
Diabetes (pre-existing, gestational, or diabetes)		O24.0, O24.1, 024.9 E10, E11
Placental conditions		O43,O44,O45,O46,O69.4
Fibroids		ICD-10 code D25 in birth or previous episode
Bleeding disorders		ICD-10 code D65-D68, or D69.9, in birth or previous episode

Table S2. Characteristics of 981 801 included compared to 252 396 excluded birth records

	Included records (n, %*)	Excluded records (n, %*)
Number of women	981 801	252 396
PPH of 1500ml or more	28 268 (2.9%)	3 798 (2.8%)
Missing	*0*	*116 274 (46.1%)*
Ethnic group		
White	705 948 (77.8%)	166 390 (74.3%)
South Asian	107 382 (11.8%)	25 503 (11.4%)
Black	42 170 (4.6%)	14 500 (6.5%)
Mixed	16 456 (1.8%)	4 763 (2.1%)
Other	35 005 (3.9%)	12 924 (5.8%)
Missing	*74 840 (7.6%)*	*28 316 (11.2%)*
Socioeconomic deprivation		
Least deprived (1)	140 872 (15.2%)	28 195 (12.0%)
2	153 007 (16.5%)	39 012 (16.6%)
3	173 295 (18.7%)	45 557 (19.4%)
4	208 409 (22.5%)	55 802 (23.7%)
Most deprived (5)	250 332 (27.0%)	66 792 (28.4%)
Missing	*55 886 (5.7%)*	*17 038 (6.8%)*
Parity		
0	404 048 (41.4%)	104 140 (43.2%)
1	360 756 (36.9%)	87 570 (36.3%)
2	128 797 (13.2%)	29 890 (12.4%)
3 or more	82 859 (8.5%)	19 425 (8.1%)
Missing	*5 341 (0.5%)*	*11 371 (4.5%)*
Previous caesarean section	138 795 (14.2%)	33 912 (13.6%)
Missing	*5 101 (0.5%)*	*2 596 (1.0%)*
Fetal characteristics		
Stillbirth	3 824 (0.4%)	802 (0.4%)
Missing	*0*	*46 810 (18.5%)*
Birthweight of 4500g or more	105 107 (10.7%)	3 313 (1.4%)
Missing	*3 003 (0.3%)*	*16 794 (6.7%)*
Gestational age		
Term (37 weeks or more)	912 875 (93.0%)	206 165 (92.1%)
Preterm <32 weeks	11 150 (1.1%)	3 944 (1.8%)
Preterm 32-36 weeks	57 776 (5.9%)	13 731 (6.1%)
Missing	*0*	*28 556 (11.3%)*
Mode of birth		
Unassisted vaginal	596 009 (60.9%)	143 789 (60.0%)
Instrumental	119 050 (12.2%)	29 614 (12.4%)
Breech	3 860 (0.4%)	1 327 (0.6%)
Emergency caesarean	153 388 (15.7%)	37 506 (15.7%)
Elective caesarean	106 989 (10.9%)	27 402 (11.4%)
Missing	*2 505 (0.3%)*	*12 758 (5.1%)*
***all percentages among non-missing values**		

Table S3. Full Characteristics of 981 801 women included in the cohort

	All women	White	S Asian	Black	Mixed	Other	Missing	p value (χ^2)
Number of women (n)		705 948	107 382	42 170	16 456	35 005	74 840	
CHARACTERISTICS (n, %)								
Socioeconomic group (quintile)								
Least deprived (1)	140 872 (15.2%)	115 577 (17.2%)	7 642 (7.7%)	1 576 (4.1%)	1 745 (11.4%)	3 799 (11.9%)	10 533 (15.1%)	<0.001
2	153 007 (16.5%)	122 314 (18.2%)	9 664 (9.7%)	2 486 (6.5%)	2 092 (13.6%)	4 158 (13.0%)	12 293 (17.6%)	
3	173 295 (18.7%)	131 731 (19.6%)	15 569 (15.6%)	4 575 (11.9%)	2 476 (16.1%)	5 215 (16.3%)	13 729 (19.6%)	
4	208 409 (22.5%)	140 615 (21.0%)	28 334 (28.5%)	11 141 (29.0%)	3 641 (23.7%)	8 145 (25.5%)	16 533 (23.6%)	
Most deprived (5)	250 332 (27.0%)	160 437 (23.9%)	38 290 (38.5%)	18 641 (48.5%)	5 418 (35.2%)	10 652 (33.3%)	16 894 (24.1%)	
Missing	*55 886 (5.7%)*	*35 274 (5.0%)*	*7 883 (7.3%)*	*3 751 (8.9%)*	*1 084 (6.6%)*	*3 036 (8.7%)*	*4 858 (6.5%)*	
Maternal age (years)								
under 20	31 537 (3.2%)	26 316 (3.8%)	762 (0.7%)	0 817 (1.9%)	0 771 (4.7%)	0 770 (2.2%)	2 101 (2.9%)	<0.001
20-24	146 154 (15.0%)	115 511 (16.5%)	10 305 (9.6%)	4 515 (10.7%)	2 724 (16.6%)	3 768 (10.8%)	9 331 (12.9%)	
25-29	275 537 (28.3%)	197 534 (28.2%)	33 535 (31.3%)	10 983 (26.1%)	4 654 (28.4%)	9 296 (26.6%)	19 535 (27.1%)	
30-34	306 576 (31.5%)	213 495 (30.5%)	38 735 (36.1%)	13 304 (31.6%)	4 743 (28.9%)	11 704 (33.5%)	24 595 (34.1%)	
35-39	172 723 (17.8%)	119 931 (17.1%)	19 686 (18.4%)	9 275 (22.0%)	2 845 (17.4%)	7 464 (21.3%)	13 522 (18.7%)	
40-44	37 428 (3.8%)	25 297 (3.6%)	3 952 (3.7%)	2 885 (6.8%)	614 (3.7%)	1 816 (5.2%)	2 864 (4.0%)	
45 or older	2 674 (0.3%)	1 604 (0.2%)	290 (0.3%)	350 (0.8%)	46 (0.3%)	143 (0.4%)	241 (0.3%)	
Missing	*9 172 (0.9%)*	*6 260 (0.9%)*	*117 (0.1%)*	*41 (0.1%)*	*59 (0.4%)*	*44 (0.1%)*	*2651 (3.5%)*	
Maternal BMI (kg/m^2)								
under 18.5	23 949 (2.9%)	16 229 (2.7%)	3 762 (4.3%)	0 603 (1.8%)	0 425 (3.1%)	1 108 (3.8%)	1 822 (3.0%)	<0.001
18.5-24.99	390 484 (47.4%)	286 577 (48.0%)	39 424 (44.9%)	10 298 (30.0%)	6 345 (45.8%)	15 487 (53.1%)	32 353 (53.0%)	
25-29.99	233 836 (28.4%)	164 648 (27.5%)	28 575 (32.6%)	11 873 (34.6%)	3 929 (28.4%)	8 018 (27.5%)	16 793 (27.5%)	
30-34.99	107 639 (13.1%)	77 268 (12.9%)	11 482 (13.1%)	7 263 (21.1%)	1 917 (13.9%)	3 188 (10.9%)	6 521 (10.7%)	
35-39.99	44 680 (5.4%)	34 183 (5.7%)	3 375 (3.8%)	2 850 (8.3%)	805 (5.8%)	1 005 (3.4%)	2 462 (4.0%)	
40 or over	23 277 (2.8%)	18 746 (3.1%)	1 143 (1.3%)	1 458 (4.2%)	419 (3.0%)	364 (1.2%)	1 147 (1.9%)	
Missing	*157 936 (16.1%)*	*108 297 (15.3%)*	*19 621 (18.3%)*	*7 825 (18.6%)*	*2 616 (15.9%)*	*5 835 (16.7%)*	*13 742 (18.4%)*	

Maternal comorbidities								
Bleeding disorders	4 369 (0.5%)	3 795 (0.6%)	307 (0.3%)	100 (0.3%)	50 (0.3%)	117 (0.4%)	237 (0.3%)	<0.001
Fibroids	1 936 (0.2%)	893 (0.1%)	271 (0.3%)	455 (1.1%)	60 (0.4%)	90 (0.3%)	167 (0.2%)	<0.001
Diabetes	58 218 (6.1%)	32 096 (4.7%)	15 012 (14.3%)	3 492 (8.6%)	1 027 (6.5%)	2 802 (8.3%)	3 789 (5.3%)	<0.001
Hypertensive disease	56 023 (5.9%)	39 701 (5.8%)	5 683 (5.4%)	3 847 (9.5%)	875 (5.5%)	1 683 (5.0%)	4 234 (5.9%)	<0.001
Placental conditions	11 772 (1.2%)	8 451 (1.2%)	1 330 (1.3%)	545 (1.3%)	191 (1.2%)	451 (1.3%)	804 (1.1%)	<0.001
Missing	*29 541 (3.0%)*	*20 501 (2.9%)*	*2 561 (2.4%)*	*1 668 (4.0%)*	*557 (3.4%)*	*1 140 (3.3%)*	*3 114 (4.2%)*	
Parity								
Nulliparous	404 048 (41.4%)	292 232 (41.6%)	36 285 (34.0%)	12 647 (30.2%)	6 496 (39.7%)	14 952 (43.0%)	41 436 (55.8%)	<0.001
1	360 756 (36.9%)	267 669 (38.1%)	38 891 (36.5%)	13 419 (32.0%)	5 830 (35.6%)	12 066 (34.7%)	22 881 (30.8%)	
2	128 797 (13.2%)	88 647 (12.6%)	18 266 (17.1%)	8 346 (19.9%)	2 365 (14.4%)	4 697 (13.5%)	6 476 (8.7%)	
3 or more	82 859 (8.5%)	54 000 (7.7%)	13 181 (12.4%)	7 486 (17.9%)	1 676 (10.2%)	3 094 (8.9%)	3 422 (4.6%)	
Missing	*5 341 (0.5%)*	*3 400 (0.5%)*	*759 (0.7%)*	*272 (0.6%)*	*89 (0.5%)*	*196 (0.6%)*	*625 (0.8%)*	
Previous caesarean section	138 795 (14.2%)	93 792 (13.4%)	20 161 (18.8%)	9 448 (22.5%)	2 411 (14.7%)	5 039 (14.5%)	7 944 (10.7%)	<0.001
Missing	*5 101 (0.5%)*	*3 856 (0.5%)*	*250 (0.2%)*	*174 (0.4%)*	*67 (0.4%)*	*140 (0.4%)*	*614 (0.8%)*	
Fetal characteristics								
Multiple birth	15 296 (1.6%)	11 267 (1.6%)	1 288 (1.2%)	0 807 (1.9%)	0 252 (1.5%)	0 501 (1.4%)	1 181 (1.6%)	<0.001
Stillbirth	3 824 (0.4%)	2 416 (0.3%)	0 587 (0.5%)	0 307 (0.7%)	0 082 (0.5%)	0 151 (0.4%)	0 281 (0.4%)	<0.001
Gestational age								
Term	912 875 (93.0%)	656 765 (93.0%)	99 336 (92.5%)	38 810 (92.0%)	15 267 (92.8%)	32 818 (93.8%)	69 879 (93.4%)	<0.001
Preterm <32 weeks	11 150 (1.1%)	7 391 (1.0%)	1 342 (1.2%)	0 805 (1.9%)	0 214 (1.3%)	0 373 (1.1%)	1 025 (1.4%)	<0.001
Preterm 32-36 weeks	57 776 (5.9%)	41 792 (5.9%)	6 704 (6.2%)	2 555 (6.1%)	0 975 (5.9%)	1 814 (5.2%)	3 936 (5.3%)	<0.001
Birthweight (g)								
0-2499	64 086 (6.5%)	42 426 (6.0%)	10 104 (9.4%)	3 465 (8.2%)	1 255 (7.6%)	2 124 (6.1%)	4 712 (6.3%)	<0.001
2500-3499	511 868 (52.3%)	349 044 (49.6%)	70 259 (65.7%)	23 872 (56.8%)	9 244 (56.3%)	19 779 (56.7%)	39 670 (53.3%)	
3500-4499	387 640 (39.6%)	300 107 (42.6%)	26 048 (24.3%)	14 206 (33.8%)	5 712 (34.8%)	12 590 (36.1%)	28 977 (38.9%)	

4500 or more	15 203 (1.6%)	12 427 (1.8%)	603 (0.6%)	495 (1.2%)	198 (1.2%)	418 (1.2%)	1 062 (1.4%)	
Missing	*3 004 (0.3%)*	*1 944 (0.3%)*	*368 (0.3%)*	*132 (0.3%)*	*47 (0.3%)*	*94 (0.3%)*	*419 (0.6%)*	
Birth characteristics								
Induction	277 450 (28.6%)	206 201 (29.6%)	28 091 (26.3%)	10 556 (25.2%)	4 398 (26.9%)	8 417 (24.2%)	19 787 (26.6%)	<0.001
Missing	*11 455 (1.2%)*	*9 711 (1.4%)*	*527 (0.5%)*	*363 (0.9%)*	*134 (0.8%)*	*202 (0.6%)*	*518 (0.7%)*	
Augmentation	140 913 (21.6%)	100 660 (21.3%)	15 007 (21.1%)	5 572 (19.5%)	2 246 (21.2%)	4 628 (19.5%)	12 800 (28.2%)	<0.001
Missing	*330 860 (33.7%)*	*234 238 (33.2%)*	*36 303 (33.8%)*	*13 646 (32.4%)*	*5 876 (35.7%)*	*11 318 (32.3%)*	*29 479 (39.4%)*	
Mode of birth								
Unassisted vaginal	596 009 (60.9%)	435 021 (61.8%)	62 488 (58.4%)	24 765 (58.9%)	10 242 (62.5%)	20 647 (59.1%)	42 846 (57.4%)	<0.001
Instrumental	119 050 (12.2%)	85 370 (12.1%)	13 366 (12.5%)	2 678 (6.4%)	1 624 (9.9%)	4 675 (13.4%)	11 337 (15.2%)	
Breech	3 860 (0.4%)	2 703 (0.4%)	425 (0.4%)	207 (0.5%)	73 (0.4%)	141 (0.4%)	311 (0.4%)	
Emergency caesarean	153 388 (15.7%)	102 408 (14.5%)	19 979 (18.7%)	9 437 (22.4%)	2 722 (16.6%)	5 755 (16.5%)	13 087 (17.5%)	
Elective caesarean	106 989 (10.9%)	78 693 (11.2%)	10 796 (10.1%)	4 961 (11.8%)	1 727 (10.5%)	3 700 (10.6%)	7 112 (9.5%)	
Missing	*2 505 (0.3%)*	*1 753 (0.2%)*	*328 (0.3%)*	*122 (0.3%)*	*68 (0.4%)*	*87 (0.2%)*	*147 (0.2%)*	
Episiotomy	149 976 (15.5%)	106 252 (15.3%)	17 923 (16.9%)	3 655 (8.8%)	1 990 (12.3%)	5 858 (17.0%)	14 298 (19.4%)	<0.001
Missing	*14 173 (1.4%)*	*10 493 (1.5%)*	*1 236 (1.2%)*	*0 532 (1.3%)*	*0 320 (1.9%)*	*0 561 (1.6%)*	*1 031 (1.4%)*	
Manual removal of placenta	16 849 (1.8%)	13 061 (1.9%)	1 320 (1.3%)	0 484 (1.2%)	0 231 (1.5%)	0 502 (1.5%)	1 251 (1.7%)	<0.001
Missing	*29 452 (3.0%)*	*20 431 (2.9%)*	*2 558 (2.4%)*	*1 666 (4.0%)*	*0 555 (3.4%)*	*1 135 (3.2%)*	*3 107 (4.2%)*	

Table S4. Complete versions of models presented in Table 3

	Crude	p value*	Model 1§	p value*	Model 2§	p value*	Model 3§	p value*
Maternal ethnic group								
White	Ref	<0.001	Ref	<0.001	Ref	<0.001	Ref	<0.001
S Asian	0.94 (0.90, 0.97)		0.98 (0.94, 1.02)		1.18 (1.13, 1.26)		1.14 (1.09, 1.19)	
Black	1.42 (1.35, 1.50)		1.36 (1.29, 1.44)		1.49 (1.41, 1.58)		1.54 (1.45, 1.63)	
Mixed	1.06 (0.97, 1.16)		1.09 (0.99, 1.19)		1.17 (1.07, 1.28)		1.20 (1.09, 1.32)	
Other	1.27 (1.20, 1.35)		1.27 (1.19, 1.35)		1.34 (1.26, 1.43)		1.37 (1.29, 1.46)	
Maternal socioeconomic deprivation (IMD)								
Least deprived (1)	Ref	<0.001	Ref	<0.001	Ref	0.02	Ref	0.007
2	0.95 (0.91,0.99)		0.97 (0.93,1.01)		0.97 (0.93,1.02)		0.97 (0.93,1.01)	
3	0.92 (0.88,0.95)		0.95 (0.91,0.99)		0.97 (0.93,1.01)		0.96 (0.92,1.00)	
4	0.86 (0.82,0.89)		0.91 (0.87,0.95)		0.94 (0.90,0.98)		0.92 (0.89,0.97)	
Most deprived (5)	0.76 (0.73,0.79)		0.85 (0.82,0.89)		0.89 (0.85,0.93)		0.88 (0.84,0.91)	
Maternal age (years)								
under 20	0.72 (0.67,0.79)	<0.001	0.64 (0.59,0.70)	<0.001	0.68 (0.63,0.75)	<0.001	0.84 (0.77,0.91)	<0.001
20-24	0.80 (0.77,0.84)		0.77 (0.74,0.81)		0.80 (0.77,0.84)		0.88 (0.84,0.92)	
25-29	Ref		Ref		Ref		Ref	
30-34	1.20 (1.16,1.24)		1.20 (1.16,1.24)		1.18 (1.14,1.22)		1.12 (1.08,1.16)	
35-39	1.37 (1.33,1.42)		1.38 (1.33,1.43)		1.35 (1.30,1.40)		1.24 (1.19,1.28)	
40-44	1.69 (1.60,1.79)		1.62 (1.53,1.72)		1.63 (1.54,1.72)		1.43 (1.34,1.51)	
45 or older	3.00 (2.59,3.47)		2.51 (2.15,2.92)		2.26 (1.93,2.65)		2.00 (1.70,2.36)	
Maternal BMI (kg/m2)								
less than 18.5	1.04 (0.98,1.10)	0.22	1.09 (1.03,1.16)	<0.001	1.07 (1.01,1.14)	<0.001	1.06 (0.99,1.12)	<0.001
18.5-24.9	Ref		Ref		Ref		Ref	
25-29.99	1.21 (1.17,1.25)		1.23 (1.19,1.26)		1.16 (1.12,1.19)		1.14 (1.10,1.17)	
30-34.99	1.28 (1.23,1.33)		1.33 (1.28,1.39)		1.23 (1.18,1.28)		1.19 (1.15,1.25)	
35-39.99	1.47 (1.40,1.55)		1.57 (1.49,1.66)		1.42 (1.34,1.50)		1.35 (1.28,1.43)	
40 or higher	1.60 (1.49,1.71)		1.71 (1.60,1.84)		1.51 (1.41,1.63)		1.43 (1.33,1.54)	

Parity								
Nulliparous	Ref	<0.001	Ref	<0.001	Ref	<0.001	Ref	<0.001
1	0.67 (0.66,0.69)		0.55 (0.53,0.57)		0.52 (0.51,0.54)		0.87 (0.84,0.90)	
2	0.63 (0.60,0.65)		0.50 (0.48,0.53)		0.47 (0.45,0.49)		0.85 (0.81,0.89)	
3 or more	0.71 (0.68,0.75)		0.49 (0.46,0.52)		0.49 (0.46,0.51)		0.91 (0.87,0.97)	
Previous caesarean birth	1.21 (1.18,1.25)	<0.001	1.29 (0.50,3.30)	0.59	1.44 (1.39,1.50)	<0.001	1.05 (1.01,1.10)	0.02
Maternal medical conditions								
Bleeding disorders	1.24 (1.06,1.45)	0.01	1.15 (0.97,1.35)	0.1	1.18 (1.00,1.39)	0.05	1.13 (0.95,1.33)	0.16
Fibroids	2.89 (2.45,3.40)	<0.001	1.87 (1.57,2.23)	<0.001	1.94 (1.62,2.31)	<0.001	1.79 (1.49,2.16)	<0.001
Diabetes	1.17 (1.12,1.23)	<0.001	0.98 (0.93,1.03)	0.48	1.00 (0.95,1.05)	0.91	0.92 (0.88,0.97)	<0.001
Placental conditions	9.20 (8.78,9.64)	<0.001	8.70 (8.29,9.13)	<0.001	9.65 (9.17,10.14)	<0.001	5.88 (5.55,6.24)	<0.001
Hypertension	1.66 (1.59,1.73)	<0.001	1.36 (1.30,1.42)	<0.001	1.41 (1.35,1.48)	<0.001	1.20 (1.15,1.26)	<0.001
Gestational age at birth								
Term								
Preterm <32 weeks	1.85 (1.70,2.02)	<0.001			1.51 (1.35,1.69)	<0.001	1.48 (1.32,1.66)	<0.001
Preterm 32-36 weeks	1.54 (1.47,1.60)	<0.001			1.43 (1.35,1.51)	<0.001	1.39 (1.31,1.48)	<0.001
Birthweight								
less than 2500g	1.59 (1.52,1.67)	<0.001			0.68 (0.64,0.73)	<0.001	0.64 (0.60,0.69)	<0.001
2500-3499g	Ref				Ref		Ref	
3500-4499	1.65 (1.61,1.69)				1.89 (1.84,1.95)		1.80 (1.75,1.85)	
4500g or more	3.58 (3.36,3.82)				4.17 (3.91,4.46)		3.55 (3.32,3.80)	
Stillbirth	2.62 (2.32,2.96)	<0.001			2.14 (1.86,2.45)	<0.001	2.64 (2.28,3.05)	<0.001
Multiple birth	3.70 (3.50,3.91)	<0.001			4.46 (4.17,4.77)	<0.001	4.00 (3.73,4.29)	<0.001
Induction of labour	1.46 (1.43,1.50)	<0.001					1.31 (1.28,1.35)	<0.001
Mode of birth								
Unassisted vaginal (vertex) birth	Ref	<0.001					Ref	<0.001
Instrumental	3.47 (3.36,3.58)						2.02 (1.92,2.13)	

Breech	1.81 (1.50,2.19)		1.00 (0.80,1.24)	
Emergency Caesarean	3.71 (3.60,3.82)		3.31 (3.19,3.44)	
Elective Caesarean	1.81 (1.73,1.88)		1.73 (1.64,1.82)	
Episiotomy	1.94 (1.89,1.99)	<0.001	1.68 (1.60,1.77)	<0.001
Manual removal of placenta	8.77 (8.41, 9.14)	<0.001	7.86 (7.47,8.28)	<0.001

§adjustment for maternal characteristics (Model 1), maternal and baby (Model 2), maternal, baby and birth (Model 3) as shown in this table.

Table S5: Numbers of women and rates of postpartum haemorrhage of 1500ml by ethnic and socioeconomic group

Socioeconomic deprivation (quintile)	Postpartum haemorrhage by ethnic group (number of women experiencing PPH, rate ((%), 95% CI)					
	White	South Asian	Black	Mixed	Other	Missing
Least deprived (1)	3 715	247	54	51	163	361
	3.2% (3.1%, 3.3%)	3.2% (2.8%, 3.6%)	3.4% (2.5%, 4.3%)	2.9% (2.1%, 3.7%)	4.3% (3.6%, 4.9%)	3.4% (3.1%, 3.8%)
2	3 685	285	95	54	172	458
	3.0% (2.9%, 3.1%)	2.9% (2.6%, 3.3%)	3.8% (3.1%, 4.6%)	2.6% (1.9%, 3.3%)	4.1% (3.5%, 4.7%)	3.7% (3.4%, 4.1%)
3	3 728	882	692	147	310	488
	2.9% (2.8%, 3.0%)	2.8% (2.5%, 3.1%)	4.3% (3.7%, 4.9%)	3.5% (2.8%, 4.2%)	4.0% (3.5%, 4.5%)	3.4% (3.1%, 3.7%)
4	3 729	757	465	106	265	539
	2.7% (2.6%, 2.7%)	2.7% (2.5%, 2.9%)	4.2% (3.8%, 4.5%)	2.9% (2.4%, 3.5%)	3.3% (2.9%, 3.6%)	3.3% (3.0%, 3.5%)
Most deprived (5)	3 728	882	692	147	310	488
	2.3% (2.2%, 2.4%)	2.3% (2.2%, 2.5%)	3.7% (3.4%, 4.0%)	2.7% (2.3%, 3.1%)	2.9% (2.6%, 3.2%)	2.9% (2.6%, 3.1%)
Missing	*975*	*200*	*149*	*35*	*107*	*156*
	2.8% (2.6%, 2.9%)	*2.5% (2.2%, 2.9%)*	*4.0% (3.3%, 4.6%)*	*3.2% (2.2%, 4.3%)*	*3.5% (2.9%, 4.2%)*	*3.2% (2.7%, 3.7%)*
Total	15 918	2 559	1 598	428	1 062	2 112
	2.8% (2.7%, 2.8%)	2.6% (2.5%, 2.7%)	3.9% (3.7%, 4.1%)	2.9% (2.7%, 3.2%)	3.5% (3.3%, 3.7%)	3.3% (3.2%, 3.4%)

Table S6. Sensitivity analyses examining risk of PPH by ethnic group (1) among primiparous women (2) when augmentation is included in the full model (3) when augmentation is included in the model (4) when the outcome is changed to PPH of 500ml or more (5) when the outcome is changed to PPH of 3000ml or more

Maternal ethnic group	Sensitivity analysis 1 (women with complete data, n = 674 867 women)	p value*	Sensitivity analysis 2 (nulliparous women with complete data, n = 268 973 women)	p value*	Sensitivity analysis 3 (inclusion of augmentation among women with complete data, n=487 087 women)	p value*
White	Ref	<0.001	Ref	<0.001	Ref	<0.001
South Asian	1.11 (1.06, 1.17)		1.27 (1.18, 1.37)		1.16 (1.10, 1.23)	
Black	1.46 (1.36, 1.56)		1.51 (1.35,1.68)		1.42 (1.31, 1.54)	
Mixed	1.22 (1.09, 1.36)		1.17 (0.99, 1.38)		1.23 (1.08, 1.40)	
Other	1.35 (1.25, 1.45)		1.43 (1.29, 1.58)		1.39 (1.28, 1.51)	

Maternal ethnic group	Sensitivity analysis 4 (PPH of 500ml or more with complete data, n = 674 867 women))	p value*	Sensitivity analysis 5 (PPH of 3000ml or more with complete data, n = 674 867 women)	p value*
White	Ref	<0.001	Ref	<0.001
South Asian	1.31 (1.28, 1.33)		1.10 (0.93, 1.29)	
Black	1.46 (1.42, 1.50)		1.34 (1.09, 1.65)	
Mixed	1.11 (1.06, 1.16)		1.03 (0.70, 1.51)	
Other	1.40 (1.36, 1.44)		1.49 (1.19, 1.87)	
***Wald test**				

Table S7. Sensitivity analysis examining correspondence between ICD-10 diagnostic code for PPH, among 907 860 women with both a record of blood loss and a linked HES record

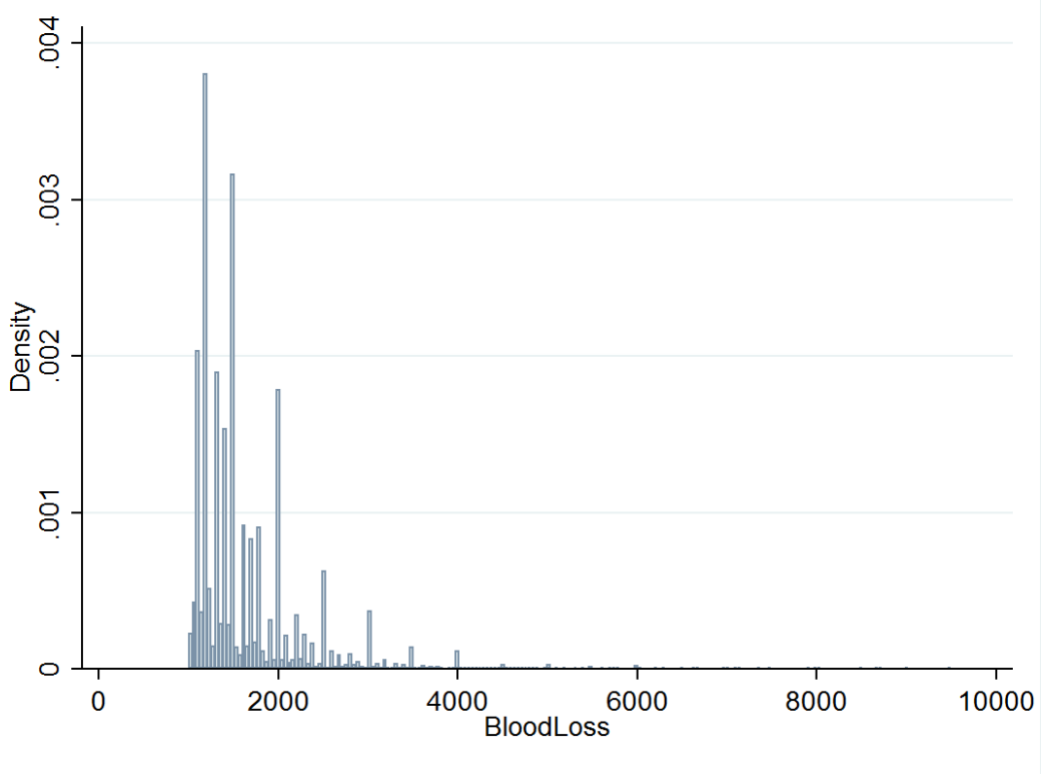
Recorded blood loss at birth (ml)	Number of women in group	Number of women recorded as having PPH in HES† (%)
500ml or less	610 608	10 001 (1.6)
500-999	228 240	85 418 (37.4)
1000-1499	43 406	33 661 (77.6)
1500-1999	14 824	12 660 (85.4)
2000-2499	6 310	5 571 (88.3)
2500-2999	2 273	2 039 (89.7)
3000 or more	2 199	1 943 (88.4)
Total	907 860	151 293 (16.7)

†Indicated by the presence of the diagnosis code O72

5.2 Further description of coding of blood loss

Blood loss is coded in the MIS dataset as a continuous variable. However, it cannot be treated as such, as there is clear evidence of rounding with an observed threshold effect. In the below histogram (Fig 5.2.1), the distribution of blood loss of over 1000ml is demonstrated (the histogram is restricted to this to allow the observation of the smaller densities above this threshold); it is possible to see clear spikes at every 100ml, and particularly at 1200, 1500, 2500 and 3000. This is because, as blood loss measurement is a combination of weighing, fluid measurement and estimation, there is practically an element of rounding. This supports the use of blood loss as a binary or ordinal variable, rather than as a continuous one.

Figure 5.2.1. Distribution of blood loss of more than 1000ml in maternity data in England and Wales



6. Results Chapter: Iatrogenic and spontaneous preterm birth

The next part of my thesis considers how best to measure preterm birth and identify the determinants of preterm birth. In this analysis, I split preterm birth into spontaneous and iatrogenic based on the mode of onset of the birth (whether it started by itself or was initiated by the healthcare provider) and used logistic regression models to explore similarities and differences between these groups.

The findings of this analysis are presented in the form of a research paper which has been submitted for publication.

6.1 Research Paper 4

Iatrogenic and spontaneous preterm birth in England: population-based cohort study

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RESEARCH PAPER COVER SHEET

Please note that a cover sheet must be completed for each research paper included within a thesis.

SECTION A – Student Details

Student ID Number	1511701	**Title**	Dr
First Name(s)	Jennifer		
Surname/Family Name	Jardine		
Thesis Title	A study of risk factors of maternity outcomes using large, routinely collected datasets		
Primary Supervisor	Kate Walker		

If the Research Paper has previously been published please complete Section B, if not please move to Section C.

SECTION B – Paper already published

Where was the work published?			
When was the work published?			
If the work was published prior to registration for your research degree, give a brief rationale for its inclusion			
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SECTION C – Prepared for publication, but not yet published

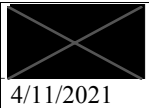
Where is the work intended to be published?	Archives of Disease in Childhood
Please list the paper's authors in the intended authorship order:	Harriet Aughey*, Jennifer Jardine*, Hannah Knight, Ipek Gurol-Urganci, Kate Walker, Tina Harris, Jan van der Meulen, Jane Hawdon, Dharmintra Pasupathy on behalf of the NMPA Project Team *joint first authors

Stage of publication	**Submitted**

SECTION D – Multi-authored work

For multi-authored work, give full details of your role in the research included in the paper and in the preparation of the paper. (Attach a further sheet if necessary)	Co-designed study with collaborative input from coauthors, conducted primary analysis, wrote first draft of methods, results, strengths and limitations, revised paper in full, co-ordinated feedback, implemented revisions from co-authors.

SECTION E

Student Signature	
Date	4/11/2021

Supervisor Signature	
Date	

Iatrogenic and spontaneous preterm birth in England: population-based cohort study

Authors

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ABSTRACT

Objective

To describe the rates and risk factors of iatrogenic and spontaneous preterm birth and the variation in rates between hospitals.

Design

We used routinely collected hospital data to identify singleton preterm births in England between 1st April 2015 and 31st March 2017. These were defined as iatrogenic or spontaneous according to the mode of onset of labour. Multivariable Poisson regression models were used to estimate adjusted risk ratios (adjRR) that represent the effect of maternal demographic and clinical risk factors.

Results

6.1% of the cohort were preterm and of these, 52.8% were iatrogenic. Both sub-groups are associated with previous preterm birth (iatrogenic adjRR 3.34 95% CI (3.22, 3.46); spontaneous adjRR 6.53 (6.32, 6.75)), socioeconomic deprivation and smoking.

Iatrogenic preterm birth is associated with older age (adjRR age >40 1.71(1.62, 1.80)), higher BMI (adjRR BMI >40 1.59 (1.50, 1.69)), and previous caesarean (adjRR 1.88 (1.83, 1.95)). Spontaneous preterm birth is more common among younger women (adjRR age <20 1.32 (1.24, 1.39)), but less common in those with a higher BMI (adjRR BMI>40 0.77 (0.70, 0.84)) and who have had a previous caesarean (adjRR 0.87 (0.83, 0.90)).

Conclusions

Iatrogenic births account for over half of liveborn singleton preterm births in England and have overlapping but different patterns of maternal demographic and clinical risk factors to spontaneous preterm births. Iatrogenic and spontaneous sub-groups should therefore be measured and monitored separately, as well as in aggregate, as each requires different prevention strategies. This is feasible using routinely acquired hospital data.

SUMMARY BOX

What is already known on this topic

Preterm birth is an important public health problem and a major challenge for obstetric practice. It may be classified into two distinct sub-groups: spontaneous and iatrogenic preterm birth. Rates of iatrogenic preterm birth are increasing in many high-income settings.

What this study adds

This study adds to the literature supporting the finding that iatrogenic and spontaneous preterm birth are associated with overlapping but different patterns of maternal demographic and clinical risk factors. Preterm birth should not be solely measured in aggregate but instead considered as two distinct outcomes requiring different prevention strategies. This study shows that is feasible to use routinely acquired hospital administrative data to measure rates of iatrogenic and spontaneous preterm birth in England.

INTRODUCTION

Preterm birth is the single largest cause of neonatal morbidity and mortality in many countries.[1][2–4] Being born preterm confers an increased lifelong risk of disability and chronic disease.[2,3] The costs of preterm birth are high, inversely related to gestation at birth, and persist throughout childhood.[4,5] Preterm birth is also associated with substantial impacts upon family life.[4] Prevention of preterm birth is, therefore, an important aim in modern obstetric practice.[6,7]

Measurement of the rate of preterm birth and comparison between providers is desirable to evaluate interventions which aim to reduce preterm birth[8] and enable clinical benchmarking. However, the aetiology of preterm birth is complex and treating it as a single outcome may hinder appropriately targeted interventions. It has been recognised that it is important to distinguish spontaneous and iatrogenic birth,[9] depending on whether birth is initiated by the provider of maternity care. Iatrogenic preterm birth is indicated in response to maternal illness or signs of fetal compromise; these are increasingly detected and acted on, with benefits to maternal health in some situations.[10] Unsurprisingly, therefore, iatrogenic preterm birth is increasing in many high-income countries[11,12,15–18] potentially limiting progress towards reducing overall rates of preterm birth.[12–14]

In the UK, overall rates of preterm birth have remained relatively static for the past decade; it is not known how the rates of iatrogenic and spontaneous preterm birth have changed within this aggregated total.[1] Using a large, routinely collected dataset, this study describes the rates of iatrogenic and spontaneous preterm birth in England, the maternal demographic and clinical risk factors associated with each group, the recorded maternal and fetal indications for iatrogenic preterm birth and the variation in preterm birth rates between hospital trusts.

METHODS

The data for this study were obtained from two population-level electronic datasets, linked together for the purposes of a national audit of maternity care, including births that occurred from 1st April 2015 to 31st March 2017.[19] Data from maternity information systems (MIS) in hospitals providing maternity services in the English National Health Services (NHS) were linked to data from the Hospital Episode Statistics (HES), the database that collects administrative data for admissions to NHS hospitals.

The MIS record contained information about gestational age, the mode of onset of labour, the birth, and maternal and neonatal characteristics including parity, ethnic group and gestational age. Socio-economic status was evaluated using the Index of Multiple Deprivation (IMD), an area-level measure of deprivation identified by the woman's recorded postcode in MIS.[20] Information about maternal diagnoses including pre-eclampsia and gestational diabetes was available in HES. Women's previous birth record, including the mode of birth and previous preterm birth, was available using a 'look-back' approach in HES where all previous records for the woman since 2000 in English NHS hospitals were considered.[21,22]

All 1 254 484 live births of at least 22 weeks of gestation in 133 NHS hospital trusts were eligible for inclusion. Births in 23 hospital trusts were excluded from the study due to poor quality data (less than 70% of records with complete information on all of: stillbirth or livebirth; gestational age; method of labour onset; and delivery method), or poor linkage (<70% of records) to HES. Stillbirths were excluded as it was not possible to identify whether a stillbirth occurred antepartum or intrapartum. Multiple births were excluded because the frequency of preterm birth in multiple pregnancies differs and therefore should be considered separately. 9 283 births without a record of labour onset were excluded, representing less than 1% of the cohort. In total 963 800 (93.1% of births in included hospitals) live singleton births with complete data about

gestational age, method of labour onset and delivery method were included in the analyses (Figure S1).

Births were considered preterm if they had a recorded gestation of less than 37 completed weeks at birth. Births were defined as iatrogenic if there was a record of induction of labour or of caesarean section (CS) before the onset of labour and as spontaneous if the recorded onset was spontaneous. Details of variable definitions are available in Supplementary Information (Table S1).

To investigate associations between risk factors and outcomes, chi-squared tests were used. Multivariable Poisson regression models with robust standard errors were used to estimate the effect of maternal risk factors for preterm birth overall and stratified into iatrogenic and spontaneous. The maternal risk factors included were age, BMI, ethnicity, socio-economic status, smoking status at booking, parity, previous CS and previous preterm birth. Interaction terms were included for parity and each of previous CS and previous preterm birth. For regression analyses, missing values were imputed using multiple imputation by chained equations with statistical coefficients obtained using 10 imputed data sets, pooled using Rubin's rules.[23] A further interaction between ethnic and socioeconomic background was considered plausible a priori. We evaluated whether there was evidence for this interaction by including an additional interaction term in the full model and using a global Wald test to compare this to the model without the interaction term. For this test $p>0.1$, so the interaction was not included in the full model.

Risk-adjusted funnel plots were used to visually explore the variation between hospital organisations in rates of preterm birth, both overall and disaggregated into iatrogenic and spontaneous. These plots 'test' whether the variation from the national mean is within the range that would be expected by chance alone.[24]

Two clinicians (JJ and DP) mapped possible indications for iatrogenic preterm birth to ICD-10 codes. These were then identified in the maternal record. Further details of codes used are available in Supplementary Information (Table S2).

Three sensitivity analyses were conducted to assess whether the effects of maternal risk factors were sensitive to the inclusion criteria and methods used. In the first, births associated with preterm prelabour rupture of membranes (PPROM) were excluded. In the second, maternal diabetes, hypertension and pre-eclampsia/ eclampsia were included in the regression models. Further details are available in Supplementary Information (Table S2). Finally, we tested whether our results were robust to alternative methods of handling missing data by repeating the regression analysis in the subset of records with complete information about all covariates. STATA v14.1 was used for all analyses.]

RESULTS

The cohort included 963 800 women who had a singleton live birth in England between 1st April 2015 and 31st March 2017 (Figure S1). 58 850 babies (6.1%) were born preterm, (Table 1), of which 31 097 (52.8%) births were iatrogenic in onset. Spontaneous preterm birth was more prevalent in the early preterm period and iatrogenic births comprised a larger proportion of late preterm births (Figure 1).

The highest rates of preterm birth were seen in women with a previous preterm birth; 12.8% of these women had spontaneous and 10.9% had iatrogenic preterm births (Table 1). Following adjustment for demographic and clinical risk factors, there remained a substantial association between both sub-groups of preterm birth and previous preterm birth; the relationship was stronger for spontaneous than iatrogenic preterm birth (iatrogenic adjRR 3.34 (3.22,3.46); spontaneous adjRR 6.53 (6.32,6.75)).

Increasing socioeconomic deprivation was associated with increasing risk of both sub-groups of preterm birth. Women in the most deprived neighbourhoods were approximately 20% more likely to have either a spontaneous (adjRR 1.21 (1.16,1.26)) or iatrogenic (adjRR 1.24 (1.19,1.29)) preterm birth compared to women in the least deprived neighbourhoods. Similarly, smoking was associated with an increased risk in both sub-groups (spontaneous, adjRR 1.61 (1.56,1.67)); iatrogenic (adjRR 1.55 (1.50,1.60)). (Table 2, Figure 2)

Opposing directions of association were found for some characteristics. Younger women were at higher risk of spontaneous preterm birth (women under 20 compared to those age 25-39, adjRR 1.32, (1.24,1.39)) and older women at higher risk of iatrogenic preterm birth (women over 40, adjRR 1.71(1.62,1.80)). (Table 2). Obese women had higher rates of iatrogenic preterm birth (adjRR for BMI >40, 1.57 (1.48,1.67)). Conversely, obesity was associated with a reduction in spontaneous preterm birth (adjRR for BMI >40, 0.77 (0.70,0.84)). (Table 2, Figure 2) Previous CS was associated with an almost doubling of the rate of iatrogenic preterm birth (adjRR 1.88 (1.83,1.95)) but a reduction in the rate of spontaneous preterm birth (adjRR 0.87 (0.83,0.90)).

South Asian women were approximately 8% more likely to have either a spontaneous (adjRR 1.08 (1.04,1.12)) or iatrogenic (adjRR 1.08 (1.04,1.12)) preterm birth when compared with White women. Black women had similar rates of spontaneous (adjRR 1.00 (0.94,1.06)) but higher rates of iatrogenic preterm birth (adjRR 1.11 (1.05,1.16)).

Our findings were not materially different in the sensitivity analyses excluding 3,842 preterm births with PPROM (14.4% of all preterm births) and restricted to complete cases. (Tables S5 and S6)

Increased rates of iatrogenic, but not spontaneous, preterm birth were seen in women with pre-existing hypertension (13.0%), diabetes (7.4%) or pre-eclampsia/eclampsia (25.7%). (Table 1) In the sensitivity analysis which included adjustment for maternal hypertensive and diabetic

disorders these conditions were strongly associated with iatrogenic preterm birth (adjRR for pre-eclampsia or eclampsia, 8.34. (8.07,8.62); adjRR for pre-existing or gestational diabetes, 2.16 (2.01,2.31)). In this analysis, the association between iatrogenic preterm birth and socioeconomic deprivation remained, the association with raised BMI was attenuated but remained (BMI of 40 or higher compared with BMI 18.5-24.9; adjRR 1.13 (1.05,1.21)) and the associations between preterm birth and maternal South Asian and Black ethnicity disappeared. (Table S7)

Fetal and maternal indications for iatrogenic preterm birth

88.4% of iatrogenic preterm births had a potential indication for delivery recorded in HES. The most common fetal indications were suspected distress (26.8%) and growth restriction (22.9%); the most common maternal indications were hypertensive disease (18.2%) and diabetes (12.4%). (Figure S2, Table S4)

Variation between hospital trusts

Risk-adjusted rates of iatrogenic preterm birth ranged from 0.95% to 4.72% (interquartile range 2.78% to 3.73%) and of spontaneous preterm birth from 1.37% to 5.96% (interquartile range 2.55% to 3.12%) in the 110 hospital trusts included in this study. The funnel plots demonstrate larger between-hospital variation in the rates of iatrogenic preterm births than rates of spontaneous preterm births (Figure 3).

DISCUSSION

Summary of results

Preterm birth accounted for 6% of all singleton live births in England in 2015-17; just over half (52.8%) were born as a result of iatrogenic intervention. This figure is larger than the 25-30% previously quoted for the UK[1,25] and is consistent with reported increases in iatrogenic preterm

birth globally, particularly in high-income settings.[7,26] Much of the observed variation seen in preterm birth rates is accounted for by iatrogenic preterm birth.

Iatrogenic and spontaneous preterm birth have areas of overlap in their risk factors. Both are strongly associated with previous preterm birth, socioeconomic deprivation and smoking. However, there are also important differences between the two sub-groups. Older women, those with higher BMI, previous caesarean and medical comorbidities are more likely to experience iatrogenic preterm birth. Spontaneous preterm birth is more common among younger women, but less common in those with a higher BMI and who have had a previous caesarean.

Our findings showed only a weak association between ethnic group and iatrogenic preterm birth which disappeared after adjustment for maternal hypertension, pre-eclampsia and diabetes, suggesting that differences in iatrogenic preterm birth between ethnic groups is largely accounted for by different prevalence of co-morbidities in non-white ethnic groups. Similarly, we show that the association between iatrogenic preterm birth and obesity is partly explained by the higher prevalence of maternal medical conditions amongst women with a raised BMI. In contrast, the association between socioeconomic deprivation and preterm birth remained consistent across all analyses.

Methodological considerations

This study uses a large contemporary dataset [19] containing rich information about maternal risk factors and neonatal characteristics. Approximately 92% of births that occurred in England in the time period were included. The main reason for exclusion was poor completeness (<70%) of records at the hospital trust level, rather than exclusion of individual patient data, minimising the risk of systematic bias. However, the adjusted results may be affected by residual confounding from information not available to us. For example, we were unable to include previous early pregnancy loss, a recognised risk factor for preterm birth.[14,27]

Our categorisation of preterm birth does not separately consider PPROM. The approach to PPROM in the literature is heterogeneous, with some studies treating it as a distinct category[9,11] and others including it as spontaneous.[14] A sensitivity analysis excluding women with PPROM from this analysis did not reveal substantial differences in the results.

Implications

This study shows that the proportion of preterm births in England that are iatrogenic in onset is greater than has previously been recognised[1,25] occurring more frequently than spontaneous preterm births. This may be partially attributable to changes in risk factor profile over time, in particular increasing maternal age and the increasing prevalence of maternal obesity,[28,29] both of which are associated with increased risk of iatrogenic preterm birth; and also, to changing obstetric practice which may lead to an increase in iatrogenic preterm birth over time.[10]

Both spontaneous and iatrogenic preterm birth are strongly associated with smoking and therefore antenatal interventions to encourage smoking cessation[8] should be prioritised.[30,31] Understanding and addressing the association between preterm birth and socioeconomic deprivation is complex and will require primary care, public health and broader societal policy interventions.

For iatrogenic preterm birth, prevention may be targeted towards modifiable upstream factors to ensure that women enter pregnancy well, with a normal BMI, as well as appropriate and timely surveillance of co-morbidities and pregnancy complications. This requires multiagency involvement extending beyond obstetric and midwifery care; our findings indicate that these efforts should be particularly focused on non-white ethnic groups. Research into complications of pregnancy, such as pre-eclampsia and diabetes must focus on identifying pregnancies for which it is possible to delay birth whilst ensuring optimal maternal outcomes.

For spontaneous preterm birth, targeted monitoring and intervention for women identified at higher risk is effective.[6,25] The identification of women at risk of preterm birth is beneficial even where primary prevention is not feasible, as this allows for optimal perinatal and neonatal management, thereby improving neonatal outcomes.[32]

The study demonstrates the feasibility of using routinely acquired hospital administrative data to measure risk-adjusted rates of iatrogenic and spontaneous preterm birth and to compare these between hospitals. This offers potential value as a tool for measuring progress towards reducing preterm birth. The primary goal of iatrogenic preterm birth is to improve outcomes for the mother and baby; avoiding or delaying iatrogenic preterm birth may be associated with poorer outcomes.[10] Nevertheless, preterm birth, be it iatrogenic or spontaneous, confers risks of significant sequalae.[2,3] The 'optimal' rate of iatrogenic preterm birth is not clear, however, variation in rates of iatrogenic preterm birth seen between NHS trusts (Figure 3) indicates variation in practice and therefore presents an opportunity for benchmarking to improve performance,[24] to reduce overall preterm birth but also to reduce, where appropriate, preventable maternal and neonatal morbidity.

Conclusions

This study adds to the literature supporting the finding that iatrogenic and spontaneous preterm birth are associated with different patterns of maternal demographic and clinical risk factors.[33] Measuring spontaneous and iatrogenic preterm birth separately as well as in aggregate will facilitate accurate evaluation of interventions aimed at preventing preterm birth, a better understanding of the impact of changes in maternity policy on preterm birth rates and more targeted identification of areas for intervention within the two sub-groups. Public health measures to decrease smoking, mitigate for ethnic and socioeconomic inequality, and reduce maternal weight at the onset of pregnancy are necessary to reduce preterm birth.

ADDITIONAL STATEMENTS

Contribution statement

DP conceived the study. All authors contributed to the design of the study. JJ performed the analyses. HA reviewed the literature. HA and JJ wrote the manuscript. All authors critically revised the manuscript for important intellectual content. All authors have given approval of the final version prior to submission.

Data access statement

The data are available for further research and service evaluation following approval from the data controllers, which are the Healthcare Quality Improvement Partnership (HQIP; www.hqip.org.uk) for the data derived from the maternity information systems and NHS Digital for Hospital Episode Statistics.

Funding

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Ethics approval

This study used data collected to evaluate service provision and performance and therefore it was exempt from ethical review by the NHS Health Research Authority. The use of data without patient consent was approved by the Confidentiality Advisory Group of the NHS Health Research Authority for the purpose of national clinical audit and health service evaluation (16/CAG/0058).

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Figure 1. Singleton iatrogenic and spontaneous births at each week of gestation among 963 800 women who gave birth in England between 1st April 2015 and 31st March 2017

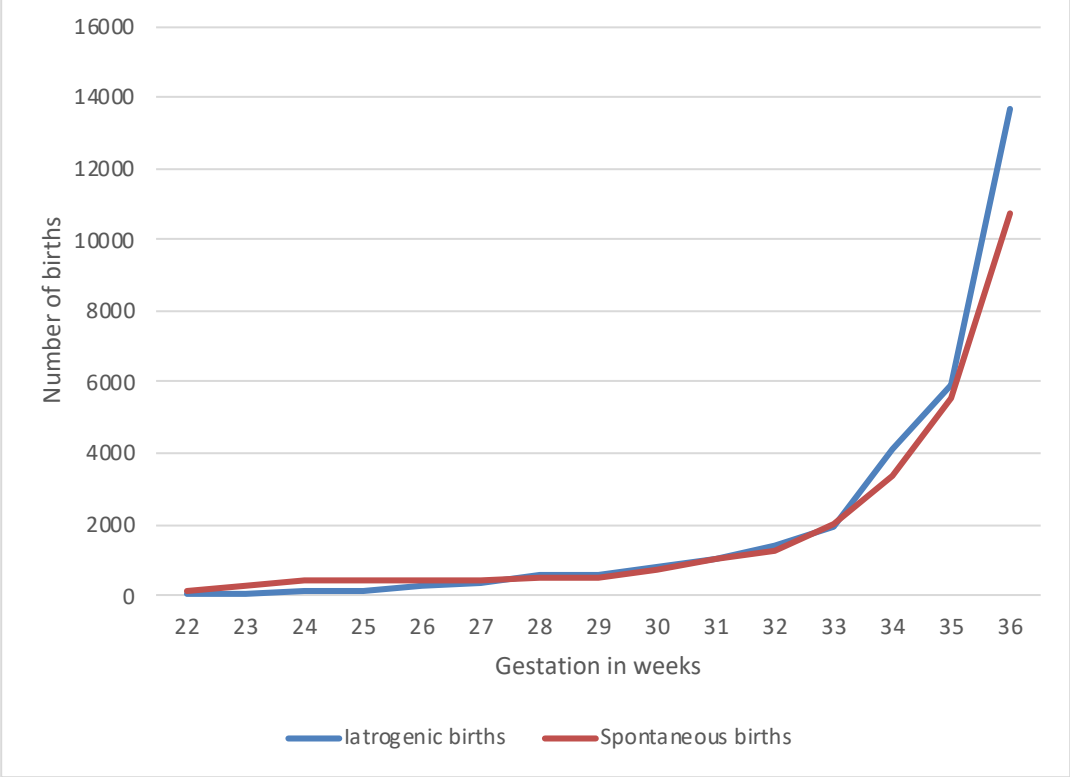
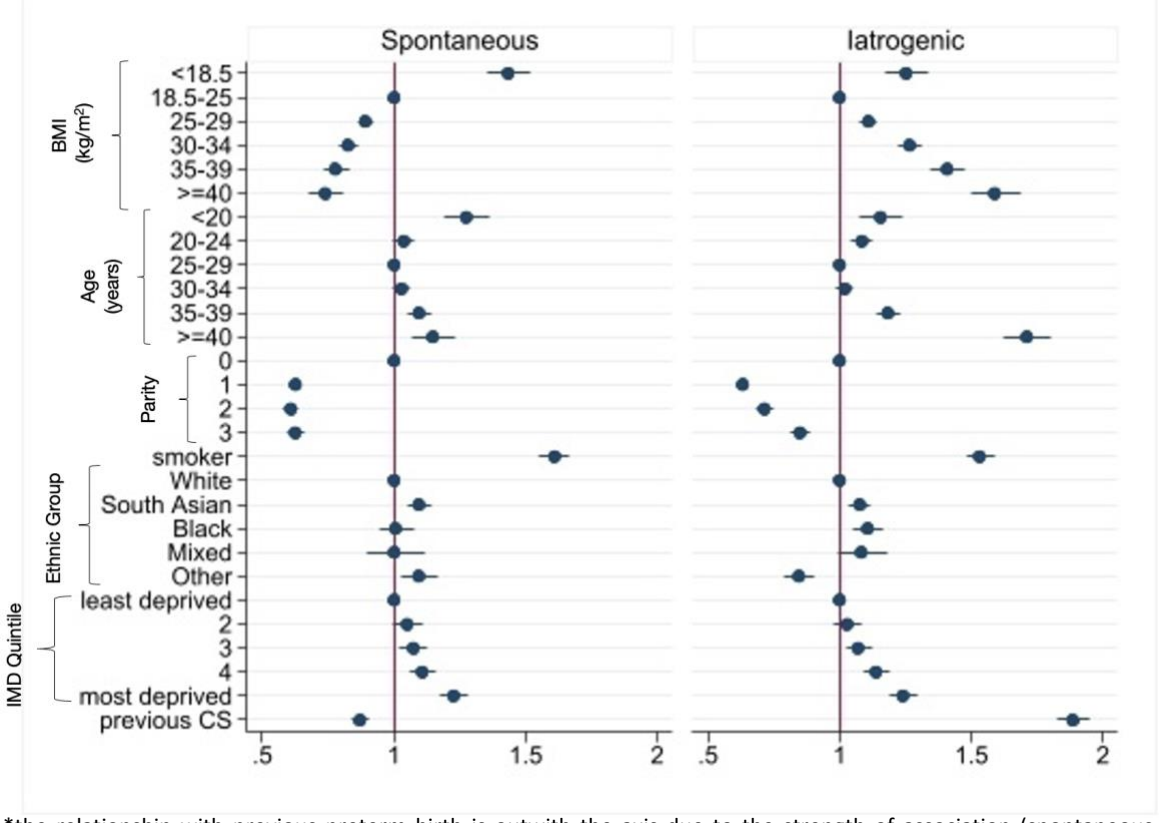
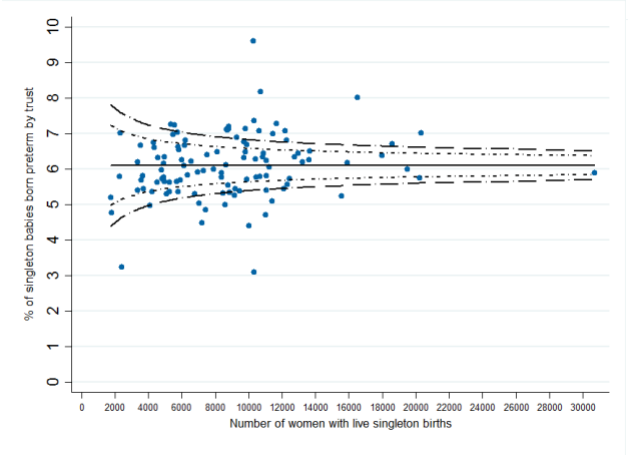


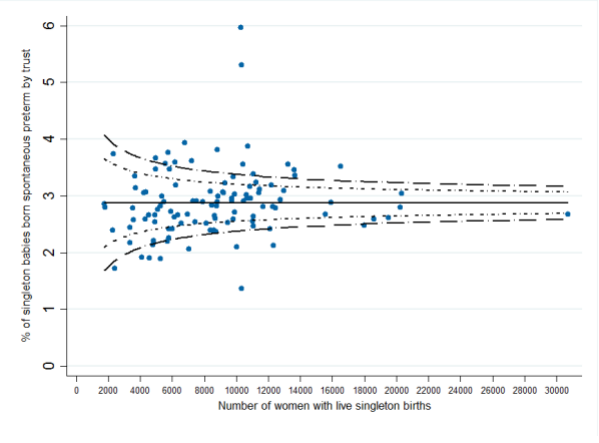
Figure 2. Risk-adjusted patterns of association for spontaneous and iatrogenic preterm birth among 963 800 women who gave birth in England between 1st April 2015 and 31st March 2017



*the relationship with previous preterm birth is outwith the axis due to the strength of association (spontaneous preterm birth adjRR 6.53 (6.32, 6.75); iatrogenic preterm birth adjRR 3.34 (3.22, 3.46)).

Figure 3. Funnel plots showing the risk-adjusted proportion of singleton preterm births by trust of birth a) total preterm birth b) spontaneous preterm birth c) iatrogenic preterm birth





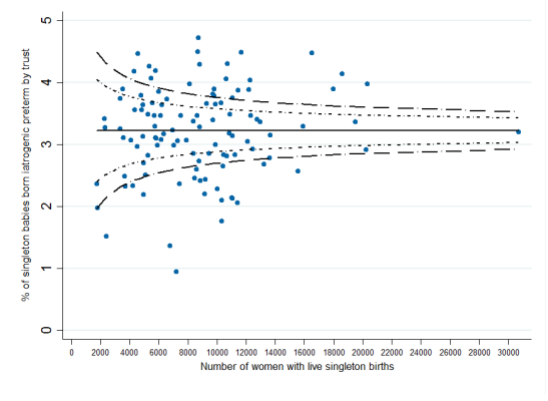


Table 1. Characteristics of 963 800 women who had singleton live births in England between 1st April 2015 and 31st March 2017

Characteristic		Number of women with characteristic (%)	Rate of preterm birth (%)		
			Preterm birth overall	Spontaneous preterm birth	Iatrogenic preterm birth
All women		963 800	58 850 (6.1)	27 753 (2.9)	31 097 (3.2)
Maternal age	<20	31 244 (3.3)	8.2	4.6	3.7
	20-24	145 091 (15.1)	6.6	3.2	3.4
	25-30	273 872 (28.5)	5.8	2.8	3.0
	30-34	301 956 (31.5)	5.7	2.7	2.9
	35-39	168 586 (17.6)	6.2	2.7	3.5
	40+	38 744 (4.0)	8.0	2.8	5.2
	Missing	*4 307 (0.5)*	*7.0*	*2.9*	*4.1*
Maternal BMI	<18.5	24 451 (3.0)	8.4	4.8	3.6
	18-24.9	391 957 (47.4)	5.6	2.9	2.7
	25-29.9	234 607 (28.4)	5.7	2.6	3.1
	30-34.9	107 898 (13.1)	6.2	2.4	3.7
	35-39.9	44 428 (5.4)	6.6	2.3	4.3
	40+	22 807 (2.8)	7.2	2.2	5.0
	Missing	*137 652 (14.3)*	*7.6*	*3.6*	*3.9*
Ethnicity	White	667 327 (76.2)	6.1	2.9	3.2
	South Asian	112 037 (12.8)	6.5	3.0	3.5
	Black	42 351 (4.8)	6.7	2.6	4.1
	Mixed	15 595 (1.8)	6.5	2.9	3.5
	Other	39 004 (4.5)	5.4	2.9	2.6
	Not stated/ missing	*87 486 (9.1)*	*5.7*	*2.9*	*2.8*
Socioeco-nomic deprivation quintile	Least deprived	150 773 (16.5)	5.0	2.4	2.6
	2	125 401 (13.7)	5.4	2.6	2.8
	3	170 630 (18.6)	5.7	2.7	3.0
	4	206 181 (22.5)	6.3	2.9	3.4
	Most deprived	263 309 (28.7)	7.3	3.3	3.9
	Missing	*47 506 (4.9)*	*6.0*	*3.1*	*2.9*
Smoking status at booking	non-smoker	693 388 (86.6)	5.5	2.5	2.9
	smoker	107 337 (13.4)	9.4	4.6	4.9
	unknown	*163 075 (16.9)*	*6.7*	*3.3*	*3.4*
Parity	0	407 989 (42.3)	6.2	3.2	3.1
	1	346 627 (36.0)	5.2	2.4	2.8
	2	126 256 (13.1)	6.4	2.8	3.6
	3+	82 928 (8.6)	8.8	3.6	5.2
Previous CS					
	Prev CS	133 907 (14.0)	8.3	2.7	5.6
	No prev CS	824 746 (86.0)	5.8	2.9	2.8
	Missing	*4 157 (0.5)*	*6.1*	*2.8*	*3.3*
Previous preterm birth		41 762 (4.3)	23.7	12.8	10.9
Comorbidity					
Pre-existing hypertension		5 339 (0.6)	15.7	2.7	13.0
Diabetes (pre-existing or gestational)		57 714 (6.0)	10.9	3.5	7.4
Pre-eclampsia or eclampsia		17 916 (1.9)	27.8	2.1	25.7

Table 2. Characteristics of women having a preterm birth (22+0 to 36+6 weeks' gestation), disaggregated into spontaneous and iatrogenic births, compared to those having a term birth, among 963 800 singleton live births in England in 2015-2017

		Spontaneous preterm birth			Iatrogenic preterm birth		
Characteristics		**Crude risk ratio (95% CI)***	**Adjusted risk ratio (95% CI)†**	**p**	**Crude risk ratio (95% CI)***	**Adjusted risk ratio (95% CI)†**	**p-value**
Maternal age	<20	1.63 (1.54, 1.72)	1.32 (1.24, 1.39)	<0.001	1.23 (1.15, 1.30)	1.16 (1.08, 1.24)	<0.001
	20-24	1.16 (1.12, 1.20)	1.05 (1.01, 1.08)		1.12 (1.08, 1.16)	1.09 (1.04, 1.13)	
	25-30	Ref	Ref		Ref	Ref	
	30-34	0.98 (0.95, 1.01)	1.05 (1.02, 1.08)		0.98 (0.95, 1.01)	1.02 (0.99, 1.05)	
	35-39	0.97 (0.93, 1.00)	1.09 (1.04, 1.13)		1.16 (1.13, 1.20)	1.18 (1.14, 1.23)	
	40+	1.01 (0.95, 1.08)	1.17 (1.10, 1.25)		1.74 (1.66, 1.82)	1.71 (1.62, 1.80)	
Maternal BMI	<18.5	1.66 (1.56, 1.76)	1.43 (1.35, 1.52)	<0.001	1.37 (1.28, 1.47)	1.25 (1.17, 1.34)	<0.001
	18.5-24.9	Ref	Ref		Ref	Ref	
	25-29.9	0.89 (0.86, 0.92)	0.90 (0.87, 0.93)		1.16 (1.12, 1.19)	1.11 (1.08, 1.14)	
	30-34.9	0.84 (0.81, 0.88)	0.84 (0.80, 0.87)		1.39 (1.34, 1.44)	1.27 (1.22, 1.31)	
	35-39.9	0.82 (0.77, 0.87)	0.79 (0.75, 0.84)		1.60 (1.53, 1.68)	1.41 (1.34, 1.48)	
	40+	0.79 (0.72, 0.86)	0.77 (0.70, 0.84)		1.87 (1.76, 1.98)	1.59 (1.50, 1.69)	
Ethnicity	White	Ref	Ref	<0.001	Ref	Ref	<0.001
	S. Asian	1.04 (1.01, 1.08)	1.08 (1.04, 1.12)		1.10 (1.06, 1.13)	1.08 (1.04, 1.12)	
	Black	0.92 (0.87, 0.97)	1.00 (0.94, 1.06)		1.27 (1.21, 1.33)	1.11 (1.05, 1.16)	
	Mixed	1.03 (0.93, 1.13)	1.00 (0.91, 1.10)		1.10 (1.01, 1.19)	1.05 (0.97, 1.14)	
	Other	0.99 (0.93, 1.05)	1.08 (1.01, 1.14)		0.80 (0.75, 0.85)	0.86 (0.80, 0.91)	
Socioeconomic deprivation quintile	Least deprived	Ref	Ref	<0.001	Ref	Ref	<0.001
	2	1.07 (1.02, 1.12)	1.04 (1.00, 1.09)		1.05 (1.01, 1.10)	1.03 (0.98, 1.08)	
	3	1.11 (1.06, 1.16)	1.06 (1.01, 1.11)		1.14 (1.09, 1.19)	1.07 (1.02, 1.12)	
	4	1.21 (1.16, 1.26)	1.11 (1.06, 1.15)		1.27 (1.22, 1.32)	1.14 (1.09, 1.19)	
	Most deprived	1.38 (1.33, 1.44)	1.21 (1.16, 1.26)		1.48 (1.43, 1.54)	1.24 (1.19, 1.29)	
Smoking status at booking	non-smoker	Ref	Ref	<0.001	Ref	Ref	<0.001
	smoker	1.78 (1.73, 1.84)	1.61 (1.56, 1.67)		1.68 (1.63, 1.73)	1.53 (1.48, 1.59)	
Parity	0	Ref	Ref	<0.001	Ref	Ref	<0.001
	1	0.77 (0.75, 0.80)	0.63 (0.61, 0.64)		0.89 (0.87, 0.92)	0.63 (0.61, 0.65)	
	2	0.87 (0.84, 0.91)	0.60 (0.58, 0.63)		1.17 (1.13, 1.21)	0.70 (0.68, 0.73)	
	3+	1.14 (1.10, 1.19)	0.63 (0.60, 0.66)		1.70 (1.64, 1.75)	0.83 (0.79, 0.86)	
Previous caesarean section		0.93 (0.90, 0.96)	0.87 (0.83, 0.90)	<0.001	1.97 (1.92, 2.02)	1.88 (1.83, 1.95)	<0.001
Previous preterm birth		5.27 (5.12, 5.42)	6.53 (6.32, 6.75)	<0.001	3.77 (3.66, 3.89)	3.34 (3.22, 3.46)	<0.001

Ref = reference category

***risk ratio compared to the reference category. †compared to reference category, adjusted for listed factors**

Supplementary Information for

Iatrogenic and spontaneous preterm birth in England: population-based cohort study

Supplementary Table 1. Definition and source of variables used in defining outcomes

Definition	Variables Required	Source	Values included in measure
Preterm birth	Gestational age	MIS[1]	<37 completed weeks
	AND Fetus outcome	MIS	10 = live birth
Iatrogenic preterm birth	Labour onset	MIS	3,4,5 = induction of labour; 2= prelabour caesarean section
	OR Delivery method	MIS	7 = elective caesarean birth
	AND Gestational age	MIS	<37 completed weeks
	AND Fetus outcome	MIS	10 = live birth
Spontaneous preterm birth	Labour onset	MIS	1 = spontaneous
	AND Delivery method	MIS	Any excluding 7
	AND Gestational age	MIS	<37 completed weeks
	AND Fetus outcome	MIS	10 = live birth
Iatrogenic preterm birth without coded indication	Diagnosis codes attributed to birth episode	HES[2]	See Supplementary table 2
Preterm birth associated with prolonged preterm rupture of membranes (PPROM)	Diagnosis codes attributed to birth episode	HES	See Supplementary table 2

1) MIS = maternity information system
2) HES = Hospital episode statistics

Supplementary Table 2. Diagnostic codes used to identify maternal medical conditions and possible indications for preterm birth

	Codes in current episode
Hypertensive disease	
Pre existing	O10, I10, I11, I12, I13, I15
New onset hypertensive disease in pregnancy	O11, O12, O13, O14, O15, O16
Diabetes	
Pre-existing diabetes	O24.0, E10, E11
Gestational diabetes	O24.1
Unspecified	O24.9
Liver conditions	O26.6
Infection	O98
Fetal malformation	O35
Fetal isoimmunisation	O36.0, O36.1
Fetal growth restriction	O36.5
Oligo or anhydramnios	O41.0
Chorioamnionitis	O36.5
Prolonged preterm rupture of membranes	O42.1
Placental conditions	O43,O44,O45,O46,O69.4
Maternal cardiac disease	O99.4
Previous poor obstetric outcome	Z35.2
Cervical abnormality	O34.3, O34.4, O71.3, Q51.1
Group B streptococcus	B95.1
Urinary tract infection	N39.0, O23
Antepartum haemorrhage	O46
Abruption	O45
Partial abortion of second twin	O31.1,O31.3
Fetal distress	O68

Supplementary Table 3. Number of births by gestation in weeks among 963 800 singleton live births in England in 2015-17 (data for figure 2)

Gestation in weeks	Overall number of births		Iatrogenic		Spontaneous	
	n	%	n	%	n	%
	963 800		417 689		546 111	
22^{+0}–22^{+6}	151	0.02%	31	0.01%	120	0.02%
23^{+0}-23^{+6}	313	0.03%	47	0.01%	266	0.05%
24^{+0}-24^{+6}	512	0.05%	102	0.02%	410	0.08%
25^{+0}-25^{+6}	569	0.06%	168	0.04%	401	0.07%
26^{+0}-26^{+6}	661	0.07%	253	0.06%	408	0.07%
27^{+0}-27^{+6}	817	0.08%	375	0.09%	442	0.08%
28^{+0}-28^{+6}	1088	0.11%	601	0.14%	487	0.09%
29^{+0}-29^{+6}	1156	0.12%	619	0.15%	537	0.10%
30^{+0}-30^{+6}	1510	0.16%	811	0.19%	699	0.13%
31^{+0}-31^{+6}	2045	0.21%	1038	0.25%	1007	0.18%
32^{+0}-32^{+6}	2667	0.28%	1385	0.33%	1282	0.23%
33^{+0}-33^{+6}	4011	0.42%	1965	0.47%	2046	0.37%
34^{+0}-34^{+6}	7448	0.77%	4117	0.99%	3331	0.61%
35^{+0}-35^{+6}	11457	1.19%	5909	1.41%	5548	1.02%
36^{+0}-36^{+6}	24445	2.54%	13676	3.27%	10769	1.97%
37^{+0}-37^{+6}	67380	6.99%	42407	10.15%	24973	4.57%
38^{+0}-38^{+6}	137210	14.24%	75804	18.15%	61406	11.24%
39^{+0}-39^{+6}	249279	25.86%	115493	27.65%	133786	24.50%
40^{+0}-40^{+6}	260912	27.07%	70048	16.77%	190864	34.95%
41^{+0}-41^{+6}	166027	17.23%	64357	15.41%	101670	18.62%
42^{+0}-42^{+6}	24142	2.50%	18483	4.43%	5659	1.04%

Supplementary Table 4. Frequency of recorded codes that may represent indications for preterm birth among 31 097 iatrogenic preterm births recorded in England in 2015 -17 (data for figure 3)

Indication	All iatrogenic preterm births		Gestation <28 weeks		Gestation 28-31 weeks		Gestation 32-36 weeks	
	n	%	n	%	n	%	n	%
Total	31097		976		6419		23702	
Hypertensive disease	5599	18.0%	231	23.7%	1794	27.9%	3574	15.1%
Diabetes	4196	13.5%	231	23.7%	670	10.4%	3483	14.7%
Liver conditions	843	2.7%	#	#	76	1.2%	763	3.2%
Infection	277	0.9%	17	1.7%	71	1.1%	189	0.8%
Fetal malformation	702	2.3%	31	3.2%	165	2.6%	506	2.1%
Fetal isoimmunisation	228	0.7%	#	#	33	0.5%	192	0.8%
Fetal growth restriction	7241	23.3%	211	21.6%	1760	27.4%	5270	22.2%
Oligo or anhydramnios	1666	5.4%	76	7.8%	422	6.6%	1168	4.9%
Chorioamnionitis	535	1.7%	129	13.2%	256	4.0%	150	0.6%
Prolonged preterm rupture of membranes	3421	11.0%	97	9.9%	423	6.6%	2901	12.2%
Placental conditions	4434	14.3%	277	28.4%	1430	22.3%	2727	11.5%
Maternal cardiac disease	245	0.8%	12	1.2%	65	1.0%	168	0.7%
Previous poor obstetric outcome	1919	6.2%	78	8.0%	365	5.7%	1476	6.2%
Cervical abnormality	281	0.9%	25	2.6%	67	1.0%	189	0.8%
Group B streptococcus	118	0.4%	5	0.5%	28	0.4%	85	0.4%
Urinary tract infection	553	1.8%	23	2.4%	136	2.1%	394	1.7%
Antepartum haemorrhage	1502	4.8%	100	10.2%	445	6.9%	957	4.0%
Abruption	1041	3.3%	108	11.1%	434	6.8%	499	2.1%
Partial abortion of second twin	28	0.1%	#	#	14	0.2%	11	0.0%
Fetal distress	7906	25.4%	211	21.6%	1909	29.7%	5786	24.4%

 # small numbers are suppressed to prevent identification

Supplementary Table 5. Complete case analysis among 646 193 women who gave birth in England between 1st April 2015 and 31st March 2017 to a singleton live infant and had complete information about all covariates

Maternal characteristics		Spontaneous preterm birth (n= 17 938)			Iatrogenic preterm birth (n= 20 790)		
		Crude rate ratio (95% CI)*	Adjusted rate ratio (95% CI)†	p	Crude rate ratio (95% CI)*	Adjusted rate ratio (95% CI)†	p-value
Maternal age	<20	1.63 (1.54, 1.72)	1.29 (1.20, 1.38)	<0.001	1.23 (1.15, 1.30)	1.17 (1.08, 1.26)	<0.001
	20-24	1.16 (1.12, 1.20)	1.05 (1.01, 1.10)		1.12 (1.08, 1.16)	1.08 (1.03, 1.13)	
	25-29	Ref	Ref		Ref	Ref	
	30-34	0.98 (0.95, 1.01)	1.03 (1.00, 1.07)		0.98 (0.95, 1.01)	1.25 (1.20, 1.30)	
	35-39	0.97 (0.93, 1.00)	1.10 (1.05, 1.15)		1.16 (1.13, 1.20)	1.41 (1.34, 1.48)	
	40+	1.01 (0.95, 1.08)	1.17 (1.09, 1.27)		1.74 (1.66, 1.82)	1.58 (1.48, 1.68)	
Maternal BMI	<18.5	1.66 (1.57, 1.76)	1.41 (1.32, 1.51)	<0.001	1.36 (1.27, 1.45)	1.26 (1.17, 1.35)	<0.001
	18.5-24.9	Ref	Ref		Ref	Ref	
	25-29.9	0.89 (0.86, 0.91)	0.87 (0.84, 0.90)		1.17 (1.13, 1.20)	1.09 (1.06, 1.13)	
	30-34.9	0.84 (0.80, 0.87)	0.80 (0.77, 0.84)		1.41 (1.36, 1.46)	1.25 (1.20, 1.30)	
	35-39.9	0.80 (0.75, 0.85)	0.76 (0.71, 0.82)		1.62 (1.55, 1.70)	1.41 (1.34, 1.48)	
	40+	0.76 (0.69, 0.83)	0.71 (0.64, 0.78)		1.90 (1.79, 2.01)	1.58 (1.48, 1.68)	
Ethnicity	White	Ref	Ref	<0.001	Ref	Ref	<0.001
	S. Asian	1.06 (1.02, 1.10)	1.11 (1.06, 1.16)		1.09 (1.05, 1.13)	1.06 (1.02, 1.10)	
	Black	0.93 (0.87, 0.98)	0.97 (0.90, 1.05)		1.26 (1.20, 1.33)	1.10 (1.04, 1.17)	
	Mixed	1.02 (0.93, 1.12)	1.01 (0.91, 1.13)		1.10 (1.01, 1.19)	1.09 (0.99, 1.20)	
	Other	1.00 (0.95, 1.07)	1.11 (1.03, 1.19)		0.79 (0.75, 0.84)	0.84 (0.78, 0.91)	
IMD (1= least deprived; 5= most deprived)	1	Ref	Ref	<0.001	Ref	Ref	<0.001
	2	1.07 (1.02, 1.12)	1.06 (1.01, 1.13)		1.06 (1.01, 1.11)	1.02 (0.97, 1.08)	
	3	1.11 (1.06, 1.16)	1.08 (1.02, 1.13)		1.14 (1.09, 1.19)	1.08 (1.03, 1.14)	
	4	1.21 (1.16, 1.26)	1.12 (1.07, 1.18)		1.28 (1.23, 1.33)	1.16 (1.10, 1.21)	
	5	1.38 (1.33, 1.44)	1.24 (1.18, 1.30)		1.49 (1.44, 1.54)	1.27 (1.21, 1.33)	
Smoking at booking		1.80 (1.75, 1.86)	1.60 (1.54, 1.66)	<0.001	1.67 (1.62, 1.72)	1.50 (1.45, 1.55)	<0.001
Parity	0	Ref	Ref	<0.001	Ref	Ref	<0.001
	1	0.77 (0.75, 0.80)	0.63 (0.61, 0.66)		0.90 (0.87, 0.92)	0.63 (0.61, 0.66)	
	2	0.87 (0.84, 0.91)	0.61 (0.58, 0.64)		1.17 (1.13, 1.21)	0.72 (0.69, 0.75)	
	3+	1.14 (1.10, 1.19)	0.63 (0.60, 0.67)		1.70 (1.64, 1.75)	0.85 (0.81, 0.90)	
Previous caesarean section		0.93 (0.90, 0.96)	0.85 (0.82, 0.89)	<0.001	1.96 (1.91, 2.01)	1.89 (1.83, 1.96)	<0.001
Previous preterm birth		5.27 (5.12, 5.42)	6.81 (6.55, 7.09)	<0.001	3.77 (3.66, 3.89)	3.27 (3.14, 3.40)	<0.001

*rate ratio compared to term births. †compared to term births, adjusted for listed factors

Supplementary Table 6. Summary results of sensitivity analysis which excluded preterm births associated with possible PPROM: results from analysis of 955 099 women who gave birth between 1st April 2015 and 31st March 2017

Maternal characteristics		Spontaneous preterm birth (n= 24 370)			Iatrogenic preterm birth (n= 25 779)		
		Crude rate ratio (95% CI)*	Adjusted rate ratio (95% CI)†	p	Crude rate ratio (95% CI)*	Adjusted rate ratio (95% CI)†	p-value
Maternal age	<20	1.21 (1.13, 1.29)	1.35 (1.27, 1.44)	<0.001	1.67 (1.57, 1.77)	1.11 (1.03, 1.19)	<0.001
	20-24	1.10 (1.06, 1.14)	1.06 (1.02, 1.10)		1.17 (1.12, 1.21)	1.06 (1.02, 1.10)	
	25-29	Ref	Ref		Ref	Ref	
	30-34	1.00 (0.96, 1.03)	1.04 (1.00, 1.07)		0.97 (0.94, 1.00)	1.03 (1.00, 1.07)	
	35-39	1.21 (1.16, 1.25)	1.09 (1.05, 1.13)		0.97 (0.93, 1.01)	1.23 (1.19, 1.28)	
	40+	1.86 (1.77, 1.96)	1.17 (1.09, 1.25)		1.01 (0.94, 1.08)	1.81 (1.72, 1.91)	
Maternal BMI	<18.5	1.37 (1.27, 1.48)	1.46 (1.37, 1.55)	<0.001	1.69 (1.59, 1.80)	1.28 (1.19, 1.39)	<0.001
	18.5-24.9	Ref	Ref		Ref	Ref	
	25-29.9	1.18 (1.14, 1.22)	0.90 (0.87, 0.93)		0.89 (0.86, 0.92)	1.11 (1.08, 1.15)	
	30-34.9	1.43 (1.38, 1.49)	0.83 (0.79, 0.87)		0.84 (0.80, 0.88)	1.28 (1.23, 1.33)	
	35-39.9	1.67 (1.59, 1.76)	0.79 (0.74, 0.85)		0.81 (0.76, 0.87)	1.44 (1.36, 1.51)	
	40+	2.00 (1.88, 2.13)	0.75 (0.68, 0.83)		0.78 (0.70, 0.85)	1.65 (1.55, 1.76)	
Ethnicity	White	Ref	Ref	0.02	Ref	Ref	<0.001
	S. Asian	1.09 (1.05, 1.13)	1.06 (1.02, 1.10)		1.03 (0.99, 1.07)	1.06 (1.02, 1.10)	
	Black	1.33 (1.26, 1.40)	0.98 (0.92, 1.05)		0.91 (0.85, 0.97)	1.13 (1.07, 1.19)	
	Mixed	1.09 (1.00, 1.19)	0.99 (0.89, 1.10)		1.01 (0.91, 1.13)	1.04 (0.95, 1.14)	
	Other	0.78 (0.73, 0.84)	1.06 (0.99, 1.13)		0.97 (0.91, 1.04)	0.83 (0.77, 0.89)	
IMD (1= least deprived; 5= most deprived)	1	Ref	Ref	<0.001	Ref	Ref	<0.001
	2	1.06 (1.01, 1.12)	1.03 (0.98, 1.09)		1.06 (1.01, 1.11)	1.04 (0.99, 1.10)	
	3	1.15 (1.10, 1.21)	1.04 (0.99, 1.09)		1.08 (1.03, 1.13)	1.10 (1.05, 1.15)	
	4	1.28 (1.23, 1.34)	1.09 (1.04, 1.14)		1.19 (1.14, 1.24)	1.17 (1.12, 1.22)	
	5	1.50 (1.44, 1.56)	1.19 (1.14, 1.24)		1.35 (1.30, 1.41)	1.27 (1.22, 1.33)	
Smoking at booking		1.66 (1.60, 1.71)	1.59 (1.54, 1.65)	<0.001	1.77 (1.71, 1.83)	1.54 (1.49, 1.60)	<0.001
Parity	0	Ref	Ref	<0.001	Ref	Ref	<0.001
	1	0.90 (0.87, 0.92)	0.63 (0.61, 0.65)		0.78 (0.76, 0.81)	0.60 (0.58, 0.62)	
	2	1.19 (1.15, 1.24)	0.61 (0.58, 0.63)		0.88 (0.85, 0.92)	0.67 (0.65, 0.70)	
	3+	1.73 (1.67, 1.80)	0.62 (0.59, 0.65)		1.13 (1.08, 1.18)	0.79 (0.75, 0.82)	
Previous caesarean section		2.16 (2.10, 2.22)	0.87 (0.84, 0.91)	<0.001	0.94 (0.91, 0.98)	2.08 (2.01, 2.15)	<0.001
Previous preterm birth		3.93 (3.80, 4.06)	6.83 (6.59, 7.08)	<0.001	5.48 (5.32, 5.65)	3.38 (3.26, 3.50)	<0.001

*rate ratio compared to term births. †compared to term births, adjusted for listed factors

Supplementary Table 7. Results of sensitivity analysis which incorporated adjustment for maternal medical conditions

Characteristic		Spontaneous preterm (n=27 753)				Iatrogenic preterm (n=31 097)			
		Rate	Crude rate ratio (95% CI)*	Adjusted rate ratio (95% CI)†	p	Rate	Crude rate ratio (95% CI)*	Adjusted rate ratio (95% CI)†	p-value
	<20	4.55	1.63 (1.54, 1.72)	1.22 (1.13, 1.32)	<0.001	3.67	1.23 (1.15, 1.30)	1.13 (1.06, 1.21)	<0.001
Maternal age	20-24	3.23	1.16 (1.12, 1.20)	0.94 (0.88, 1.00)		3.36	1.12 (1.08, 1.16)	1.08 (1.04, 1.12)	
	25-30	2.79	Ref	Ref		2.99	Ref	Ref	
	30-34	2.73	0.98 (0.95, 1.01)	1.09 (1.03, 1.15)		2.93	0.98 (0.95, 1.01)	0.99 (0.95, 1.02)	
	35-39	2.70	0.97 (0.93, 1.00)	1.09 (1.01, 1.17)		3.48	1.16 (1.13, 1.20)	1.09 (1.05, 1.13)	
	40+	2.83	1.01 (0.95, 1.08)	0.90 (0.78, 1.05)		5.20	1.74 (1.66, 1.82)	1.45 (1.38, 1.53)	
Maternal BMI	<18.5	4.83	1.66 (1.56, 1.76)	1.43 (1.34, 1.52)	<0.001	3.61	1.37 (1.28, 1.47)	1.28 (1.20, 1.38)	<0.001
	18.5-24.9	2.91	Ref	Ref		2.66	Ref	Ref	
	25-29.9	2.58	0.89 (0.86, 0.92)	0.88 (0.85, 0.91)		3.10	1.16 (1.12, 1.19)	1.03 (1.00, 1.06)	
	30-34.9	2.43	0.84 (0.81, 0.88)	0.81 (0.77, 0.85)		3.74	1.39 (1.34, 1.44)	1.09 (1.04, 1.13)	
	35-39.9	2.33	0.82 (0.77, 0.87)	0.78 (0.72, 0.84)		4.31	1.60 (1.53, 1.68)	1.12 (1.07, 1.19)	
	40+	2.21	0.79 (0.72, 0.86)	0.72 (0.65, 0.80)		5.04	1.87 (1.76, 1.98)	1.13 (1.05, 1.21)	
Ethnicity	White	2.86	Ref	Ref	0.002	3.22	Ref	Ref	<0.001
	S. Asian	3.02	1.04 (1.01, 1.08)	1.09 (1.04, 1.14)		3.52	1.10 (1.06, 1.13)	0.97 (0.94, 1.01)	
	Black	2.65	0.92 (0.87, 0.97)	0.98 (0.91, 1.05)		4.06	1.27 (1.21, 1.33)	0.98 (0.92, 1.03)	
	Mixed	2.93	1.03 (0.93, 1.13)	1.01 (0.90, 1.13)		3.53	1.10 (1.01, 1.19)	1.08 (0.99, 1.18)	
	Other	2.87	0.99 (0.93, 1.05)	1.08 (1.01, 1.16)		2.55	0.80 (0.75, 0.85)	0.82 (0.76, 0.87)	
IMD (1= least deprived; 5= most deprived)	1	2.41	Ref	Ref	<0.001	2.62	Ref	Ref	<0.001
	2	2.58	1.07 (1.02, 1.12)	1.06 (1.00, 1.12)		2.77	1.05 (1.01, 1.10)	1.03 (0.97, 1.08)	
	3	2.68	1.11 (1.06, 1.16)	1.06 (1.01, 1.12)		2.99	1.14 (1.09, 1.19)	1.06 (1.01, 1.11)	
	4	2.92	1.21 (1.16, 1.26)	1.10 (1.05, 1.16)		3.35	1.27 (1.22, 1.32)	1.11 (1.07, 1.16)	
	5	3.34	1.38 (1.33, 1.44)	1.21 (1.44, 1.27)		3.90	1.48 (1.43, 1.54)	1.21 (1.16, 1.26)	
Smoking status at booking	non-smoker	2.52	Ref	Ref		2.92	Ref	Ref	<0.001
	smoker	4.55	1.78 (1.73, 1.84)	1.67 (1.58, 1.76)	<0.001	4.88	1.68 (1.63, 1.73)	1.59 (1.54, 1.65)	
Parity	0	3.15	Ref	Ref	<0.001	3.09	Ref	Ref	<0.001
	1	2.44	0.77 (0.75, 0.80)	0.53 (0.35, 0.80)		2.76	0.89 (0.87, 0.92)	0.73 (0.70, 0.75)	
	2	2.75	0.87 (0.84, 0.91)	0.49 (0.37, 0.64)		3.61	1.17 (1.13, 1.21)	0.85 (0.82, 0.89)	
	3+	3.59	1.14 (1.10, 1.19)	0.83 (0.68, 1.01)		5.24	1.70 (1.64, 1.75)	1.02 (0.98, 1.07)	
Previous caesarean section		2.70	0.93 (0.90, 0.96)	0.86 (0.82, 0.90)	<0.001	5.57	1.97 (1.92, 2.02)	1.74 (1.69, 1.80)	<0.001
Previous preterm birth		12.8	5.27 (5.12, 5.42)	6.73 (6.47, 7.00)	<0.001	10.9	3.77 (3.66, 3.99)	2.90 (2.80, 3.01)	<0.001
Comorbidity									
Pre-existing hypertension		2.70	0.94 (0.80, 1.10)	0.88 (0.73, 1.06)	0.09	13.02	4.10 (3.83, 4.40)	2.77 (2.54, 3.00)	<0.001
Diabetes (previous or gestational)		3.52	1.24 (1.19, 1.30)	1.25 (1.14, 1.38)	<0.001	7.38	2.49 (2.42, 2.57)	2.16 (2.01, 2.31)	<0.001
Pre-eclampsia or eclampsia		2.09	0.72 (0.65, 0.80)	0.68 (0.56, 0.72)	<0.001	25.73	9.19 (8.94, 9.45)	8.34 (8.07, 8.62)	<0.001
*rate ratio compared to term births. †compared to term births, adjusted for listed factors and interaction between BMI and diabetes									

7. Results Chapter: Risk of complicated birth at term in nulliparous and multiparous women

In this part of the thesis, I evaluate the NICE risk classification typically used for recommending place of birth, with two purposes: first, to evaluate its clinical use in predicting risk of complicated birth sufficiently to guide place of birth, and second, to understand whether it could be used as a transparent form of describing clinical risk in both further studies and the NMPA. The findings of this analysis have been published as a research paper.

7.1 Research Paper 5

Risk of complicated birth at term in nulliparous and multiparous women using routinely collected maternity data in England: cohort study

This article has been accepted for publication in the *BMJ* 2020;371:m3377 following peer review and can also be accessed online at http://dx.doi.org/10.1136/bmj.m3377

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Student ID Number	1511701	**Title**	Dr
First Name(s)	Jennifer		
Surname/Family Name	Jardine		
Thesis Title	A study of risk factors of maternity outcomes using large, routinely collected electronic datasets		
Primary Supervisor	Kate Walker		

If the Research Paper has previously been published please complete Section B, if not please move to Section C.

SECTION B – Paper already published

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When was the work published?	August 2020		
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Risk of complicated birth at term in nulliparous and multiparous women using routinely collected maternity data in England: cohort study

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ABSTRACT

OBJECTIVES

To determine the rate of complicated birth at term in women classified at low risk according to the National Institute for Health and Care Excellence guideline for intrapartum care (no pre-existing medical conditions, important obstetric history, or complications during pregnancy) and to assess if the risk classification can be improved by considering parity and the number of risk factors.

DESIGN

Cohort study using linked electronic maternity records.

PARTICIPANTS

276 766 women with a singleton birth at term after a trial of labour in 87 NHS hospital trusts in England between April 2015 and March 2016.

MAIN OUTCOME MEASURE

A composite outcome of complicated birth, defined as a birth with use of an instrument, caesarean delivery, anal sphincter injury, postpartum haemorrhage, or Apgar score of 7 or less at five minutes.

RESULTS

Multiparous women without a history of caesarean section had the lowest rates of complicated birth, varying from 8.8% (4879 of 55 426 women, 95% confidence interval 8.6% to 9.0%) in those without specific risk factors to 21.8% (613 of 2811 women, 20.2% to 23.4%) in those with three or more. The rate of complicated birth was higher in nulliparous women, with corresponding rates varying from 43.4% (25 805 of 59 413 women, 43.0% to 43.8%) to 64.3% (364 of 566 women, 60.3% to 68.3%); and highest in multiparous women with previous caesarean section, with corresponding rates varying from 42.9% (3426 of 7993 women, 41.8% to 44.0%) to 66.3% (554 of 836 women, 63.0% to 69.5%).

CONCLUSIONS

Nulliparous women without risk factors have substantially higher rates of complicated birth than multiparous women without a previous caesarean section even if the latter have multiple risk factors. Grouping women first according to parity and previous mode of birth, and then within these groups according to presence of specific risk factors would provide greater and more informed choice to women, better targeting of interventions, and fewer transfers during labour than according to the presence of risk factors alone.

WHAT IS ALREADY KNOWN ON THIS TOPIC

In many countries, women at low risk of complications at birth are advised that it is safe to give birth at home or in a midwife led unit

A National Institute for Health and Care Excellence guideline on intrapartum care used a consensus approach to identify women with specific risk factors for whom care in an obstetric unit is expected to reduce risk to mother or baby

The NICE guideline does not distinguish between women in their first pregnancy and those who have previously given birth

WHAT THIS STUDY ADDS

Parity and history of a caesarean section are considerably stronger determinants of the risk of a complicated birth than other risk factors identified by NICE

Giving more weight to parity and obstetric history would provide greater choice for many women, expand the proportion of women advised to consider giving birth in a midwife led unit, and reduce transfers to obstetric led care after the onset of labour

Introduction

Risk assessment is an essential part of antenatal and intrapartum care. In middle and high income settings, women are typically considered to be at low risk of complications in pregnancy or at birth if they do not have specific conditions or comorbidities.[1-12] In the United Kingdom, a national guideline for intrapartum care, developed by the National Institute for Health and Care Excellence, includes a set of risk factors that provide the basis of a risk classification system.[4] These risk factors, including a woman's age, body mass index (BMI), and the presence of specific clinical and obstetric conditions, are considered to identify women at increased risk of complications during labour and birth and to inform recommendations on place of birth.[4]

Women considered to be at low risk of complications are advised that a low risk setting such as their home or a midwife led unit is a suitable place for them to give birth,[4] whereas women considered to be at increased risk are advised to give birth in an obstetric unit. The NICE guideline recommends that women with characteristics that indicate they are at a higher risk of complications, but who according to its risk classification do not fall into the increased risk group (referred to as the intermediate risk group in this paper) should have an individual discussion about place of birth with their obstetric and midwifery team. The risk classification according to the NICE guideline does not distinguish between women with a single risk factor and those with multiple risk factors. Importantly, the listed factors that identify women as being at increased risk do not include a reference to parity (except for women who have had four or more pregnancies), even though the rate of complications and interventions

during labour are different between nulliparous and multiparous women.[4]

We evaluated the set of risk factors identified in the NICE guideline as a tool to identify women at increased risk of complications during labour and birth, using routinely collected maternity data. Firstly, we determined the numbers of women classified according to the NICE guideline as being at low, intermediate, and increased risk at the time of birth. Then we determined the rate of complications and interventions that are generally considered to require action by an obstetric or neonatal team, according to these risk groups. Finally, we assessed the extent to which the risk classification could be improved by considering the number of risk factors present in a woman and by distinguishing between nulliparous women and multiparous women with and without a previous caesarean section.

Methods

Data sources

We used a national maternity dataset that was collated from extracts of the routinely collected electronic Maternity Information Systems (MIS) of English National Health Service hospitals by the National Maternity and Perinatal Audit.[13 14] In England, more than 99% of births occur within the NHS.[15] MIS extracts were provided by 124 of the 134 NHS hospital trusts that provide maternity services in England. After cleaning, the dataset contains information on mothers and babies for 573 336 babies born in England between 1 April 2015 and 31 March 2016 (85.9% of all babies born that year) to 564 000 women (fig 1).[14]

MIS data were linked at patient level to records from Hospital Episode Statistics (HES), an administrative database containing records of all admissions to English NHS hospitals. NHS Digital carried out the linkage using a deterministic algorithm based on the woman and baby's NHS numbers, dates of birth, and postcode. Of the 573 336 MIS records, 536 924 (93.6%) could be linked. When information was available in both datasets, we used the MIS data. If a woman had given birth twice during the study period, we only considered the first birth.

Study population

We first restricted the study population to 411 690 women aged 15-45 who gave birth in the 87 hospital trusts with high levels of completeness of key data items (>70% of records complete on all of maternal BMI, maternal age, and gestational age) and within these hospitals to the 356 251 women with a record of a singleton pregnancy linked to HES with available data on these key data items (fig 1). We identified 322 949 women who gave birth at term (37+0 to 41+6 weeks gestation), and the 276 766 women who gave birth at term after a trial of labour (elective caesarean births excluded) were included in the analyses (fig 1). We compared the characteristics of included and non-included hospital trusts and the complete and incomplete records within those trusts.

Definition of risk group

From the NICE guideline, we derived a list of characteristics and diagnosis and procedure codes that can be used to identify women at an increased risk of birth complications.[4] Diagnoses in HES records are coded using ICD-10 (international statistical classification of diseases and related health problems, 10th revision)[16] and procedure codes using the operating procedure codes (OPCS) classification of interventions and procedures used by NHS hospitals in the UK (see supplementary table S1).[17] When no precise match was possible for the condition defined, we included all diagnosis codes that could be used as a proxy for the condition. To assess concurrent validity, we also checked coded frequencies against known rates of particular conditions in the UK population (table 1, see full details in supplementary table S1).

As it is not possible to define exactly when a diagnosis code was assigned in the HES records, we made assumptions about the time of onset of conditions. We assumed that illnesses of pregnancy such as gestational diabetes or pre-eclampsia occurred after booking but before birth.

For some types of medical conditions, most notably asthma, hypothyroidism, and cardiac disease, HES does not give enough information about severity. For these three conditions, the most common level of severity was assumed for all women. Therefore, we assumed women with asthma or hypothyroidism to be stable and at low risk and women with cardiac conditions to be at increased risk. We carried out a sensitivity analysis in which we classified women with asthma and hypothyroidism in the increased risk group.

We distinguished five types of risk factors: previous caesarean section, BMI of 35 or more, pre-existing medical conditions, important obstetric history, and complications in the current pregnancy (table 1).

Definition of outcomes

When possible we defined outcomes using previously published coding frameworks.[18 19] A composite outcome of complicated birth was defined as a birth with any of the following events: use of an instrument (forceps or vacuum device), emergency caesarean delivery, obstetric anal sphincter injury, postpartum haemorrhage, or neonate born with an Apgar score of 7 or less at five minutes. We chose this composite outcome as it represents a birth that typically requires the attention of an obstetric or neonatal team. It also closely matches a definition of complicated birth used in a recent Danish study.[20]

As about 90% of stillbirths occur before the onset of labour and as information was not available on the timing of stillbirths in this dataset, we considered all stillbirths to be antepartum and therefore they were excluded.[21] We carried out a sensitivity analysis in which we considered all stillbirths as intrapartum and included stillbirth as a component of the complicated birth outcome.

To assess the sensitivity of the results to the dominance of instrumental birth among nulliparous

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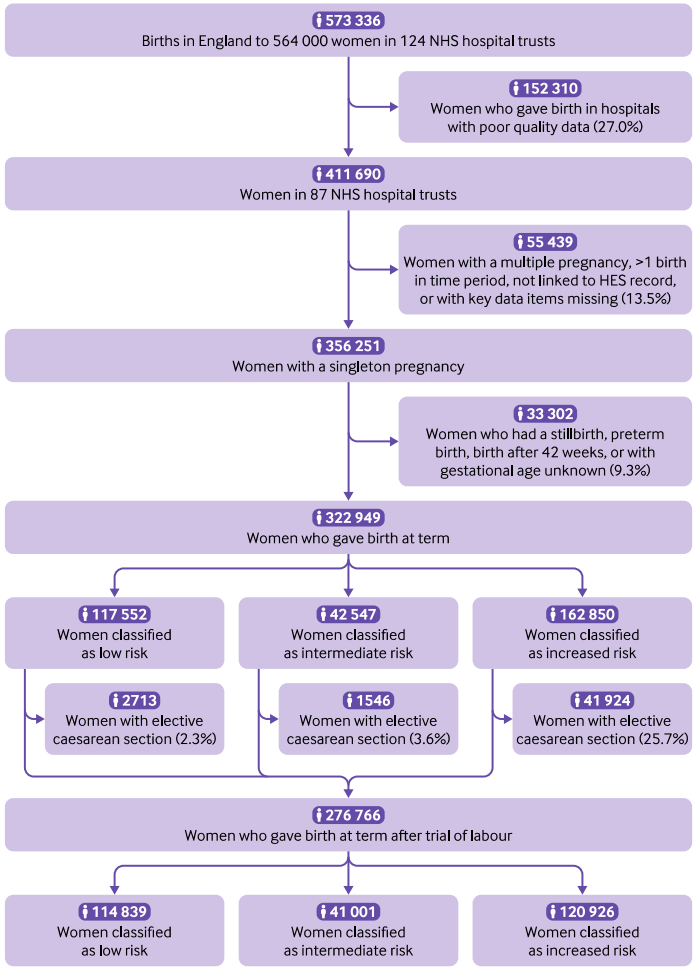

Fig 1 | Flowchart of cohort selection. NHS=national health service; HES=Hospital Episode Statistics

women, we conducted a sensitivity analysis with instrumental birth excluded from the outcome.

Statistical analysis

Firstly, we used proportions to describe the women's characteristics. Then we compared frequencies and the 95% confidence intervals of complicated births in women who gave birth at term after a trial of labour in three groups: nulliparous women, multiparous women with previous vaginal deliveries only, and multiparous women with a previous caesarean section. We used Poisson regression with robust standard errors to estimate risk ratios comparing the likelihood of complicated birth compared with a reference group of multiparous women with no additional risk factors. Finally, for these three groups we compared frequencies of the individual components of the composite outcome between the risk groups separately.

Patient and public involvement

This study was motivated by discussions with the Women and Families Group of the National Maternity and Perinatal Audit, which represents women and their families accessing maternity care in the UK. This group helped to refine the research question.

Results

Risk classification groups at birth

Of the 322 949 women who gave birth at term, 117 552 (36.4%) were considered to be at low risk, 42 547

Table 1 | Summary of risk classification derived from National Institute for Health and Care Excellence guideline CG90: intrapartum care for healthy women and babies[4]

	Risk group		
Risk factors	Low	Intermediate	Increased
Age (years)	<35	≥35	–
Body mass index	<30	30-34.99	≥35
Pre-existing medical conditions	Stable mild medical conditions (asthma, hypothyroidism)	Mild medical conditions	Comorbidity (eg, hypertension), previous uterine surgery (eg, myomectomy)
Important obstetric history	No important history	Parity of ≥4, previous events that are unlikely to recur (eg, stillbirth of known cause), previous mild complications not known to occur in this pregnancy (eg, mild pre-eclampsia)	Previous caesarean section, previous events that might recur (eg, severe pre-eclampsia or stillbirth of unknown cause)
Complications in current pregnancy	None	–	Conditions or suspected conditions in mother, such as pre-eclampsia, fetal complications such as anomaly, multiple pregnancy, or suspected macrosomia

(13.2%) at intermediate risk, and 162 850 (50.4%) at increased risk at the time of birth according to the risk factors derived from the NICE guideline (table 2). Women in the low risk group were more often younger than 25 years (22.4%) and nulliparous (51.9%) than the women in the intermediate risk group (18.4% and 38.8%, respectively) and the increased risk group (16.3% and 31.8%, respectively). Women in the intermediate risk and increased risk groups were more often of black ethnicity and from more socioeconomically deprived backgrounds.

Of the 162 850 women in the increased risk group, 25 705 (15.8%) had a BMI of 35 or higher, 100 759 (61.9%) had at least one pre-existing medical condition, and 95 300 (58.5%) had complications in the current pregnancy (table 2). In total, 64 410 women at increased risk (39.6%) had more than one of the five types of risk factors: previous caesarean section, BMI of ≥35, pre-existing medical conditions, important obstetric history, and complications in the current pregnancy.

Of the 322 949 women who gave birth at term, 46 183 (14.3%) had an elective caesarean section and 276 766 (86.7%) had a trial of labour (fig 1). The elective caesarean section rate was lowest in multiparous women in the low risk group (1.9%) and highest in multiparous women with a previous caesarean section (59.0%) (table 3). Induction rates increased according to risk group, both in nulliparous women (from 24.8% in the low risk group to 40.2% in the increased risk group) and in multiparous women without a previous caesarean section (from 18.3% in the low risk group to 37.8% in the increased risk group).

Outcomes in women who had a trial of labour, by risk group

Among the 276 766 women who gave birth at term after a trial of labour, multiparous women without a previous caesarean section had the lowest rates of complicated birth (table 4, fig 2), with rates varying from 8.8% (95% confidence interval 8.6% to 9.0%) in those at low risk to 21.8% (20.2% to 23.4%) in those at increased risk with three or more types of risk factor. The rate of complicated birth was higher in nulliparous women across all risk groups, with rates varying from 43.4% (43.0% to 43.8%) in those at low risk to 64.3% (60.3% to 68.3%) in those at increased risk with three or more types of risk factor. This is confirmed by risk ratios presented in supplementary table S3.

Multiparous women with a previous caesarean section had the highest rates of complicated birth, with rates varying from 42.9% (41.8% to 44.0%) in those who had a previous caesarean section but no additional risk factors to 66.3% (63.0% to 69.5%) in those with three or more additional risk factors.

Figure 2 shows that parity and a previous caesarean section are the dominant risk factors for a complicated birth in women experiencing a trial of labour at term, with substantially higher rates of complicated birth in nulliparous women and multiparous women with a previous caesarean section compared with multiparous women without a previous caesarean section. In contrast, not taking into account parity and history of a caesarean section, women classified as low, intermediate, and increased risk using the risk factors identified in the NICE guideline had rates of complicated birth of 26.7% (26.5% to 27.0%), 24.1% (23.7% to 24.5%), and 38.0% (37.7% to 38.2%), respectively (table 4).

Components of the composite outcome

Table 5 presents the components of the composite outcome according to risk group. The most common components of the composite outcome were instrumental birth and emergency caesarean section, especially in nulliparous women and in multiparous women with a previous caesarean section. For example, the increase in the rate of complicated birth in nulliparous women from 43.4% in the low risk group to 57.5% in the increased risk group is mainly driven by emergency caesarean section. Also, more than 90% of the complicated births in multiparous women with a previous caesarean resulted from instrumental birth or emergency caesarean section (table 5). For multiparous women with no previous caesarean section, the risks were low for all components of the composite outcome.

Sensitivity analyses

A sensitivity analysis was conducted to examine the impact of not having information about the severity of asthma and hypothyroidism. In this sensitivity analysis, 9672 women were classified as having unspecified asthma or hypothyroidism in the increased risk group rather than in the low risk group, as was done for the

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Table 2 | Characteristics of 322 949 women who gave birth at term, according to risk classification. Values are numbers (percentages) unless stated otherwise

	Risk group		
Characteristics	Low (n=117 552)	Intermediate (n=42 547)	Increased (n=162 850)
Age (years):			
15-24	26 284 (22.4)	7836 (18.4)	26 573 (16.3)
25-34	91 268 (77.6)	14 089 (33.1)	105 838 (65.0)
35-44	–	20 622 (48.5)	30 439 (18.7)
Parity:			
0 (nulliparous)	61 039 (51.9)	16 491 (38.8)	51 850 (31.8)
1-3	56 513 (48.1)	22 072 (51.9)	103 523 (63.6)
≥4	–	3984 (9.4)	7477 (4.6)
IMD (national fifth)*:			
1st (least deprived)	20 308 (18.5)	7607 (19.0)	25 181 (16.5)
2nd	16 497 (15.0)	5821 (14.5)	20 782 (13.7)
3rd	21 761 (19.8)	7454 (18.6)	28 476 (18.7)
4th	24 382 (22.2)	8782 (21.9)	33 909 (22.3)
5th (most deprived)	26 746 (24.5)	10 409 (26.0)	43 843 (28.8)
Missing	7858	2474	10 659
Ethnicity:			
White	85 553 (79.2)	31 674 (80.0)	116 010 (75.9)
Black	5005 (4.6)	2410 (6.1)	11 006 (7.2)
Asian	12 960 (12.0)	3826 (9.7)	19 857 (13.0)
Other	4463 (4.1)	1648 (4.2)	5999 (3.9)
Unknown	9571	2989	9978
Body mass index:			
<18	–	–	9361 (5.7)
18-24.9	77 821 (66.2)	15 039 (35.3)	61 513 (37.8)
25-29.9	39 731 (33.8)	8385 (19.7)	43 594 (26.8)
30-34.9	–	19 123 (44.9)	22 677 (13.9)
≥35	–	–	25 705 (15.8)
Pre-existing medical conditions:			
Cardiac	–	–	2514 (1.5)
Endocrine/renal	–	–	3245 (2.0)
Neurological	–	–	9262 (5.7)
Psychiatric	–	–	12 682 (7.8)
Haematological	–	–	7473 (4.6)
Other	–	–	65 583 (40.3)
None	117 552 (100)	42 547 (100)	62 091 (38.1)
Important obstetric history:			
Caesarean birth	–	–	48 331 (29.7)
Uterine surgery	–	–	6827 (4.2)
Previous tear	–	–	5267 (3.2)
Other	–	–	21 029 (12.9)
None	117 552 (100)	42 547 (100)	91 018 (55.9)
Complications in current pregnancy:			
Hypertension	–	–	16 880 (10.4)
Fetal complication	–	–	30 956 (19.0)
Diabetes	–	–	15 690 (9.6)
Other	–	–	45 471 (27.9)
None	117 552 (100)	42 547 (100)	67 550 (41.5)

IMD=index of multiple deprivation.
Comparisons between risk groups were made using two sided x^2 tests. All comparisons were statistically significant, at P<0.001.
*Combines socioeconomic information about a postcode area.

main analysis. This had little impact on the rate of a complicated birth according to the risk classification. The biggest changes were seen in nulliparous women with increased risk whose risk of a complicated birth decreased from 57.5% to 55.3% and in multiparous women at increased risk with no previous caesarean section whose risk decreased from 17.0% to 16.0%.

A further sensitivity analysis examined the impact of not having information about the timing of stillbirth in the dataset. In this sensitivity analysis, all 1271 stillbirths were considered to have occurred intrapartum rather than antepartum, and these stillbirths were therefore included in the analysis as a complicated birth. The rate of stillbirth was low among all women with a singleton pregnancy (0.36%). The stillbirth rate was highest in nulliparous women and thus the largest difference in results was seen in nulliparous women, with an associated increase in the rate of complicated birth from 43.4% to 43.6% in women at low risk, from 45.8% to 45.9% in those at intermediate risk, and from 57.5% to 57.7% in those at increased risk.

Table 3 | Mode of onset of labour according to risk group in 322 949 women who gave birth at term

	Risk group		
Onset of labour by parity	Low (n=117 552)	Intermediate (n=42 547)	Increased (n=162 850)
Nulliparous women			
No in group:	n=61 039	n=16 491	n=51 850
Spontaneous	44 260 (72.5)	10 372 (62.9)	23 048 (44.5)
Induced	15 153 (24.8)	5 244 (31.8)	20 854 (40.2)
Elective caesarean section	1626 (2.7)	875 (5.3)	7948 (15.3)
Multiparous women			
No previous caesarean section:	n=56 513	n=26 056	n=63 003
Spontaneous	45 075 (79.8)	19 221 (73.8)	33 506 (53.2)
Induced	10 351 (18.3)	6164 (23.7)	23 824 (37.8)
Elective caesarean section	1087 (1.9)	671 (2.6)	5673 (9.0)
Previous caesarean section:			47 997
Spontaneous	–	–	13 979 (29.1)
Induced	–	–	5715 (11.9)
Elective caesarean section	–	–	28 303 (59.0)

A final sensitivity analysis evaluated whether the dominance of instrumental delivery in the composite outcome influenced the pattern of associations for nulliparous women. If instrumental delivery was not included in the composite outcome, a similar pattern of results was, however, observed (supplementary table S4).

Table 4 | Rates of complicated birth in 276 766 women who gave birth at term after a trial of labour (elective caesarean births excluded*)

	Nulliparous women		Multiparous women without a previous caesarean section		Multiparous women with a previous caesarean section		All women	
Risk classification†	No in group	Complicated births; % (95% CI)	No in group	Complicated birth; % (95% CI)	No in group	Complicated births; % (95% CI)	No in group	Complicated births; % (95% CI)
Low risk	59 413	25 805; 43.4 (43.0 to 43.8)	55 426	4879; 8.8 (8.6 to 9.0)	–	–	114 839	30 684; 26.7 (26.5 to 27.0)
Intermediate risk	15 616	7153; 45.8 (45.0 to 46.6)	25 385	2712; 10.7 (10.3 to 11.1)	–	–	41 001	9870; 24.1 (23.7 to 24.5)
BMI 30-34 alone	6671	2933; 44.0 (42.9 to 45.2)	8700	771; 8.9 (8.3 to 9.5)	–	–	–	–
Age ≥35 alone	8134	3799; 46.7 (45.6 to 47.8)	11 284	1449; 12.8 (12.2 to 13.5)	–	–	–	–
Parity ≥4 alone	0	0	2022	100; 4.9 (4.0 to 5.9)	–	–	–	–
No of risk factor types:								
1	14 805	6732; 45.5 (44.7 to 46.3)	22 006	2320; 10.5 (10.1 to 11.0)	–	–	–	–
2	811	421; 51.9 (48.4 to 55.4)	3032	364; 12.0 (10.9 to 13.2)	–	–	–	–
3	–	–	347	28; 8.1 (5.4 to 11.5)	–	–	–	–
Increased risk	43 902	25 230; 57.5 (57.0 to 57.9)	57 330	9767; 17.0 (16.7 to 17.4)	19 694	10 908; 55.4 (54.7 to 56.1)	120 926	45 905; 38.0 (37.7 to 38.2)
Previous caesarean section alone	–	–	–	–	7 993	3 426; 42.9 (41.8 to 44.0)	–	–
BMI ≥35 alone*	7063	3260; 46.2 (45.0 to 47.3)	8134	917; 11.3 (10.6 to 12.0)	790	317; 40.1 (36.6 to 43.6)	–	–
Pre-existing medical conditions alone*	9920	5098; 51.4 (50.4 to 52.4)	11 446	1445; 12.6 (12.0 to 13.2)	1217	571; 46.9 (44.1 to 49.8)	–	–
Important obstetric history alone*	–	–	8415	1511; 18.0 (17.1 to 18.8)	1110	505; 45.5 (42.5 to 48.5)	–	–
Complications in current pregnancy alone*	19 464	12 456; 64.0 (63.3 to 64.7)	13 230	2826; 21.4 (20.6 to 22.1)	4601	3480; 75.6 (74.4 to 76.9)	–	–
No of risk factor types*:								
1	36 447	20 814; 57.1 (56.6 to 57.6)	41 225	6709; 16.3 (15.9 to 16.6)	7718	4873; 63.1 (62.0 to 64.2)	–	–
2	6889	4052; 58.8 (57.6 to 60.0)	13 294	2445; 18.4 (17.7 to 19.1)	3147	2055; 65.3 (63.6 to 67.0)	–	–
≥3	566	364; 64.3 (60.3 to 68.3)	2811	613; 21.8 (20.2 to 23.4)	836	554; 66.3 (63.0 to 69.5)	–	–
All	118 931	58 188; 48.9 (48.6 to 49.2)	138 141	17 358; 12.6 (12.4 to 12.7)	19 694	10 908; 55.4 (54.7 to 56.1)	276 766	86 459; 31.2 (31.1 to 31.4)

*In addition to previous caesarean section for multiparous women with previous caesarean section.
†According to National Institute for Health and Care Excellence guidelines.

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Discussion

In this study we found that parity and a history of caesarean section are considerably stronger determinants for risk of a complicated birth in women with a trial of labour at term than the other factors of the risk classification derived from the clinical guideline for intrapartum care developed by NICE in the UK. Low risk nulliparous women have substantially higher rates of complicated birth than increased risk multiparous women without a previous caesarean section even if the latter have multiple risk factors.

Methodological considerations

We used routinely collected data to determine the risk of complications during childbirth at the onset of term labour in the English NHS. About 60% of births in England could be included. Most exclusions were related to poor data completeness at hospital level rather than missing data at individual level. Comparison of included and excluded NHS hospital trusts showed similar maternal and hospital characteristics for number of deliveries each year and region. A comparison among women with a singleton term birth showed that women in the included hospital trusts were younger, more often of white ethnicity, and less often living in socioeconomically deprived areas (supplementary table S5). However, as these differences were small they will have had minimal impact on our findings.

We were not able to conduct any direct validation of the clinical information recorded in the MIS or HES data. It is possible that owing to under-recording of diagnostic and procedure data in routinely collected datasets, some women in the low risk group were misclassified. As a result, we might have overestimated the risk of a complicated birth in the low risk group, but it is unlikely that this will have had a major impact on our results given that the observed risk of complications in multiparous women classified as low risk is low (8.8%). Furthermore, the routinely collected maternity data included little information about severity of specific medical conditions. However, a sensitivity analysis assessing the impact of moving women with asthma and hypothyroidism from the low risk group to the increased risk group had little effect on our results.

A further limitation is that our data reflect real world practice and as a result the risk factors included in the NICE guideline will have influenced the women's chosen place of birth. This will in turn have affected the rate of complicated birth that we report, given that the use of instrumental delivery or emergency caesarean section is higher in obstetric led care.[13] This limitation cannot, however, explain the substantially higher rates of complicated birth we found in nulliparous women compared with multiparous women without a previous caesarean section. Nulliparous women were more often classified as low risk according to the risk factors derived from the NICE guideline (50.0% of those who had a trial of labour at term) than multiparous women without a previous caesarean section (40.1%).

Lastly, we did not have information about the timing of stillbirth and assumed for the main analyses that all stillbirths had occurred before the onset of labour. A sensitivity analysis that included stillbirths as if all had occurred after the onset of labour did not change our results appreciably. Importantly, the stillbirth rate varied little according to the risk classification and it was highest in nulliparous women. The results of this sensitivity analysis are in line with the main analysis, adding to the evidence that parity and a history of caesarean birth are stronger determinants of the rates of complicated birth than other risk factors identified in the NICE guideline.

Comparison with other studies

Other studies have classified women as low risk using a similar risk classification as recommended by NICE.[1-3 5-12 22] A study of about 10 million births in the United States found that 38% of women were low risk according to the absence of risk factors at the time of birth and, similar to our results, 29% of these women had a complication requiring an obstetric or neonatal intervention.[8] A Dutch study, using a similar risk classification, estimated the proportion of women at low risk of complications as 42.5%.[10] This Dutch study did not, however, have access to information about BMI, which is a major reason why women in our study were classified in the intermediate risk or increased risk groups.

The Birthplace in England study, which included 45 000 births between April 2008 and April 2010, was designed to look at place of birth for women at low risk of complications, defined in a similar way as the risk classification recommended by NICE.[23] The primary outcome in this study was a composite of perinatal mortality and adverse neonatal outcomes. The neonatal component of our outcome, a low Apgar score (≤7) at five minutes, was chosen as it represents a baby requiring additional involvement from the neonatal team. It is also a proxy for adverse neonatal outcomes. Evidence suggests that a low Apgar score at five minutes is associated with perinatal mortality,[24] poorer cognitive development,[25 26] and cerebral palsy.[27]

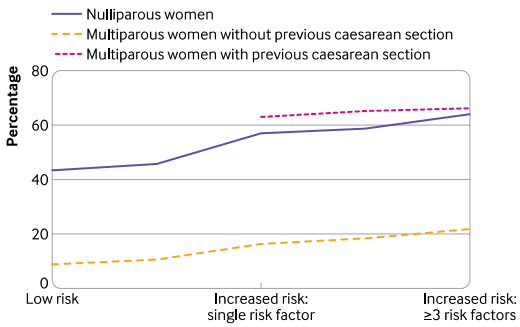

Fig 2 | Association between number of types of risk factors and rates of complicated birth among women who gave birth at term after a trial of labour in England, 2015-16

Table 5 | Components of composite outcome by risk group, parity and obstetric history in 276 766 women who gave birth at term after a trial of labour (elective caesarean births excluded*)

	Low risk		Intermediate risk		Increased risk	
Components of composite outcome	No with outcome	% (95% CI)	No with outcome	% (95% CI)	No with outcome	% (95% CI)
Nulliparous with trial of labour	59 413		15 616		43 902	
Complicated birth:	25 805	43.4 (43.0 to 43.8)	7153	45.8 (45.0 to 46.6)	25 230	57.5 (57.0 to 57.9)
Instrumental birth	15 377	25.9 (25.5 to 26.3)	3830	24.5 (23.8 to 25.2)	11 935	27.2 (26.8 to 27.6)
Emergency caesarean birth	7445	12.5 (12.2 to 12.9)	2657	17.0 (16.4 to 17.6)	11 274	25.7 (25.3 to 26.1)
Obstetric anal sphincter injury	3565	6.0 (5.8 to 6.2)	755	4.8 (4.5 to 5.2)	2266	5.2 (5.0 to 5.4)
Postpartum haemorrhage	1561	2.6 (2.5 to 2.8)	468	3.0 (2.7 to 3.3)	1903	4.3 (4.1 to 4.5)
Apgar score ≤7 at 5 minutes	696	1.2 (1.0 to 1.3)	194	1.2 (1.1 to 1.4)	820	1.9 (1.7 to 2.0)
Multiple components (≥2)	2839	4.8 (4.6 to 5.0)	751	4.8 (4.5 to 5.2)	2968	11.7 (11.4 to 12.2)
Multiparous no previous caesarean with trial of labour	55 426		25 385		57 330	
Complicated birth:	4879	8.8 (8.6 to 9.0)	2712	10.7 (10.3 to 11.1)	9767	17.0 (16.9 to 17.2)
Instrumental birth	2140	3.9 (3.7 to 4.0)	1098	4.3 (4.1 to 4.6)	3317	5.8 (5.6 to 6.0)
Emergency caesarean birth	976	1.8 (1.6 to 1.9)	749	3.0 (2.7 to 3.2)	3589	6.3 (6.1 to 6.5)
Obstetric anal sphincter injury	1125	2.0 (1.9 to 2.1)	485	1.9 (1.7 to 2.1)	1541	2.7 (2.6 to 2.8)
Postpartum haemorrhage	689	1.2 (1.1 to 1.3)	414	1.6 (1.5 to 1.7)	1515	2.6 (2.5 to 2.8)
Apgar score ≤7 at 5 minutes	318	0.6 (0.5 to 0.6)	185	0.7 (0.6 to 0.8)	645	1.1 (1.0 to 1.2)
Multiple components (≥2)	369	0.7 (0.6 to 0.7)	219	0.9 (0.8 to 1.0)	840	1.5 (1.4 to 1.6)
Multiparous with previous caesarean with trial of labour					19 694	
Complicated birth:	–	–	–	–	10 908	55.4 (55.0 to 55.7)
Instrumental birth	–	–	–	–	3416	17.3 (16.8 to 17.9)
Emergency caesarean birth	–	–	–	–	6748	34.3 (33.6 to 34.9)
Obstetric anal sphincter injury	–	–	–	–	747	3.8 (3.5 to 4.1)
Postpartum haemorrhage	–	–	–	–	1322	6.7 (6.4 to 7.1)
Apgar score ≤7 at 5 minutes	–	–	–	–	575	2.9 (2.7 to 3.2)
Multiple components (≥2)	–	–	–	–	1900	9.6 (9.2 to 10.1)

In line with our findings, the Birthplace in England study found that the chances of a baby having serious medical problems were higher for low risk nulliparous women (about 5 per 1000 births) than for low risk multiparous women (about 3 per 1000 births), irrespective of planned place of birth. For nulliparous women planning a home birth, this risk was even higher (about 10 per 1000 births). The study also found that about one in three nulliparous women who had planned to give birth in a midwife led unit were transferred before delivery to an obstetric unit compared with fewer than one in 10 multiparous women.[23] These results support our findings that the risk of requiring the attention of an obstetric or neonatal team is much higher in nulliparous women than in multiparous women and highlight the importance of considering parity when planning place of birth.

Substantial literature evaluates the importance of previous mode of birth for multiparous women.[28-30] In agreement with these studies, we found that the risk of a complicated birth for multiparous women with a previous caesarean section is similar to the risk observed in nulliparous women.[29] The risk in women with a previous caesarean section who also had a vaginal delivery either before or after the caesarean section is, however, much lower, and offers opportunities for further refinement of a risk group based on parity and obstetric history.[19]

Implications

Our results indicate that it is appropriate to consider modifying the risk classification used to give advice to women who are planning where to give birth. For multiparous women without a previous caesarean section, the chance of a complicated birth is low, irrespective of whether or not they have additional risk factors, and planning to give birth in a midwife led setting is appropriate, even for women with additional risk factors. However, nulliparous women, including those without additional risk factors, have considerably higher risks of a complicated birth, and they could consider giving birth in a setting that enables rapid access to care by an obstetric or neonatal team, including midwife led units. These considerations are especially relevant for those women considering a home birth. There are no obvious reasons why these findings in the English NHS are not applicable to other countries with similar models of care.

Giving more weight to parity when assessing the risk in women giving birth at term might lead to substantial shifts in where women choose to give birth, which in turn could have substantial implications for workforce and capacity planning. For example, 45% of women who labour at term are multiparous without a history of caesarean section. In contrast, the risk classification system recommended by NICE identifies only 36% of women who labour at term as low risk and therefore as candidates for a low risk birth setting. These shifts would not only expand the proportion of women who are advised to consider giving birth in midwife led settings but would also have an impact on the proportion of women actually giving birth in these settings, given that the transfer rate during labour to obstetric led care is far lower for multiparous women than for nulliparous women.[23]

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Conclusion

Parity and obstetric history are key determinants of the risk of a complicated birth in women who labour at term. Grouping women first according to parity and previous mode of birth, and then within these groups according to the presence of specific risk factors would allow better planning of place of birth and targeting of interventions, with greater and more informed choice for many women and fewer undesired transfers to obstetric led care after the onset of labour.

This study was based on data collected by the National Maternity Perinatal Audit linked to Hospital Episode Statistics made available by NHS Digital (https://digital.nhs.uk/data-andinformation/data-tools-and-services/data-services/hospital-episode-statistics).

Contributors: JvdM, KW, and DP are joint senior authors and contributed equally to this study and manuscript. They supervised all phases of design and analysis and drafted and revised the paper. JJ conceived the idea, wrote the analysis plan, cleaned and analysed the data, drafted and revised the paper, and is guarantor. AB and HK reviewed the concept and analysis plan and revised the paper. IG-U reviewed the analysis plan and revised the paper. TH and JH reviewed the concept and revised the paper. The corresponding author attests that all listed authors meet authorship criteria and that no others meeting the criteria have been omitted.

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Ethical approval: This study used data collected to evaluate service provision and performance and therefore was exempt from ethical review by the NHS Health Research Authority. The use of personal data without patients' consent was approved by the NHS Health Research Authority (16/CAG/0058). This study has also been considered and approved by the London School of Hygiene and Tropical Medicine research ethics committee (reference 14544).

Data sharing: The data are available for further research and service evaluation after approval from the data controllers, which are the Healthcare Quality Improvement Partnership for the data derived from the maternity information systems and NHS Digital for Hospital Episode Statistics.

The lead author (JJ) affirms that this manuscript is an honest, accurate, and transparent account of the study being reported; that no important aspects of the study have been omitted; and that any discrepancies from the study as planned (and, if relevant, registered) have been explained.

Dissemination to participants and related patient and public communities: We disseminate results through patient organisations and representative groups of women giving birth in the UK.

Provenance and peer review: Not commissioned; externally peer reviewed.

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Supplementary information: additional tables, S1 to S5

Risk of complicated birth at term in nulliparous and multiparous women using routinely collected maternity data in England: a cohort study

SUPPORTING INFORMATION TABLES

List of Tables

Table S1: Coding structures used to identify women at increased, intermediate and low risk according to NICE intrapartum care guideline

Factor	ICD – 10 code	Frequencies		Classified as
		n	%	
Medical conditions indicating increased risk suggesting planned birth at an obstetric unit				
Confirmed cardiac disease	I01 I05-09 I20-28 I30-I52 I97-98	2852	0.80%	Increased risk
Hypertensive disorders	O10-O11 I10-I16	2031	0.06%	Increased risk
Asthma requiring an increase in treatment or hospital treatment	J45 - not possible to restrict by treatment	37314	10.47%	Low risk
Cystic fibrosis	E84	36	0.01%	Increased risk
Haemoglobinopathies – sickle-cell disease, beta-thalassaemia major	D570, D571, D572, D578, D561	467	0.13%	Increased risk
History of thromboembolic disorders	I74-I76, I63, I26, O88, I80-I82	843	0.24%	Increased risk
Immune thrombocytopenia purpura or other platelet disorder or platelet count below 100×10^9/litre	D693, D691, D694, D695, D696	1522	0.43%	Increased risk
Von Willebrand's disease	D680	183	0.05%	Increased risk
Bleeding disorder in the woman	D68, D65, D66, D67, D699	1811	0.51%	Increased risk
Bleeding disorder in the unborn baby	Not possible			Not included
Atypical antibodies which carry a risk of haemolytic disease of the newborn	P55, P56; O361; O360	1511	0.42%	Increased risk
Hyperthyroidism	E05	838	0.24%	Increased risk
Diabetes	E10-E14, O24	2859	0.80%	Increased risk
Hepatitis B/C with abnormal liver function tests	B180, B181, B16, B171, B182 (+ R945)	680	0.19%	Increased risk
Carrier of/infected with HIV	B20-B24 ; Z21 ; O987	<5	<0.01%	Increased risk
Toxoplasmosis – women receiving treatment	B58	9	0.00%	Increased risk
Current active infection of chicken pox/rubella/genital herpes in the woman or baby	B01; B06; A60	13	0.00%	Increased risk
Tuberculosis under treatment	A15,A17,A18,A19	12	0.00%	Increased risk
Systemic lupus erythematosus	M32	293	0.08%	Increased risk
Scleroderma	M34; L940	30	0.01%	Increased risk
Abnormal renal function or renal disease requiring supervision by a renal specialist	N17-N19; P96; D594; K767; R392 E87 (most commonly renal) I12, I13, N00-N19; N25; N28; N29	2811	0.79%	Increased risk
Epilepsy	G40	2859	0.80%	Increased risk
Myasthenia gravis	G70	44	0.01%	Increased risk
Previous cerebrovascular accident	I60-I66 through lookback	102	0.03%	Increased risk
Liver disease associated with current abnormal liver function tests	K70-K77 (+ R945 OR R748)	225	0.06%	Increased risk
Psychiatric disorder requiring current inpatient care [inclusive approach as under outpatient care also included]	F20-31, F322, F323, F332, F333, F42, F431, F500, F502, F503, F60,	14517	4.07%	Increased risk
Other factors indicating increased risk suggesting planned birth at an obstetric unit: (1) Previous complications				
Unexplained stillbirth/neonatal death or previous death related to intrapartum difficulty	Previous stillbirth using look back approach; Z352	3604	1.01%	Increased risk
Previous baby with neonatal encephalopathy	Not possible			

Pre-eclampsia requiring preterm birth	Previous pre-term and pre-eclampsia using combination of codes in lookback approach O13, O14	17799	5.00%	Increased risk
Placental abruption with adverse outcome	O45 ; not possible to define adverse outcome	1022	0.29%	Increased risk
Eclampsia	O15	220	0.06%	Increased risk
Uterine rupture	O710 O711	146	0.04%	Increased risk
Primary postpartum haemorrhage requiring additional treatment or blood transfusion	O72, X33 (OPCS)	44896	12.60%	Increased risk
Retained placenta requiring manual removal in theatre	O73	2986	0.84%	Increased risk
Caesarean section	Indication of previous caesarean section in either MIS or HES lookback	45104	12.66%	Increased risk
Shoulder dystocia	O660	2908	0.82%	Increased risk
Other factors indicating increased risk suggesting planned birth at an obstetric unit: (2) Current pregnancy				
Multiple birth	O30, numberinfant>1	excluded from cohort		Increased risk
Placenta praevia	O44	2138	0.60%	Increased risk
Pre-eclampsia or pregnancy-induced hypertension	O10-O16	23022	6.46%	Increased risk
Preterm labour or preterm prelabour rupture of membranes	Gestational age not term, O60, O42	21198	5.95%	Increased risk
Placental abruption	O45	1410	0.40%	Increased risk
Anaemia – haemoglobin less than 85 g/litre at onset of labour	Not possible		0.00%	Low risk
Confirmed intrauterine death	from maternity information system data	1271	0.36%	Increased risk
Substance misuse or alcohol misuse	F10-16; F18-19; Z86.4;	1322	0.37%	Increased risk
Gestational diabetes	O244; O249	17210	4.83%	Increased risk
Malpresentation – breech or transverse lie	Uses fetal presentation recorded in maternity information system and in delivery method; assumes cephalic if missing	27606	7.75%	Increased risk
BMI at booking >35	Uses BMI recorded in maternity information system	39330	11.04%	Increased risk
Recurrent APH	O46 (note this is any APH)	39324	11.04%	Increased risk
Small for gestational age in this pregnancy (less than 5th centile, or reduced growth velocity on US)	O365	5337	1.50%	Increased risk
Abnormal FHR/Doppler studies	O363, O365	16759	4.70%	Increased risk
Ultrasound diagnosis of oligo- or polyhydramnios	O40, O41	11090	3.11%	Increased risk
Previous myomectomy	O342 [previous]	13118	3.68%	Increased risk
Previous hysterotomy	Not able to be identified separately from previous caesarean section			Increased risk
Medical conditions indicating individual assessment when planning place of birth				
Cardiac disease without intrapartum implications	I20-I52 *note no severity available	2852	0.80%	Increased risk

Atypical antibodies not putting the baby at risk of haemolytic disease	As previous	1511	0.42%	Increased risk
Sickle-cell trait	D573	1973	0.55%	Increased risk
Thalassaemia trait	D563, D569	1703	0.48%	Increased risk
Anaemia – haemoglobin 85–105 g/litre at onset of labour	O990 but not able to differentiate whether ante- or postpartum	642	0.18%	Low risk
Hepatitis B/C with normal liver function tests	B180, B181, B16, B171, B182 (not able to differentiate)	680	0.19%	Increased risk
Non-specific connective tissue disorders	M30-M31, M33-M36	1099	0.31%	Increased risk
Unstable hypothyroidism such that a change in treatment is required	E018, E03, E063 - not possible to differentiate treatment	6683	1.88%	Low risk
Spinal abnormalities	M40-M43	1709	0.48%	Increased risk
Previous fractured pelvis	Previous S32	193	0.05%	
Neurological deficits	G13-G99	10425	2.93%	Increased risk
Liver disease without current abnormal liver function	K70-K77	225	0.06%	Increased risk
Crohn's disease	K50	996	0.28%	Increased risk
Ulcerative colitis	K51	877	0.25%	Increased risk
Other factors indicating individual assessment when planning place of birth (1): previous complications				
Stillbirth/neonatal death with a known non-recurrent cause	Use prev_sb from lookback	3604	1.01%	Increased risk
Pre-eclampsia developing at term	O14, O15 + no evidence of preterm delivery previously	17799	5.00%	Increased risk
Placental abruption with good outcome	O45 in lookback	1022	0.29%	Increased risk
History of previous baby more than 4.5 kg	O366 in previous record	5029	1.41%	Low risk
Extensive vaginal, cervical, or third- or fourth-degree perineal trauma	Able to differentiate previous third- or fourth- degree tear only from HES lookback: O702,O703,O704 or procedure code R322, R325	5614	1.58%	Increased risk
Previous term baby with jaundice requiring exchange transfusion	Nil			Unable to measure
Other factors indicating individual assessment when planning place of birth (1): current pregnancy				
Antepartum bleeding of unknown origin (single episode after 24 weeks of gestation)	O46	39324	11.04%	Increased risk
BMI at booking of 30–35 kg/m^2	Use BMI	46422	13.03%	Intermediate risk
Blood pressure of 140 mmHg systolic or 90 mmHg diastolic or more on 2 occasions	Not possible without diagnostic			Not possible
Clinical or ultrasound suspicion of macrosomia	O366	2061	0.58%	Increased risk
Para 4 or more	Use parity	13143	3.69%	Intermediate risk
Recreational drug use	Unable to distinguish from substance misuse above			Increased risk
Under current outpatient psychiatric care	Unable to distinguish from psychiatric conditions above			Increased risk
Age over 35 at booking	Uses age in maternity information system	62786	17.62%	Intermediate risk
Fetal abnormality	O35	2464	0.69%	Increased risk
Previous major gynaecological surgery; Previous cone biopsy or large loop excision of the transformation zone	O342, O346, O348 in lookback or current; previous record of procedures Q238, Q239, Q24, Q01, Q05, Q544, Q555, Q556, Q557	7771	2.18%	Increased risk
Previous fibroids	O341 D25 in lookback	667	0.19%	Increased risk

Supplementary material Table S2: Components of composite outcome by risk sub-group, parity and obstetric history in 41 001 women who gave birth at term following a trial of labour, and were intermediate risk at the onset of labour (*elective caesarean births excluded)

	Low risk women		Intermediate risk						
			BMI 30.0-34.9		Age 35-44		Parity≥4		All
	n	%	n	%	n	%	n	%	
Primiparous	61039		6943		8656				16491
without ELCS	59413		6671		8134				15616
Spontaneous vaginal delivery	36586	61.58%	4065	60.94%	4636	57.00%			9127
Instrumental birth	15377	25.88%	1391	20.85%	2263	27.82%			3830
Emergency caesarean birth	7445	12.53%	1215	18.21%	1233	15.16%			2657
Postpartum haemorrhage	1561	2.56%	210	3.02%	221	2.55%			468
Obstetric anal sphincter injury	3565	6.00%	336	5.04%	388	4.77%			755
Apgar score less than 7 at 5 minutes	696	1.14%	92	1.33%	92	1.06%			194
Complicated birth	25838	43.49%	2938	44.04%	3806	46.79%			8451
Multiparous	56513		8875		11674		2042		26056
without ELCS	55426		8700		11284		2022		25385
Spontaneous vaginal delivery	52302	94.36%	8178	94.00%	10297	91.25%	1954	96.64%	23530
Instrumental birth	2140	3.86%	283	3.25%	650	5.76%	34	1.68%	1098
Emergency caesarean birth	976	1.76%	237	2.72%	334	2.96%	32	1.58%	749
Postpartum haemorrhage	689	1.22%	143	1.61%	191	1.64%	17	0.83%	414
Obstetric anal sphincter injury	1125	2.03%	123	1.41%	306	2.71%	7	0.35%	485
Apgar score less than 7 at 5 minutes	318	0.56%	52	0.59%	76	0.65%	16	0.78%	185
Complicated birth	4929	8.89%	771	8.86%	1449	12.84%	1922	95.05%	22673

Supplementary material Table S3: Risk ratios for complicated birth in 276 766 women who gave birth at term following a trial of labour (*elective caesarean births excluded).

NICE risk classification	Nulliparous women				Multiparous women without previous CS				Multiparous women with previous CS			
	Number in group	Complicated births	%	Risk ratio‡ (95% CI)†	Number in group	Complicated births	%	Risk ratio‡ (95% CI)†	Number in group	Complicated births	%	Risk ratio‡ (95% CI)†
Low risk	59 413	25 805	43·4	4.89 (4.75 to 5.03)	55 426	4 879	8·8	Reference				
Intermediate risk	15 616	7 153	45·8	5.16 (5.00 to 5.33)	25 385	2 712	10·7	1.20 (1.15 to 1.26)				
BMI 30 to 34 alone	6 671	2 933	44·0	4.95 (4.76 to 5.14)	8 700	771	8·9	1.00 (0.93 to 1.07)				
Age 35+ alone	8 134	3 799	46·7	5.26 (5.08 to 5.45)	11 284	1 449	12·8	1.44 (1.37 to 1.53)				
Parity 4+ alone	0	0		-	2 022	100	4·9	0.56 (0.46 to 0.67)				
Multiple risk factors	811	421	51·9	5.84 (5.44 to 6.27)	3 379	392	11·6	1.35 (1.22 to 1.49)				
Increased risk	43 902	25 230	57·5	6.46 (6.28 to 6.64)	57 330	9 767	17·0	1.92 (1.86 to 1.98)	19 694	10 908	55·4	6.23 (6.05 to 6.41)
Previous caesarean section alone									7 993	3 426	42·9	4.82 (4.65 to 5.00)
BMI 35+ alone*	7 063	3 260		5.19 (5.00 to 5.38)	8 134	917	11·3	1.27 (1.19 to 1.35)	790	317	40·1	4.51 (4.13 to 4.93)
Pre-existing medical conditions alone*	9 920	5 098	51·4	5.78 (5.59 to 5.97)	11 446	1 445	12·6	1.42 (1.34 to 1.50)	1 217	571	46·9	5.28 (4.94 to 5.63)
Significant obstetric history alone*					8 415	1 511	18·0	2.02 (1.92 to 2.13)	1 110	505	45·5	5.12 (4.77 to 5.48)
Complications in current pregnancy alone*	19 464	12 456	64·0	7.20 (6.99 to 7.41)	13 230	2 826	21·4	2.40 (2.30 to 2.51)	4 601	3 480	75·6	8.51 (8.24 to 8.78)
Number of risk factor types												
1*	36 447	20 814	57·1	6.42 (6.24 to 6.60)	41 225	6 709	16·3	1.83 (1.77 to 1.89)	7 718	4 873	63·1	7.10 (6.88 to 7.33)
2*	6 889	4 052	58·8	6.61 (6.40 to 6.84)	13 294	2 445	18·4	2.07 (1.98 to 2.16)	3 147	2 055	65·3	7.34 (7.08 to 7.62)
3+*	566	364	64·3	7.23 (6.76 to 7.73)	2 811	613	21·8	2.49 (2.31 to 2.68)	836	554	66·3	7.45 (7.05 to 7.87)

* significant obstetric history, not including previous CS
‡ Risk in low-risk multiparous women was used as the reference category.
† all p values, except the comparison with multiparous women with BMI 30-34 as the only risk factor (highlighted with a $), are less than 0.001. $p=

Supplementary material Table S4. Components of composite outcome without instrumental delivery by risk group, parity and obstetric history in 276 766 women who gave birth at term following a trial of labour (*elective caesarean births excluded)

	Low risk women		Intermediate risk		Increased risk	
	Women with outcome		Women with outcome		Women with outcome	
	n	% (95% CI)	n	% (95% CI)	n	% (95% CI)
Nulliparous with a trial of labour	59 413		15 616		43 902	
Complicated birth	12 492	21.0 (20.7 to 21.4)	3 808	24.4 (23.7 to 25.1)	15 013	34.2 (33.8 to 34.6)
Emergency caesarean birth	7 445	12.5 (12.2 to 12.9)	2 657	17.0 (16.4 to 17.6)	11 274	25.7 (25.3 to 26.1)
Obstetric anal sphincter injury	3 565	6.0 (5.8 to 6.2)	755	4.8 (4.5 to 5.2)	2 266	5.2 (5.0 to 5.4)
Postpartum haemorrhage	1 561	2.6 (2.5 to 2.8)	468	3.0 (2.7 to 3.3)	1 903	4.3 (4.1 to 4.5)
5-minute Apgar ≤7	696	1.2 (1.0 to 1.3)	194	1.2 (1.1 to 1.4)	820	1.9 (1.7 to 2.0)
Multiparous no previous caesarean section with a trial of labour	55 426		25 385		57 330	
Complicated birth	2 939	5.3 (5.1 to 5.5)	1 676	6.6 (6.3 to 6.9)	6 737	11.8 (11.5 to 12.0)
Emergency caesarean birth	976	1.8 (1.6 to 1.9)	749	3.0 (2.7 to 3.2)	3 589	6.3 (6.1 to 6.5)
Obstetric anal sphincter injury	1 125	2.0 (1.9 to 2.1)	485	1.9 (1.7 to 2.1)	1 541	2.7 (2.6 to 2.8)
Postpartum haemorrhage	689	1.2 (1.1 to 1.3)	414	1.6 (1.5 to 1.7)	1 515	2.6 (2.5 to 2.8)
5-minute Apgar ≤7	318	0.6 (0.5 to 0.6)	185	0.7 (0.6 to 0.8)	645	1.1 (1.0 to 1.2)
Multiparous with previous caesarean section with a trial of labour					19 694	
Complicated birth					7995	40.6 (40.0 to 41.3)
Emergency caesarean birth					6 748	34.3 (33.6 to 34.9)
Obstetric anal sphincter injury					747	3.8 (3.5 to 4.1)
Postpartum haemorrhage					1 322	6.7 (6.4 to 7.1)
5-minute Apgar ≤7					575	2.9 (2.7 to 3.2)

Supplementary material Table S5: Characteristics of included and excluded NHS hospital trusts, and women who gave birth to a singleton infant at term within those trusts

	Included **Number (%)**	**Not included** **Number (%)**	**p value**[†]
	87 NHS hospital trusts	**37 NHS hospital trusts**	
Trust size (births per annum)			0.70
<2500 births	13	4	
2500-3999 births	18	11	
4000-5999 births	35	13	
6000+	21	9	
Region of England			0.68
London	11	5	
South East/Home Counties	17	9	
East of England	2	1	
Midlands	14	10	
Northeast and Yorkshire	16	5	
Southwest	12	4	
North West	15	3	
	322 949 women	**159 792 women**	
Age (year)			<0.001
15-24	60 693 (18.8%)	30 478 (19.1%)	
25-34	211 195 (65.4%)	95 387 (59.8%)	
35-44	51 061 (15.8%)	33 729 (21.1%)	
Missing	n/a	*198*	
Ethnicity of women giving birth			<0.001
White	233 237 (77.6%)	109 312 (76.3%)	
Black	18 421 (6.1%)	9 638 (6.7%)	
Asian	36 643 (12.2%)	18 331 (12.8%)	
Other	12 110 (4.0%)	6 008 (4.2%)	
Unknown	*22 538*	*1650*	
Index of multiple deprivation			<0.001
1 (least deprived)	53 096 (17.6%)	24 958 (16.7%)	
2	43 100 (14.3%)	20 390 (13.6%)	
3	57 691 (19.1%)	26 594 (17.8%)	
4	67 073 (22.2%)	33 941 (22.7%)	
5 (most deprived)	80 998 (26.8%)	43 625 (29.2%)	
Missing	*20 991*	*10 284*	

[†]using chi2 tests to compare proportions
*For this comparison, we have restricted to singleton term live births in women aged 15-45 within excluded trusts

7.2 Induction of Labour Supplementary Analysis

A criticism of this paper post-publication was that its findings could have been explained entirely by differences in induction of labour (IOL) rates by parity. I conducted a further supplementary analysis which demonstrated that, although women with IOL were more likely to have a complicated birth, relative patterns of risk were similar within these cohorts. These are included in the thesis here.

Table 7.1. Rates of complicated birth in 189 461 women who gave birth at term after a spontaneous onset of labour

	Nulliparous women		Multiparous women without previous caesarean section		Multiparous women with a previous caesarean section	
	N women	Complicated births; % (95% CI)	N women	Complicated births; % (95% CI)	N women	Complicated births; % (95% CI)
Low risk	44 260	17 299; 39.1 (38.6, 39.5)	45 075	3 608; 8.0 (7.8, 8.3)	-	
Intermediate risk	10 372	4 104; 39.6 (38.6, 40.5)	19 221	1 728; 9.0 (8.6, 9.4)	-	-
Increased risk	23 048	12 113; 52.6 (51.9, 53.2)	33 506	5 021; 15.0 (14.6, 15.4)	13 979	7 423; 53.1 (52.3, 53.9)

Table 7.2. Rates of complicated birth in 87 305 women who gave birth at term after an induced onset of labour

	Nulliparous women		Multiparous women without previous caesarean section		Multiparous women with a previous caesarean section	
	N women	Complicated births; % (95% CI)	N women	Complicated births; % (95% CI)	N women	Complicated births; % (95% CI)
Low risk	15 153	8 539; 56.4 (55.6, 57.1)	10 351	1 321; 12.8 (12.1, 13.4)	-	-
Intermediate risk	5 244	3 061; 58.4 (57.0, 59.7)	6 164	984; 16.0 (15.1, 16.9)		
Increased risk	20 854	13 117; 62.9 (62.2, 63.6)	23 824	4 746; 19.9 (19.4, 20.4)	5 715	3 485; 61.0 (59.7, 62.2)

8. Results Chapter: Adverse pregnancy outcomes attributable to socioeconomic and ethnic inequality

In this part of the research, I used crude and adjusted population attributable fractions to estimate the proportion of adverse pregnancy outcomes attributable to ethnic and socioeconomic inequality. The findings of this analysis have been published as a research paper.

8.1 Research Paper 6

Adverse pregnancy outcomes attributable to socioeconomic and ethnic inequalities in England: a national cohort study

This article has been accepted for publication in the *Lancet* (volume 398, issue 10314, p1905-1912, November 20, 2021) following peer review and can also be accessed online at https://doi.org/10.1016/S0140-6736(21)01595-6

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SECTION A – Student Details

Student ID Number	1511701	**Title**	Dr
First Name(s)	Jennifer		
Surname/Family Name	Jardine		
Thesis Title	A study of risk factors of maternity outcomes using large, routinely collected electronic datasets		
Primary Supervisor	Kate Walker		

If the Research Paper has previously been published please complete Section B, if not please move to Section C.

SECTION B – Paper already published

Where was the work published?	The Lancet		
When was the work published?	November 2021		
If the work was published prior to registration for your research degree, give a brief rationale for its inclusion	n/a		
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SECTION E

Student Signature	[redacted]
Date	4/11/2021

Supervisor Signature	[redacted]
Date	16/11/2021

Adverse pregnancy outcomes attributable to socioeconomic and ethnic inequalities in England: a national cohort study

Jennifer Jardine, Kate Walker, Ipek Gurol-Urganci, Kirstin Webster, Patrick Muller, Jane Hawdon, Asma Khalil*, Tina Harris*, Jan van der Meulen*, on behalf of the National Maternity and Perinatal Audit Project Team†*

Summary

Background Socioeconomic deprivation and minority ethnic background are risk factors for adverse pregnancy outcomes. We aimed to quantify the magnitude of these socioeconomic and ethnic inequalities at the population level in England.

Methods In this cohort study, we used data compiled by the National Maternity and Perinatal Audit, based on birth records from maternity information systems used by 132 National Health Service hospitals in England, linked to administrative hospital data. We included women who gave birth to a singleton baby with a recorded gestation between 24 and 42 completed weeks. Terminations of pregnancy were excluded. We analysed data on stillbirth, preterm birth (<37 weeks of gestation), and fetal growth restriction (FGR; liveborn with birthweight <3rd centile by the UK definition) in England, and compared these outcomes by socioeconomic deprivation quintile and ethnic group. We calculated attributable fractions for the entire population and specific groups compared with least deprived groups or White women, both unadjusted and with adjustment for smoking, body-mass index (BMI), and other maternal risk factors.

Findings We identified 1 233 184 women with a singleton birth between April 1, 2015, and March 31, 2017, of whom 1 155 981 women were eligible and included in the analysis. 4505 (0·4%) of 1 155 981 births were stillbirths. Of 1 151 476 livebirths, 69 175 (6·0%) were preterm births and 22 679 (2·0%) were births with FGR. Risk of stillbirth was 0·3% in the least socioeconomically deprived group and 0·5% in the most deprived group (p<0·0001), risk of a preterm birth was 4·9% in the least deprived group and 7·2% in the most deprived group (p<0·0001), and risk of FGR was 1·2% in the least deprived group and 2·2% in the most deprived group (p<0·0001). Population attributable fractions indicated that 23·6% (95% CI 16·7–29·8) of stillbirths, 18·5% (16·9–20·2) of preterm births, and 31·1% (28·3–33·8) of births with FGR could be attributed to socioeconomic inequality, and these fractions were substantially reduced when adjusted for ethnic group, smoking, and BMI (11·6% for stillbirths, 11·9% for preterm births, and 16·4% for births with FGR). Risk of stillbirth ranged from 0·3% in White women to 0·7% in Black women (p<0·0001); risk of preterm birth was 6·0% in White women, 6·5% in South Asian women, and 6·6% in Black women (p<0·0001); and risk of FGR ranged from 1·4% in White women to 3·5% in South Asian women (p<0·0001). 11·7% of stillbirths (95% CI 9·8–13·5), 1·2% of preterm births (0·8–1·6), and 16·9% of FGR (16·1–17·8) could be attributed to ethnic inequality. Adjustment for socioeconomic deprivation, smoking, and BMI only had a small effect on these ethnic group attributable fractions (13·0% for stillbirths, 2·6% for preterm births, and 19·2% for births with FGR). Group-specific attributable fractions were especially high in the most socioeconomically deprived South Asian women and Black women for stillbirth (53·5% in South Asian women and 63·7% in Black women) and FGR (71·7% in South Asian women and 55·0% in Black women).

Interpretation Our results indicate that socioeconomic and ethnic inequalities were responsible for a substantial proportion of stillbirths, preterm births, and births with FGR in England. The largest inequalities were seen in Black and South Asian women in the most socioeconomically deprived quintile. Prevention should target the entire population as well as specific minority ethnic groups at high risk of adverse pregnancy outcomes, to address risk factors and wider determinants of health.

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See Comment page 1855

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Introduction

In many high-income countries, women from more deprived socioeconomic backgrounds and minority ethnic groups experience poorer outcomes in pregnancy and birth than do women from less deprived socioeconomic backgrounds and White women, with higher rates of stillbirth, preterm births, fetal growth restriction (FGR), and neonatal and infant mortality.[1–3] These outcomes have long-term ramifications for children and families, health-care systems, and economies.[4,5]

Reduction of inequalities in pregnancy outcomes by socioeconomic status and ethnicity is a key objective of health policies in many countries.[6] For example, the National Health Service (NHS) in England set a target to reduce the overall rates of stillbirth and neonatal mortality by 50% and preterm birth by 25% between 2019

For more on the **NHS Long Term Plan** see https://longtermplan.nhs.uk

Research in context

Evidence before this study

Socioeconomic deprivation and a minority ethnic background are associated with adverse perinatal outcomes. However, there is a paucity of evidence on the strength of these risk factors and on the scale of their effect at population level. We searched MEDLINE from database inception to Jan 1, 2021, for reviews of studies done in the UK using the following search terms: ("inequality", "disparity", "socioeconomic", "ethnicity", or "race") and ("stillbirth", "preterm", or "fetal growth restriction"). A 2012 systematic literature review of the relation between socioeconomic deprivation and adverse pregnancy outcomes reported that risks of adverse pregnancy outcomes in women in the most deprived group were between 1·5 times (for stillbirth) and 1·8 times (for low birthweight) higher than in women in the most affluent group. A 2019 review on inequalities and stillbirth reported that research investigating inequalities and stillbirth was underdeveloped, and therefore estimation of the potential stillbirth reduction if inequalities were reduced is not possible.

Added value of this study

This study of more than 1 million births in the English National Health Service found that a substantial proportion of stillbirths, preterm births, and fetal growth restriction would not have occurred if all women had the same risk as women in the least deprived socioeconomic group and women from White ethnic groups. The largest increases in the risk of stillbirth and fetal growth restriction occurred in Black and South Asian women. These results show that initiatives to reduce adverse birth outcomes focusing on individual women's choices and behaviour and on antenatal care will have limited effects.

Implications of all the available evidence

Concerted action is needed to reduce socioeconomic and ethnic inequalities in pregnancy outcomes. This action must involve midwives and obstetricians, public health professionals, and politicians, and target the entire population as well as Black and South Asian women in deprived socioeconomic groups. Prevention should address wider determinants of health and specific risk factors including maternal smoking and obesity.

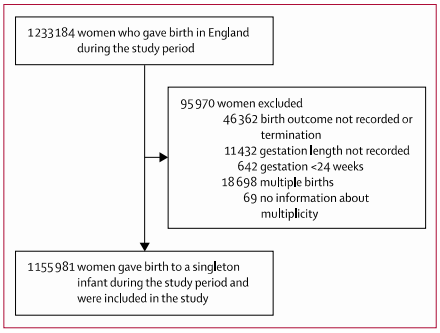


Figure 1: **Study design**

and 2025. However, efforts to improve pregnancy outcomes and to mitigate inequalities are impeded by a paucity of information about how these inequalities are related to women's societal circumstances and pre-existing health and which groups are most strongly affected. Research into inequalities in pregnancy outcomes is underdeveloped in the UK, as in many other high-income countries.[7] Clear measures are needed to communicate the size of these inequalities in pregnancy outcomes to clinicians, to women and their families, and to public health professionals and policy makers.[8,9]

We aimed to quantify socioeconomic and ethnic inequalities in stillbirth, preterm birth, and FGR in England, taking account of health at the onset of pregnancy and complications that arise during pregnancy.

Methods

Study design and data sources

In this national cohort study, we used a dataset compiled by the National Maternity and Perinatal Audit that was based on records of each birth from maternity information systems used by NHS maternity services in England to record care throughout pregnancy and birth.[10] These records were linked to the Hospital Episode Statistics, an administrative database with records of all hospital episodes in the English NHS. The resulting dataset captured approximately 94% of all births that occurred in England during the study period.[10] This study used data collected to evaluate service provision and performance and therefore was exempt from ethical review by the NHS Health Research Authority. The use of personal data without patients' consent was approved by the NHS Health Research Authority (16/CAG/0058).

Participants

We included all women who gave birth to a singleton baby with a recorded gestation between 24 and 42 completed weeks, if information was available on whether the baby was born alive or stillborn. Terminations of pregnancy were excluded.

Outcomes

We collected and assessed data on stillbirth, preterm birth, and FGR. Stillbirth was defined as any recorded birth of a stillborn baby of at least 24 completed weeks of gestation. Preterm birth was defined as the recorded birth of a liveborn baby between 24 and 37 completed weeks of gestation. FGR was defined as the birth of a liveborn baby of at least 24 completed weeks with a

	n (%)
All	1 155 981
Socioeconomic deprivation quintile	
Total with available data (n)	1 087 776
Least deprived	158 401 (14·6%)
Less deprived	178 676 (16·4%)
Median deprived	203 698 (18·7%)
More deprived	246 266 (22·6%)
Most deprived	300 735 (27·6%)
Maternal ethnic group	
Total with available data (n)	1 061 417
White	818 982 (77·2%)
South Asian	126 262 (11·9%)
Black	52 361 (4·9%)
Other stated	44 251 (4·2%)
Mixed	19 561 (1·8%)
Maternal characteristics at start of pregnancy	
Age	
Total with available data (n)	1 142 227
<20 years	37 394 (3·3%)
20–34 years	857 074 (75·0%)
35–39 years	201 336 (17·6%)
≥40 years	46 423 (4·1%)
Parity	
Total with available data (n)	1 148 742
0	485 555 (42·3%)
1	414 993 (36·1%)
2	150 518 (13·1%)
3 or more	97 676 (8·5%)
Previous caesarean section	
Total with available data (n)	1 131 546
Yes	163 267 (14·4%)
No	968 279 (85·6%)
Smoking status	
Total with available data (n)	950 233
Non-smoker	821 549 (86·5%)
Smoker	128 684 (13·5%)
BMI (kg/m²)	
Total with available data (n)	966 324
Underweight (<18·5)	28 200 (2·9%)
Ideal weight (18·5–24·9)	457 385 (47·3%)
Overweight (25·0–29·9)	274 338 (28·4%)
Grade I obese (30·0–34·9)	126 644 (13·1%)
Grade II obese (35·0–39·9)	52 496 (5·4%)
Grade III obese (≥40·0)	27 261 (2·8%)
Presence of conditions considered high risk by NICE	
Total with available data (n)	925 996
Pre-existing medical conditions	140 980 (15·2%)
Previous birth complication	67 946 (7·3%)
Conditions in current pregnancy	248 781 (26·9%)

(Table 1 continues in next column)

(Continued from previous column)

	n (%)
Pregnancy outcomes	
Overall	
Liveborn	1 151 476 (99·6%)
Stillborn	4505 (0·4%)
Term babies	
Liveborn	1 082 301 (99·8%)
Stillborn	1683 (0·2%)
Gestational age	
Preterm (<37 completed weeks)	71 997 (6·2%)
Term	1 083 984 (93·8%)
Among liveborn babies	
Preterm (<37 completed weeks)	69 175 (6·0%)
Term	1 082 301 (94·0%)
Birthweight centile among liveborn babies	
Total with available data (n)	1 146 909
<3rd	22 679 (2·0%)
3rd to 9th	66 049 (5·8%)
10th to 89th	955 177 (83·3%)
≥90th	103 004 (9·0%)

Percentages are presented for women with available data only. BMI=Body-mass index. NICE=National Institute for Health and Care Excellence.

Table 1: **Patient characteristics and outcomes**

birthweight below the 3rd centile for gestational age according to UK-WHO growth charts.[11]

We used the Index of Multiple Deprivation (IMD) as a measure of socioeconomic status (appendix p 3). The IMD provides an area-level measure of deprivation derived from information about income, education, employment, crime, and the living environment. We categorised women into five socioeconomic groups according to national quintiles of IMD rankings of 32 844 Lower Super Output Areas in England with typically 1500 inhabitants.[12]

See Online for appendix

We coded maternal ethnicity using the Office for National Statistics categorisation system from the 2001 UK census.[13] Ethnicity data was considered missing if it was coded as not stated (appendix p 3). Ethnic origin was collapsed into five groups: White, South Asian, Black, Mixed, and Other (including Chinese). Coding of all included variables is described in the appendix (pp 2–3).

Statistical analysis

We compared outcomes between quintiles of deprivation and ethnic groups by use of χ^2. We used the data for each outcome for women in the least deprived quintile or from a White ethnic background as the reference rate, which were then applied to the women in the entire population or in a specific group to estimate the expected number of women with an adverse pregnancy outcome. Attributable fractions were defined as the difference in the observed and expected number of women with an

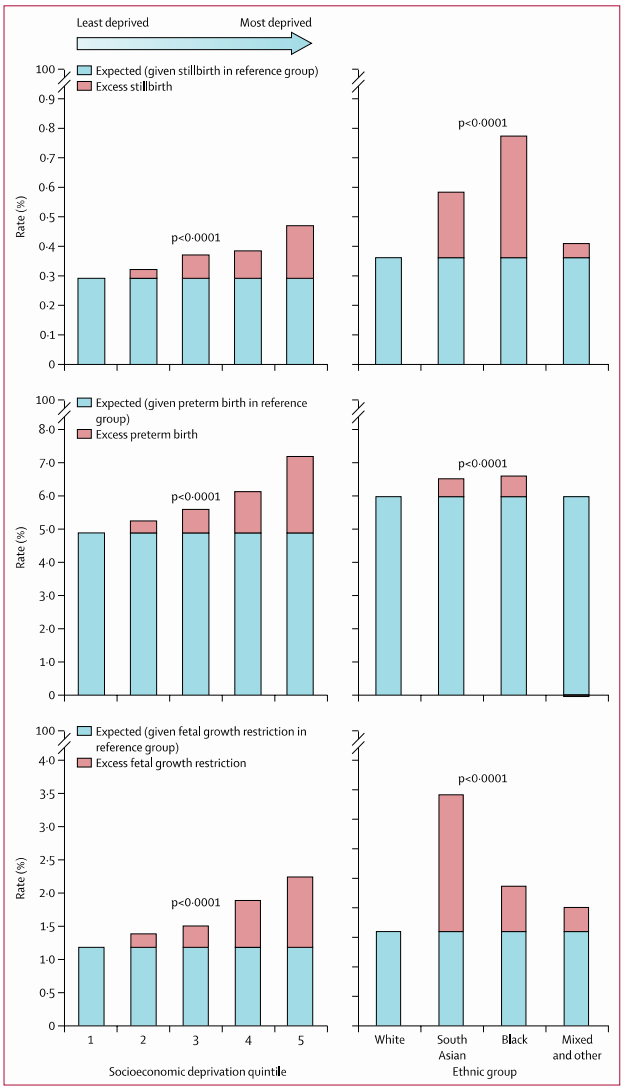


Figure 2: **Stillbirth, preterm birth, and fetal growth restriction rates by socioeconomic deprivation quintile and ethnic group**
(A) Stillbirths. (B) Preterm birth. (C) Birth with fetal growth restriction (less than 3rd centile birthweight). p values calculated using χ^2.

adverse pregnancy outcome, divided by the observed number. The attributable fraction described the proportion of adverse outcome that would not have occurred were the rates of the outcome the same as in the women in the reference group. The attributable fraction compares the reference group either with the entire population, producing a population attributable fraction, or with a specific group, producing a group-specific attributable fraction, also known as attributable fraction in the exposed.[9]

We used logistic regression models to estimate expected numbers of women with adverse pregnancy outcomes, adjusting for ethnicity or deprivation, maternal smoking, and body-mass index (BMI) at the onset of pregnancy. We also adjusted for other maternal risk factors, including maternal age, maternal parity, previous caesarean section, pre-existing medical conditions, previous obstetric complications, and complications in the current pregnancy defined according to the National Institute for Health and Care Excellence (appendix p 3).[14] An interaction term between parity and previous caesarean birth was included in all models in which both these terms were included. A full description of the models and a graphical representation of their goodness of fit is included in the appendix (pp 7–9, 12–13).

We calculated the adjusted attributable fractions again using the expected numbers of adverse outcomes predicted by the logistic regression models. We calculated 95% CIs for the attributable fractions after use of logarithmic transformation to normalise the distribution and stabilise the variance.[15]

Unadjusted attributable fractions were calculated including only women with complete information about socioeconomic deprivation or ethnicity. All regression analyses were restricted to women who had complete information about the outcome under consideration (100% of women for stillbirth and preterm birth and 99·6% for FGR). When estimating adjusted results, we imputed missing maternal risk factors, including socioeconomic deprivation and ethnicity, using chained equations to create ten data sets. We pooled the results for each data set using Rubin's rules.[16]

To examine the robustness of our results to different population definitions, we did sensitivity analyses of stillbirth and FGR only including babies born at term (at or after 37 weeks of gestation). To examine the robustness of results to different outcome definitions, we did sensitivity analyses with preterm birth defined as a birth before 34 weeks of gestation and babies born small defined as those born with a birthweight below the tenth centile (small for gestational age). Our final sensitivity analysis was a complete-case analysis (in other words, excluding records with missing values for maternal risk factors rather than imputing missing data).

All analyses were done with Stata version 14.1, StataCorp, College Station, TX, USA.

Role of the funding source

The funder of the study had no role in study design, data collection, data analysis, data interpretation, or writing of the report.

Results

We identified 1 233 184 women who gave birth in England between April 1, 2015, and March 31, 2017. 46 362 records did not include birth outcome, or the outcome was termination. 18 767 were not reported as singleton births, 18 698 were multiple births, and 69 records did not include information about multiplicity. Gestation length was not reported in 11 432 women, and gestation was less than 24 completed weeks in 643 women. 1 155 981 eligible women were included in the analysis (figure 1), of whom 4505 had a stillbirth (0·4%). Of the 1 151 476 women who had a livebirth, 69 175 (6·0%) had a preterm birth and 22 679 (2·0%) had a birth with FGR (table 1).

1 087 776 women had complete information about their socioeconomic status. Risk of stillbirth increased with socioeconomic deprivation, from 0·29% in the least socioeconomically deprived group to 0·47% in the most deprived group (figure 2, appendix p 4; p<0·0001). The population attributable fraction for socioeconomic status was 23·6% (95% CI 16·7–29·8) unadjusted; 19·0% when adjusted for ethnic group; and 11·6% when adjusted for ethnic group, smoking, and BMI (table 2). The population attributable fraction was similar at 12·4% (95% CI 3·5–20·4) with further adjustment for other maternal risk factors.

Risk of a preterm birth in liveborn babies increased with socioeconomic deprivation, from 4·9% in the least deprived group to 7·2% in the most deprived group (figure 2, appendix p 4; p<0·0001). The population attributable fraction for preterm birth was 18·5% (95% CI 16·9–20·2) unadjusted; 18·4% when adjusted for ethnic group; and 11·9% when adjusted for ethnic group, smoking, and BMI (table 2). Additional adjustment for other risk factors reduced the population attributable fraction to 10·1% (8·0–12·1).

The risk of FGR was 1·2% in the least deprived group and 2·2% in the most deprived group (figure 2; p<0·0001). The attributable fraction was 31·1% (95% CI 28·3–33·8) unadjusted; 25·3% when adjusted for ethnic group; and 16·4% when adjusted for ethnic group, smoking, and BMI. Additional adjustment for other risk factors had little effect on the population attributable fraction (16·5%, CI 12·7–20·2).

1 061 417 women had complete information about their ethnic group. Risk of stillbirth varied according to maternal ethnicity, and ranged from 0·34% in White women to 0·70% in Black women (appendix p 4; p<0·0001). The population attributable fraction for ethnicity was 11·7% (95% CI 9·8–13·5) unadjusted. Adjustment for socioeconomic deprivation, smoking, BMI, and other maternal risk factors had little effect and the population attributable fraction was 12·6% (10·4–14·7) with full adjustment.

Variation in the risk of preterm birth according to ethnicity was small, and ranged from 6·0% in White women to 6·5% in South Asian women and 6·6% in Black women (appendix p 4; p<0·0001). The corresponding population attributable fraction was 1·2% (95% CI 0·8–1·6) unadjusted and 1·2% (0·7–1·7) when adjusted for socioeconomic deprivation, smoking, BMI, and the other maternal risk factors.

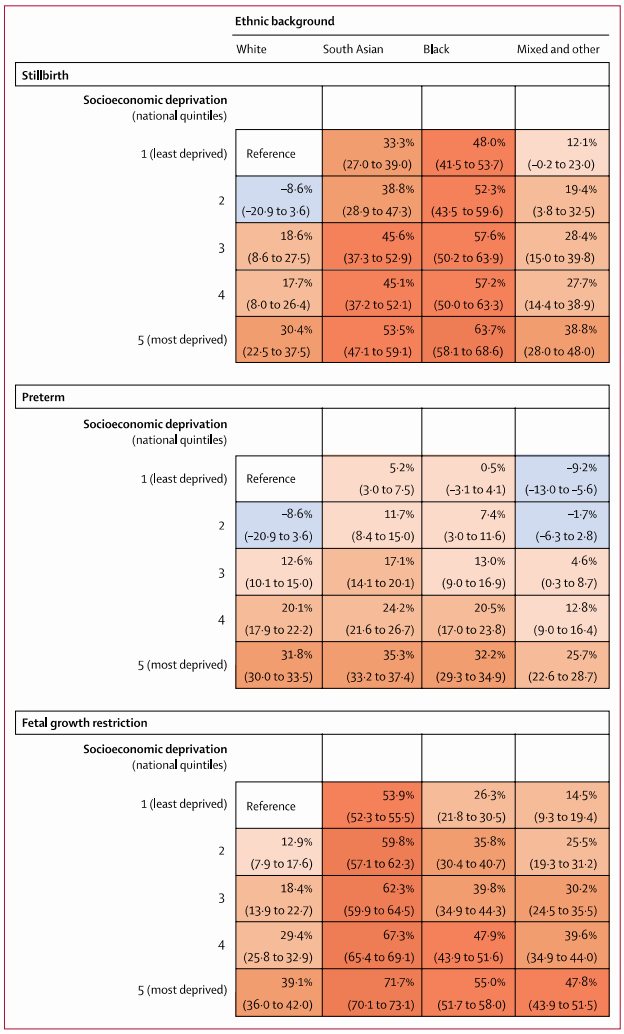
	Stillbirth	Preterm birth	Birth with fetal growth restriction
Socioeconomic deprivation*			
No adjustment	23·6% (16·7 to 29·8)	18·5% (16·9 to 20·2)	31·1% (28·3 to 33·8)
Adjustment			
Ethnic group	19·0% (11·8 to 25·7)	18·4% (16·7 to 20·0)	25·3% (22·3 to 28·2)
Ethnic group, smoking, BMI	11·6% (3·6 to 19·0)	11·9% (10·1 to 13·7)	16·4% (13·0 to 19·6)
Ethnic group, smoking, BMI, all maternal factors†	12·4% (3·5 to 20·4)	10·1% (8·0 to 12·1)	16·5% (12·7 to 20·2)
Ethnic group‡			
No adjustment	11·7% (9·8 to 13·5)	1·2% (0·8 to 1·6)	16·9% (16·1 to 17·8)
Adjustment			
Socioeconomic group	10·8% (8·9 to 12·6)	0·1% (–0·3 to 0·5)	15·2% (14·3 to 16·1)
Socioeconomic group, smoking, BMI	13·0% (11·1 to 14·8)	2·6% (2·2 to 3·0)	19·2% (18·4 to 20·1)
Socioeconomic group, smoking, BMI, all maternal factors†	12·6% (10·4 to 14·7)	1·2% (0·7 to 1·7)	19·5% (18·6 to 20·4)

Data are % (95% CI). BMI=body-mass index. *Compared with those in the least deprived quintile. †Age, parity, pre-existing medical conditions, previous obstetric complications, and conditions in the current pregnancy sufficient to recommend that the woman gives birth in an obstetric-led setting. ‡Compared with White women.

Table 2: **Population attributable fractions of stillbirth, preterm birth, and birth with fetal growth restriction by socioeconomic deprivation and ethnicity**

The risk of FGR varied according to ethnicity, from 1·4% in White women to 3·5% in South Asian women (figure 2; p<0·0001) with a corresponding population attributable fraction of 16·9% (95% CI 16·1–17·8). Adjustment for socioeconomic deprivation, smoking, BMI, and other risk factors had little effect and produced a population attributable fraction of 19·5% (18·6–20·4).

The proportion of stillbirths that would not have occurred if all women had the same stillbirth risk as the least deprived White women was substantially increased in women from more deprived socioeconomic backgrounds and minority ethnic groups (figure 3). More detailed information about the distribution of maternal risk factors by ethnicity and socioeconomic deprivation is available in the appendix (p 10). Attributable fractions for stillbirth were especially high in women in the most deprived socioeconomic group if they were Black (63·7%, 95% CI 58·1–68·6), South Asian (53·5%, 47·1–59·1), or from Mixed or other ethnic background (38·8%, 28·0–48·0). Similarly, high attributable fractions were found for FGR in women in the most deprived socioeconomic group if they were South Asian (71·7%, 70·1–73·1), Black (55·0%, 51·7–58·0), or from Mixed or other ethnic background (47·8%, 43·9–51·5). Similar results were seen in analyses of stillbirth and FGR risk in term births, in analyses in which preterm birth was defined as a birth before 34 completed weeks of gestation and in which a small baby was defined as birthweight under the 10th centile (small for gestational age; appendix p 5), and



Socioeconomic deprivation (national quintiles)	White	South Asian	Black	Mixed and other
Stillbirth				
1 (least deprived)	Reference	33·3% (27·0 to 39·0)	48·0% (41·5 to 53·7)	12·1% (−0·2 to 23·0)
2	−8·6% (−20·9 to 3·6)	38·8% (28·9 to 47·3)	52·3% (43·5 to 59·6)	19·4% (3·8 to 32·5)
3	18·6% (8·6 to 27·5)	45·6% (37·3 to 52·9)	57·6% (50·2 to 63·9)	28·4% (15·0 to 39·8)
4	17·7% (8·0 to 26·4)	45·1% (37·2 to 52·1)	57·2% (50·0 to 63·3)	27·7% (14·4 to 38·9)
5 (most deprived)	30·4% (22·5 to 37·5)	53·5% (47·1 to 59·1)	63·7% (58·1 to 68·6)	38·8% (28·0 to 48·0)
Preterm				
1 (least deprived)	Reference	5·2% (3·0 to 7·5)	0·5% (−3·1 to 4·1)	−9·2% (−13·0 to −5·6)
2	−8·6% (−20·9 to 3·6)	11·7% (8·4 to 15·0)	7·4% (3·0 to 11·6)	−1·7% (−6·3 to 2·8)
3	12·6% (10·1 to 15·0)	17·1% (14·1 to 20·1)	13·0% (9·0 to 16·9)	4·6% (0·3 to 8·7)
4	20·1% (17·9 to 22·2)	24·2% (21·6 to 26·7)	20·5% (17·0 to 23·8)	12·8% (9·0 to 16·4)
5 (most deprived)	31·8% (30·0 to 33·5)	35·3% (33·2 to 37·4)	32·2% (29·3 to 34·9)	25·7% (22·6 to 28·7)
Fetal growth restriction				
1 (least deprived)	Reference	53·9% (52·3 to 55·5)	26·3% (21·8 to 30·5)	14·5% (9·3 to 19·4)
2	12·9% (7·9 to 17·6)	59·8% (57·1 to 62·3)	35·8% (30·4 to 40·7)	25·5% (19·3 to 31·2)
3	18·4% (13·9 to 22·7)	62·3% (59·9 to 64·5)	39·8% (34·9 to 44·3)	30·2% (24·5 to 35·5)
4	29·4% (25·8 to 32·9)	67·3% (65·4 to 69·1)	47·9% (43·9 to 51·6)	39·6% (34·9 to 44·0)
5 (most deprived)	39·1% (36·0 to 42·0)	71·7% (70·1 to 73·1)	55·0% (51·7 to 58·0)	47·8% (43·9 to 51·5)

Figure 3: **Attributable fractions of stillbirth, preterm birth, and birth with fetal growth restriction by socioeconomic deprivation and ethnic group**
Data are attributable fraction (95% CI), calculated by comparison with White women or women in the least deprived quintile. Darker colours indicate higher group attributable fraction.

in analyses that excluded births with missing data on maternal risk factors (appendix p 6).

Discussion

In this study of more than 1 million births in England, 24% of stillbirths, 19% of preterm livebirths, and 31% of livebirths with FGR would not have occurred if all women had the same risk of adverse pregnancy outcomes as women in the least deprived socioeconomic group. These population attributable fractions were considerably lower when adjusted for ethnicity, maternal smoking, and BMI at the onset of pregnancy, which suggests that much of the socioeconomic inequalities in pregnancy outcomes can be explained by the combined influences of these maternal characteristics.

12% of stillbirths, 1% of preterm births, and 17% of births with FGR would not have occurred if all women had the same risks as White women. Adjustment for socioeconomic deprivation, maternal smoking, and BMI had little effect on these population attributable fractions.

About half of stillbirths and about three quarters of births with FGR in South Asian women in the most deprived areas could be attributed to socioeconomic and ethnic inequalities. Similarly, about two thirds of stillbirths and about half of births with FGR in Black women from the most deprived areas could be attributed to socioeconomic and ethnic inequalities.

We used a large set of routinely collected data including 94% of births that occurred in England during the study period. A few NHS hospitals were unable to contribute to the National Maternity and Perinatal Audit, primarily because of limitations of their local clinical information systems.[10] This provides strong support for the representativeness of our findings.

Our study has several limitations. We used an aggregate area-based measure to capture the level of socioeconomic deprivation. The socioeconomic status of people living in a particular area can vary, which will have led to non-differential misclassification of the socioeconomic status of some women and probably led to regression dilution, so our results might underestimate the true extent of socioeconomic differences in pregnancy outcomes.[17] Deprivation measures covering smaller areas (or even individual households) are needed to quantify more accurately the effect of socioeconomic deprivation on adverse pregnancy outcomes and overall health.

There are ongoing concerns about the accuracy of the coding of ethnic groups in the Hospital Episode Statistics database. However, comparison of ethnicity codes in 59 000 patients in the database against self-reported ethnicity information indicated a high level of agreement, especially for the distinction between patients with a White and those with another ethnic background (agreement level 98%). The level of agreement was worse for distinguishing specific minority ethnic groups such as Indian, Pakistani, and Bangladeshi, and therefore we used higher-level ethnic categories.[18]

The interpretation of the attributable fraction as the percentage of adverse outcomes that would not have occurred if women were not exposed to a different background depends on the assumption that biases are absent and that there is no effect modification.[9] It is unlikely that this assumption is fully met in the context

of our study, because exposures such as socioeconomic deprivation and ethnicity are linked to many other circumstances, including overall health, health-related behaviour, nutrition, lifestyle factors, and wider aspects of adversity that are all recognised risk factors of poor pregnancy outcomes.[19]

Socioeconomic and ethnic inequalities in birth outcomes in the UK and many other high-income countries are widely reported.[20] There are many possible reasons for these inequalities and causal pathways are long and complex.[21] Socioeconomic deprivation and minority ethnic background are typically linked to a wider pattern of adverse circumstances, including increased rates of maternal smoking, obesity, and mental illness. Other pathways through which socioeconomic and ethnic inequalities can influence pregnancy outcomes are environmental or pollution exposure; social isolation and paucity of social cohesion; poor access to maternity care and health care in general; and increased chronic stress because of economic strain, insecure employment, and more frequent stressful life events.[22]

Increased stillbirth and FGR birth rates in women from minority ethnic backgrounds are not explained by socioeconomic deprivation alone. Other factors related to discrimination based on race, religion, and culture can contribute to a societal disadvantage and increase the risk of poor pregnancy outcomes.[23] In addition, physiological differences between ethnic groups might lead to differences in maternal immunological, vascular, and endocrine responses.[24] All this indicates that more detailed causal mediation analysis is a research priority.

Policy initiatives to reduce stillbirth, preterm birth, and FGR in England should take these causal complexities into account. Most initiatives that aim to reduce adverse pregnancy outcomes recommend that maternity services focus on individual risk factors and specific groups identified as at high risk.[25,26] Our results suggest that initiatives focusing on individual choices and behaviour and the antenatal care that they receive will have limited effects, because this approach puts the onus on individual women to control risk factors that are at least partly due to social context and societal attitudes. Clinical interventions available to maternity services to mitigate the risk of adverse perinatal outcomes, such as monitoring fetal growth more precisely and frequently[27] and considering elective birth at term,[28] can only have limited impact as they tackle the consequences of socioeconomic and ethnic inequalities.

Our results highlight the potential effect of public health approaches in reducing the risk of adverse pregnancy outcomes. For example, the population attributable fraction of socioeconomic inequalities for stillbirth and FGR reduced considerably if we took maternal smoking and obesity at the onset of pregnancy into account. Initiatives to reduce smoking and improve dietary habits in the community, as part of wider public health initiatives addressing a broader range of lifestyle factors and adverse maternal circumstances, provide important opportunities to improve the health of mothers and birth outcomes.

Attempts to address inequalities in pregnancy outcomes or wider inequalities in health will have to move from addressing the downstream factors such as specific clinical conditions and lifestyle factors, to the conditions that ultimately influence the choices that individuals can make about their own lives.[29] These upstream factors include access to high-quality education, employment, and fairness in terms of income and welfare support.[29] As risk is spread across the whole population, interventions must address the whole population to achieve their maximum benefit.[30]

The largest increases in excess risk of stillbirth and birth with FGR occurred in women from South Asian and Black ethnic backgrounds in the more deprived socioeconomic groups. Our estimates suggest that two thirds of stillbirths in Black women in the most deprived socioeconomic group would not have occurred if they had the same risk as White women in the least deprived socioeconomic group. Similarly, about three quarters of birth with FGR would not have occurred in the most deprived South Asian women if they had same risk as the least deprived White women. These observations underscore the relevance of the complementary nature of the population and high-risk approaches to prevention of adverse births outcomes.[31]

National programmes to make pregnancy safer can only be realistically achieved through plans that include midwives and obstetricians, public health professionals, and politicians. High-quality audits of maternity care and pregnancy outcomes linked to quality improvement initiatives are key to monitoring the outcome of these clinical interventions[31]—for example, by use of a score card that is being implemented in Australia[32] to focus on indicators of antenatal and intrapartum care and on social marginalisation and disadvantage.[3]

Concerted action is needed to reduce inequalities in pregnancy outcomes. Maternity services and public health professionals should work closely with politicians to address the full complexity of the pathways that contribute to the socioeconomic and ethnic differences in pregnancy outcomes, targeting the entire population and those groups at the highest risk.

Contributors

JJ, KW, JH, AK, TH, and JvdM conceived the study. All authors were involved in the design. JJ and JvdM analysed the data. All authors interpreted the results. JJ and JvdM wrote the report with contributions from all other authors. JH, AK, TH, and JvdM are joint senior authors. JJ and IG-U accessed and verified the underlying data. JvdM and JJ had final responsibility for the decision to submit for publication.

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Declaration of interests
All authors declare funding from the Healthcare Quality Improvement Partnership to deliver the National Maternity and Perinatal Audit Programme. We declare no other competing interests.

Data sharing
Data used in this study were collected for the National Maternity and Perinatal Audit and are available on request to the data controllers (the Healthcare Quality Improvement Partnership for Maternity Information System data and NHS Digital for HES data). Please contact the authors if you require further guidance.

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Adverse pregnancy outcomes attributable to socioeconomic and ethnic inequalities in England: a national cohort study

SUPPLEMENTARY APPENDIX

List of items

Supplementary Table 1. Definitions of outcomes

Outcome	Denominator	Numerator
Stillbirth	All births with recorded birth outcome (all births in cohort)	Births recorded as stillbirth
Preterm birth	Births recorded as livebirth with recorded gestational age of 24 weeks or more (all livebirths in cohort)	All livebirths with recorded gestational age below 37 weeks
Preterm birth (<34 weeks)	Births recorded as livebirth with recorded gestational age of 24 weeks or more (all livebirths in cohort)	All livebirths with recorded gestational age below 34 weeks
Term stillbirth	All births with recorded birth outcome with recorded gestational age of 37 weeks or more	All births recorded as stillbirth with recorded gestational age of or above 37 weeks
Preterm stillbirth	All births with recorded birth outcome with recorded gestational age of less than 37 weeks	All births recorded as stillbirth with recorded gestational age of less than 37 weeks
Fetal growth restriction	Births recorded as livebirth with recorded gestational age of 24 weeks or more, with complete information about birthweight	Births recorded as livebirth with recorded gestational age of 24 weeks or more, with recorded birthweight less than 3rd centile
Fetal growth restriction at term	Births recorded as livebirth with recorded gestational age of 37 weeks or more, with complete information about birthweight	Births recorded as livebirth with recorded gestational age of 37 weeks or more, with recorded birthweight less than 3rd centile
Small for gestational age	Births recorded as livebirth with recorded gestational age of 37 weeks or more, with complete information about birthweight	Births recorded as livebirth with recorded gestational age of 37 weeks or more, with recorded birthweight less than 10th centile

Supplementary Table 2. Definitions of maternal characteristics and pregnancy outcomes

Variable	Data Source	Detail	Coding framework
Socioeconomic deprivation: Index of Multiple Deprivation	Primary – MIS Secondary – HES	Postcodes matched to Lower Super Output Areas in 2015[1]	Separated into quintiles of the national distribution
Ethnic group	Primary – MIS Secondary - HES		Grouped into White, South Asian, Black, Mixed and Other according to ONS categories[2]
Birth outcome	MIS		
Gestational age in weeks	MIS		
Parity	Primary – MIS Secondary – HES	When HES is used, lookback method is used[3]	Parity of 3 or more grouped together
Previous caesarean section	Primary – MIS Secondary – HES		
Maternal age	MIS		
Smoking status at booking	MIS		
Body mass index	MIS		
Birthweight centile	Primary – MIS Secondary - HES	Birthweight centile derived using WHO growth charts[4]	
Risk factors identified	HES and MIS	Methodology described in full elsewhere[5]	Separated into previous obstetric complications, previous medical history, and conditions in current pregnancy

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Supplementary Table 3. Stillbirth, preterm birth and fetal growth restriction attributable to inequality in England in 2015-17, by index of multiple deprivation and ethnic group, among those with complete information for socioeconomic or ethnic group only (data for Figure 2)

	Number of women in group	Observed number of women with outcome	Rate of outcome	Number of women with outcome, if rate the same as reference group	Excess outcome	Attributable fraction
Stillbirth						
Ethnic group						
White (Ref)	818982	2807	0.34%	2807	Ref	
South Asian	126262	682	0.54%	433	249	36.5%
Black	52361	368	0.70%	179	189	51.2%
Mixed and Other‡	63812	261	0.41%	219	42	16.2%
Total		*4118*		*3638*	*480*	
Socioeconomic deprivation						
least deprived 20%	158401	462	0.29%	462	Ref	
less deprived 21-40%	178676	574	0.32%	521	53	9.2%
median deprived 41-59%	203698	755	0.37%	594	161	21.3%
more deprived 61-80%	246266	947	0.38%	718	229	24.2%
most deprived 80-100%	300735	1412	0.47%	877	535	37.9%
Total		*4150*		*3173**	*977**	
Preterm birth						
Ethnic group						
White (Ref)	816175	48740	5.97%	48740	Ref	
South Asian	125580	8178	6.51%	7499	679	8.3%
Black	51993	3429	6.60%	3105	324	9.5%
Mixed and Other‡	63551	3551	5.59%	3795	-244	-6.9%
Total		*63898*		*63139*	*759*	
Socioeconomic deprivation						
least deprived 20%	157939	7709	4.88%	7709	Ref	
less deprived 21-40%	178102	9338	5.24%	8693	645	6.9%
median deprived 41-59%	202943	11346	5.59%	9906	1440	12.7%
more deprived 61-80%	245319	15024	6.12%	11974	3050	20.3%
most deprived 80-100%	299323	21509	7.19%	14610	6899	32.1%
Total		*64926*		*52892*	*12034*	
FGR						
Ethnic group						
White (Ref)	766107	10873	1.42%	10873	Ref	
South Asian	117158	4077	3.48%	1663	2414	59.2%
Black	48480	1018	2.10%	688	330	32.4%
Mixed and Other	59888	1067	1.78%	850	217	20.3%
Total		*17035*		*14074*	*2961*	
Socioeconomic deprivation						
least deprived 20%	149973	1772	1.18%	1772	Ref	
less deprived 21-40%	168460	2333	1.38%	1990	343	14.7%
median deprived 41-59%	191229	2876	1.50%	2259	617	21.4%
more deprived 61-80%	229842	4335	1.89%	2716	1619	37.4%
most deprived 80-100%	277261	6213	2.24%	3276	2937	47.3%
Total		*17529*		*12014**	*5515**	
*discrepancy due to rounding error, the total here is correct.						

Supplementary Table 4. Alternative definitions of outcomes: The fractions of term and preterm stillbirth, preterm birth under 34 weeks, fetal growth restriction at term and babies born small for gestational age under the 10th centile which are attributable to deprivation and to ethnic group, following adjustment for other possible modifiers of association, among complete cases

	Stillbirth (term only)	Stillbirth (preterm)	Preterm (<34wk)	Fetal growth restriction (term only)	Small for gestational age (<10th centile)
Socioeconomic deprivation†					
No adjustment	17.6% (5.9 to 27.9)	11.0% (0.6 to 20.4)	23.2% (19.8 to 26.4)	31.5% (28.4 to 34.4)	23.9% (22.4 to 25.3)
Adjusted for:					
Ethnic group	14.1% (1.1 to 25.4)	6.7% (-4.9 to 16.9)	23.8% (20.3 to 27.2)	26.4% (22.9 to 29.7)	19.2% (17.6 to 20.8)
Ethnic group, smoking, BMI	4.6% (-11.8 to 18.5)	10.1% (-3.5 to 21.9)	17.4% (12.8 to 21.8)	16.3% (11.7 to 20.6)	12.1% (10.1 to 14.0)
Ethnic group, smoking, BMI, all maternal factors*	7.8% (-8.4 to 21.5)	12.7% (-1.1 to 24.6)	16.8% (12.0 to 21.3)	17.7% (13.1 to 22.1)	12.5% (10.5 to 14.4)
Ethnic group‡					
No adjustment	9.7% (6.6 to 12.6)	11.5% (9.1 to 13.8)	3.6% (2.8 to 4.5)	17.4% (16.5 to 18.3)	14.3% (13.9 to 14.7)
Adjusted for:					
Socioeconomic group	9.1% (5.9 to 12.1)	10.5% (8.1 to 12.9)	1.9% (1.0 to 2.8)	15.2% (14.2 to 16.2)	12.6% (12.2 to 13.0)
Socioeconomic group, smoking, BMI	10.5% (7.0 to 13.9)	10.6% (7.7 to 13.4)	4.7% (3.6 to 5.8)	20.0% (18.9 to 21.0)	16.4% (15.9 to 16.9)
Socioeconomic group, smoking, BMI, all maternal factors*	10.4% (6.8 to 13.9)	11.5% (8.5 to 14.4)	3.5% (2.4 to 4.6)	20.1% (19.0 to 21.2)	16.7% (16.2 to 17.1)

†Compared to those in the least deprived quintile.

‡Compared to women from a White ethnic background.

*These include age, parity, pre-existing medical conditions, previous obstetric complications and conditions in the current pregnancy sufficient to recommend that the woman gives birth in an obstetric-led setting.

Supplementary Table 5. The fractions of stillbirth, preterm birth and FGR which are attributable to deprivation and to ethnic group, following adjustment for other possible modifiers of association, among complete cases

	Stillbirth	Preterm birth	Birth with FGR
Socioeconomic deprivation†			
No adjustment	23.6% (16.7 to 29.8)	18.5% (16.9 to 20.2)	31.1% (28.3 to 33.8)
Adjusted for:			
Ethnic group	20.4% (12.8 to 27.3)	19.3% (17.5 to 21.0)	26.3% (23.1 to 29.3)
Ethnic group, smoking, BMI	14.6% (5.0 to 23.2)	12.4% (10.2 to 14.5)	15.8% (11.7 to 19.8)
Ethnic group, smoking, BMI, all maternal factors*	16.3% (6.7 to 25.1)	11.1% (8.9 to 13.3)	17.0% (12.8 to 21.0)
Ethnic group‡			
No adjustment	11.7% (9.8 to 13.5)	1.2% (0.8 to 1.6)	16.9% (16.1 to 17.8)
Adjusted for:			
Socioeconomic group	10.0% (8.1 to 12.0)	-0.3% (-0.7 to 0.2)	14.8% (13.9 to 15.6)
Socioeconomic group, smoking, BMI	11.9% (9.7 to 14.1)	2.1% (1.6 to 2.6)	19.9% (18.9 to 20.8)
Socioeconomic group, smoking, BMI, all maternal factors*	11.7% (9.4 to 13.9)	0.8% (0.3 to 1.3)	19.7% (18.7 to 20.7)

†Compared to those in the least deprived quintile.

‡Compared to women from a White ethnic background.

*These include age, parity, pre-existing medical conditions, previous obstetric complications and conditions in the current pregnancy sufficient to recommend that the woman gives birth in an obstetric-led setting.

Supplementary Tables 6a-c. Adjustment models for Table 2: stillbirth, preterm birth and FGR (models used to generate PAFs shown in Table 2)

6a. Stillbirth

Maternal characteristics	Unadjusted Odds Ratio (OR)	Adjusted ORs†		
		Socioeconomic and ethnic group	Socioeconomic and ethnic group, smoking, BMI	Socioeconomic and ethnic group, smoking, BMI, maternal factors
IMD decile				
least deprived 20%	Ref	Ref	Ref	Ref
less deprived 21-40%	1.10 (0.98,1.24)	1.09 (0.97,1.23)	1.06 (0.94,1.19)	1.05 (0.91,1.20)
median deprived 41-59%	1.27 (1.13,1.43)	1.23 (1.09,1.38)	1.15 (1.03,1.37)	1.20 (1.05,1.37)
more deprived 61-80%	1.32 (1.19,1.47)	1.22 (1.09,1.36)	1.10 (0.98,1.23)	1.13 (1.00,1.28)
most deprived 80-100%	1.63 (1.46,1.81)	1.45 (1.30,1.61)	1.23 (1.11,1.38)	1.22 (1.08,1.38)
Ethnic group				
White	Ref	Ref	Ref	Ref
South Asian	1.59 (1.46,1.73)	1.51 (1.39,1.64)	1.73 (1.58,1.89)	1.69 (1.53,1.86)
Black	2.08 (1.87,2.32)	1.92 (1.72,2.15)	2.07 (1.85,2.32)	1.96 (1.73,2.22)
Mixed	1.34 (1.09,1.65)	1.29 (1.05,1.59)	1.33 (1.08,1.64)	1.33 (1.05,1.68)
Other	1.14 (0.99,1.33)	1.11 (0.95,1.29)	1.24 (1.07,1.44)	1.26 (1.06,1.49)
Smoker at booking			1.66 (1.53,1.82)	1.64 (1.49,1.80)
BMI				
<18.5			0.97 (0.79,1.20)	0.97 (0.79,1.20)
18.5-24.9			Ref	Ref
25.0-29.9			1.16 (1.07,1.26)	1.13 (1.04,1.22)
30.0-34.9			1.23 (1.12,1.36)	1.15 (1.04,1.28)
35.0-39.9			1.51 (1.34,1.70)	1.34 (1.17,1.53)
40.0 or over			1.87 (1.60,2.18)	1.54 (1.30,1.82)
Age				
Under 20				1.25 (1.14,1.36)
20-34				Ref
35-39				1.50 (1.29,1.73)
40 or older				0.96 (0.79,1.17)
Parity				
0				Ref
1				0.52 (0.47,0.57)
2				0.56 (0.50,0.64)
3 or more				0.58 (0.50,0.67)
Previous caesarean				0.59 (0.29,1.23)
Pre-existing conditions				1.48 (1.37,1.61)
Previous complications				4.87 (4.45,5.34)
Conditions in pregnancy				1.08 (0.99,1.17)

†Adjusted for all listed covariates. Models which include parity and previous caesarean also include an interaction term

6b. Preterm birth

Maternal characteristics	Unadjusted Odds Ratio (OR)	Adjusted ORs†		
		Socioeconomic and ethnic group	Socioeconomic and ethnic group, smoking, BMI	Socioeconomic and ethnic group, smoking, BMI, maternal factors
IMD decile				
least deprived 20%	Ref	Ref	**Ref**	Ref
less deprived 21-40%	1.08 (1.04,1.11)	1.08 (1.04,1.11)	1.05 (1.02,1.08)	1.04 (1.01,1.08)
median deprived 41-59%	1.15 (1.12,1.19)	1.15 (1.12,1.19)	1.09 (1.06,1.12)	1.08 (1.05,1.12)
more deprived 61-80%	1.27 (1.24,1.31)	1.27 (1.23,1.30)	1.15 (1.12,1.19)	1.13 (1.10,1.17)
most deprived 80-100%	1.51 (1.47,1.55)	1.50 (1.46,1.54)	1.29 (1.25,1.32)	1.24 (1.20,1.28)
Ethnic group				
White	Ref	Ref	Ref	Ref
South Asian	1.13 (1.10,1.16)	1.06 (1.03,1.08)	1.20 (1.18,1.24)	1.14 (1.11,1.18)
Black	1.12 (1.08,1.16)	1.01 (0.98,1.05)	1.15 (1.11,1.19)	0.98 (0.94,1.02)
Mixed	1.05 (0.99,1.11)	1.00 (0.95,1.06)	1.03 (0.98,1.10)	1.00 (0.94,1.07)
Other	0.89 (0.86,0.93)	0.86 (0.82,0.89)	0.94 (0.90, 0.98)	0.95 (0.90,1.00)
Smoker at booking			1.77 (1.73,1.81)	1.66 (1.62,1.70)
BMI				
<18.5			1.49 (1.43,1.55)	1.38 (1.32,1.45)
18.5-24.9			Ref	Ref
25.0-29.9			0.98 (0.96,1.00)	0.94 (0.92,0.96)
30.0-34.9			1.05 (1.02,1.08)	0.91 (0.89,0.94)
35.0-39.9			1.14 (1.10,1.19)	0.90 (0.87,0.94)
40.0 or over			1.28 (1.22,1.34)	0.89 (0.85,0.94)
Age				
Under 20				1.06 (1.03,1.08)
20-34				Ref
35-39				1.26 (1.21,1.32)
40 or older				1.18 (1.12,1.23)
Parity				
0				Ref
1				0.56 (0.54,0.57)
2				0.62 (0.60,0.64)
3 or more				0.71 (0.69,0.74)
Previous caesarean				1.38 (1.21,1.56)
Pre-existing conditions				2.03 (1.99,2.08)
Previous complications				3.97 (3.87,4.08)
Conditions in pregnancy				1.89 (1.85,1.93)

†Adjusted for all listed covariates. Models which include parity and previous caesarean also include an interaction term

6c. FGR

Maternal characteristics	Unadjusted Odds Ratio (OR)	Adjusted ORs†		
		Socioeconomic and ethnic group	Socioeconomic and ethnic group, smoking, BMI	Socioeconomic and ethnic group, smoking, BMI, maternal factors
IMD decile				
least deprived 20%	Ref	Ref	Ref	Ref
less deprived 21-40%	1.16 (1.10,1.23)	1.15 (1.08,1.21)	1.11 (1.05,1.17)	1.07 (1.00,1.14)
median deprived 41-59%	1.29 (1.22,1.36)	1.23 (1.16,1.29)	1.14 (1.08,1.20)	1.12 (1.06,1.19)
more deprived 61-80%	1.58 (1.50,1.66)	1.41 (1.34,1.49)	1.24 (1.18,1.30)	1.25 (1.18,1.32)
most deprived 80-100%	1.89 (1.80,1.98)	1.64 (1.56,1.72)	1.33 (1.26,1.39)	1.37 (1.29,1.45)
Ethnic group				
White	Ref	Ref	Ref	Ref
South Asian	2.40 (2.32,2.48)	2.22 (2.15,2.30)	2.84 (2.75,2.95)	2.87 (2.75,2.98)
Black	1.54 (1.46,1.63)	1.38 (1.30,1.46)	1.89 (1.78,2.00)	1.89 (1.76,2.02)
Mixed	1.51 (1.37,1.65)	1.43 (1.30,1.57)	1.50 (1.37,1.65)	1.61 (1.45,1.78)
Other	1.14 (1.06,1.23)	1.09 (1.01,1.17)	1.26 (1.17,1.35)	1.24 (1.15,1.35)
Smoker at booking			2.73 (2.64,2.83)	2.92 (2.80,3.04)
BMI				
<18.5			1.74 (1.64,1.84)	1.68 (1.57,1.79)
18.5-24.9			Ref	Ref
25.0-29.9			0.76 (0.73,0.82)	0.76 (0.73,0.79)
30.0-34.9			0.69 (0.65,0.72)	0.65 (0.62,0.69)
35.0-39.9			0.63 (0.58,0.67)	0.56 (0.51,0.60)
40.0 or over			0.60 (0.54,0.67)	0.50 (0.45,0.56)
Age				
Under 20				1.12 (1.07,1.16)
20-34				Ref
35-39				1.16 (1.07,1.26)
40 or older				0.85 (0.79,0.92)
Parity				
0				Ref
1				0.46 (0.44,0.48)
2				0.44 (0.41,0.47)
3 or more				0.43 (0.40,0.46)
Previous caesarean				0.64 (0.49,0.82)
Pre-existing conditions				1.08 (1.04,1.12)
Previous complications				1.27 (1.20,1.35)
Conditions in pregnancy				3.43 (3.31,3.54)

†Adjusted for all listed covariates. Models which include parity and previous caesarean also include an interaction term

Supplementary Table 7. Maternal risk factors by socioeconomic and ethnic group

	Ethnic group			
	White	**South Asian**	**Black**	**Mixed/Other**
IMD Quintile				
Least deprived 20%				
Age ≥35yrs*	30557/129094 (23.7)	2139/8515 (25.1)	488/1797 (27.2)	1847/6263 (29.5)
BMI ≥30*	17206/109028 (15.8)	780/7121 (11.0)	403/1553 (26.0)	639/5282 (12.1)
Smoker*	6475/107998 (6.0)	55/7207 (0.8)	31/1520 (2.0)	178/5360 (3.3)
Less deprived 21-40%				
Age ≥35yrs*	27099/140702 (19.3)	2383/11155 (21.4)	794/2978 (26.7)	1779/7607 (23.4)
BMI ≥30*	21952/120153 (18.3)	1373/9607 (14.3)	736/2594 (28.4)	875/6607 (13.2)
Smoker*	11120/118828 (9.4)	124/9652 (1.3)	66/2629 (2.5)	327/6636 (4.9)
Median deprived 41-59%				
Age ≥35yrs*	24939/151214 (16.5)	3305/17910 (18.5)	1470/5627 (26.1)	2060/9662 (21.3)
BMI ≥30*	27362/130325 (21.0)	2509/15581 (16.1)	1617/4925 (32.8)	1365/8451 (16.2)
Smoker*	16766/127760 (13.1)	203/15432 (1.3)	178/4972 (3.6)	509/8283 (6.2)
More deprived 61-80%				
Age ≥35yrs*	21491/161944 (13.3)	5039/32375 (15.6)	3208/13367 (24.0)	2638/14530 (18.2)
BMI ≥30*	33214/138574 (24.0)	4883/26257 (18.6)	3748/11192 (33.5)	2231/12378 (18.0)
Smoker*	26287/135915 (19.3)	464/26802 (1.7)	422/11267 (3.8)	1072/12174 (8.8)
Most deprived 81-100%				
Age ≥35yrs*	17237/186178 (9.3)	6985/46911 (14.9)	5509/23733 (23.2)	3062/20393 (15.0)
BMI ≥30*	43521/156691 (27.8)	8461/38402 (22.0)	6876/19458 (35.3)	3729/16932 (22.0)
Smoker*	48241/155466 (31.0)	1089/38312 (2.8)	822/18982 (4.3)	2288/16373 (14.0)
*numerator/denominator (%) of cases with complete information about covariates				

Supplementary Figure 1. Percentage of stillbirth, preterm birth and fetal growth restriction attributable to socioeconomic and ethnic inequality in England, 2015-17 (complete cases only)

Stillbirth

Socioeconomic deprivation (national quintiles)	**Ethnic group** White	South Asian	Black	Mixed and Other
1 (least deprived)	Reference	32.6% (26.3 to 38.3)	47.0% (40.4 to 52.9)	10.9% (-1.9 to 22.1)
2	8.8% (-3.7 to 19.8)	38.5% (28.3 to 47.3)	51.7% (42.6 to 59.3)	18.7% (2.4 to 32.4)
3	20.5% (10.2 to 29.6)	46.4% (37.9 to 53.7)	57.8% (50.2 to 64.3)	29.2% (15.3 to 40.7)
4	17.9% (7.6 to 27.0)	44.6% (36.3 to 51.9)	56.5% (49.0 to 62.8)	26.8% (12.8 to 38.6)
5 (most deprived)	32.8% (24.9 to 40.0)	54.7% (48.3 to 60.3)	64.4% (58.7 to 69.3)	40.1% (29.2 to 49.4)

Preterm

Socioeconomic deprivation (national quintiles)	**Ethnic group** White	South Asian	Black	Mixed and Other
1 (least deprived)	Reference	2.6% (0.2 to 4.9)	-0.3% (-4.0 to 3.3)	-10.4% (-14.3 to -6.6)
2	7.1% (4.2 to 9.9)	9.5% (5.9 to 12.9)	6.8% (2.3 to 11.1)	-2.5% (-7.3 to 2.1)
3	13.4% (10.9 to 16.0)	15.7% (12.5 to 18.7)	13.2% (9.1 to 17.1)	4.6% (0.2 to 8.8)
4	21.4% (19.2 to 23.6)	23.4% (20.7 to 26.1)	21.2% (17.6 to 24.6)	13.4% (9.6 to 17.1)
5 (most deprived)	32.8% (31.0 to 34.5)	34.5% (32.2 to 36.6)	32.6% (29.7 to 35.3)	26.0% (22.8 to 29.0)

Fetal growth restriction

Socioeconomic deprivation (national quintiles)	**Ethnic group** White	South Asian	Black	Mixed and Other
1 (least deprived)	0	54.3% (52.6 to 55.8)	26.1% (21.5 to 30.4)	13.9% (8.6 to 19.0)
2	12.4% (7.0 to 17.4)	59.8% (57.0 to 62.4)	35.2% (29.5 to 40.4)	24.6% (18.0 to 30.6)
3	18.4% (13.7 to 22.9)	62.5% (60.1 to 64.9)	39.6% (34.5 to 44.3)	29.7% (23.8 to 35.2)
4	30.3% (26.5 to 33.9)	67.9% (65.9 to 69.7)	48.4% (44.2 to 52.2)	39.9% (35.1 to 44.5)
5 (most deprived)	39.8% (36.6 to 42.8)	72.2% (70.6 to 73.7)	55.3% (51.9 to 58.5)	48.1% (44.0 to 51.9)

Supplementary Figure 2a-c. Calibration of models used to generate PAFs demonstrated in Table 2 (models detailed in Supplementary Tables 6a-c; models used in these plots are 'full' models incorporating socioeconomic and ethnic group, smoking, BMI and other maternal risk factors).

Figure 2a. Calibration of full model for stillbirth, by decile of predicted risk

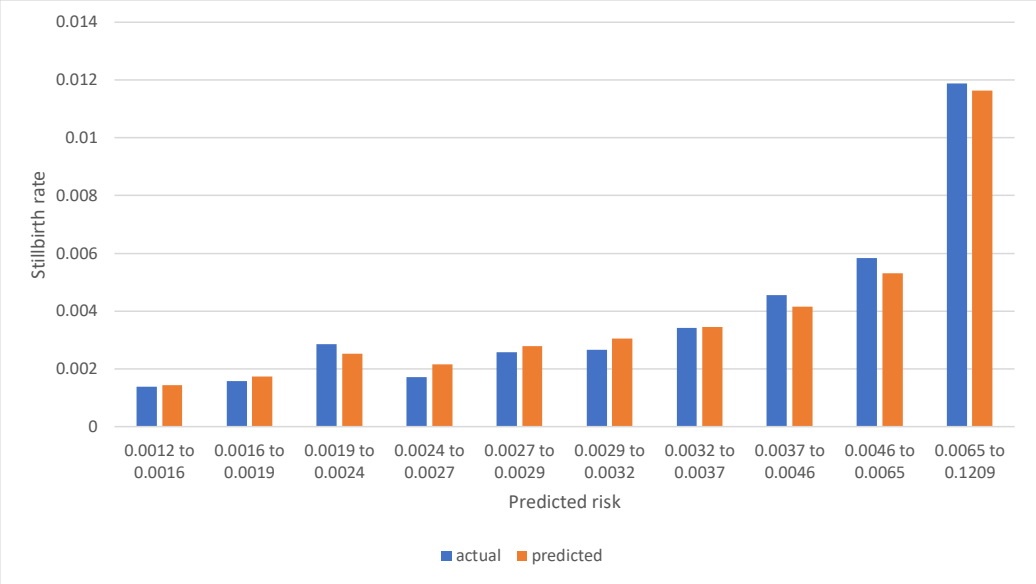


Figure 2b. Calibration of full model for preterm birth, by decile of predicted risk

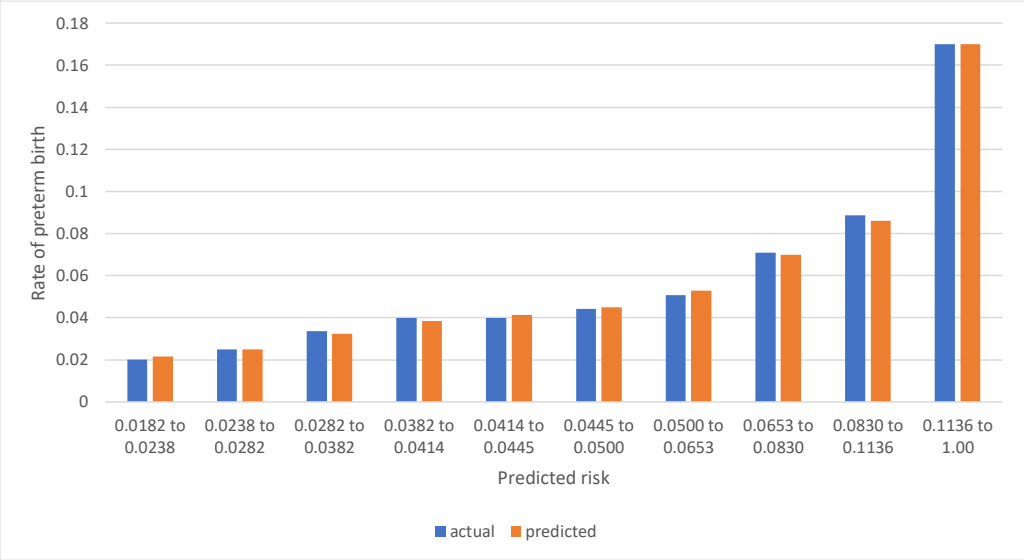
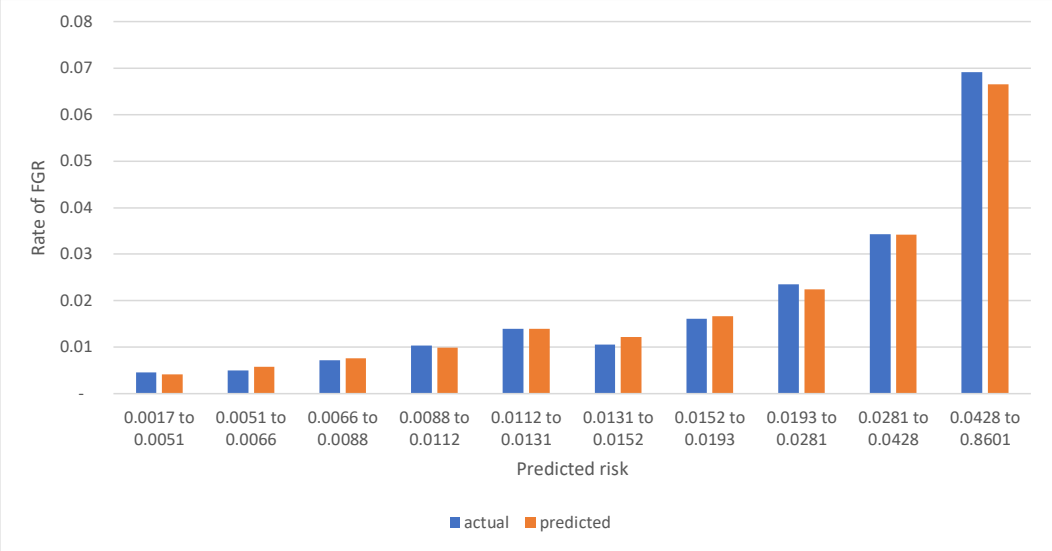


Figure 2c. Calibration of full model for small-for-gestational-age, by decile of predicted risk



9. Discussion

This programme of research has addressed several questions relevant to prognosis in women giving birth and understanding maternity care within the NHS. In this section, I summarise my findings, discuss overall strengths and limitations of the work, and then discuss implications of this research for clinical care, policy, and future research.

9.1 Summary of main findings

This thesis addressed four related issues in maternity care in the UK. These are:

(1) The quality of coding of ethnicity in electronic health record data.

(2) Risk factors for adverse pregnancy outcomes
    a. Associations between ethnicity and admission to intensive care among women giving birth
    b. Associations between ethnicity and postpartum haemorrhage
    c. Risk factors for preterm birth, split into iatrogenic (provider-initiated) and spontaneous

(3) Risk of complicated birth at term in nulliparous and multiparous women

(4) The proportion of adverse pregnancy outcomes (stillbirth, preterm birth and fetal growth restriction) which are attributable to socioeconomic and ethnic inequality

The studies use linked datasets comprising information captured during routine clinical care and seek to address common concerns about the validity and usefulness of these data.

The first issue addressed by this thesis, in Chapter 3, is the quality of the recording and coding of ethnicity in maternal health records. This work underpins the later investigation of inequalities in maternity outcomes by providing both a validation of ethnicity coding in the dataset and an understanding of the limitations of the use of electronic health record data to examine differences by ethnic group. This study used two datasets both of which record the self-declared ethnicity of women giving birth: Hospital Episode Statistics (HES) records for the birth episode, and Maternity Information Systems (MIS) records. The overall agreement between datasets was good; the most disagreement was seen in women coded as mixed ethnicity in either dataset. I found that regardless of dataset used, rates of obstetric events and complications by ethnicity were similar. These findings support the use of ethnicity

collapsed into groups, with caution over results for women with mixed ethnicity; analyses using more granular classifications should also be interpreted with caution. Based on these findings, later analyses using these datasets are restricted to handling ethnicity in aggregate groups.

The next part of the thesis investigates risk factors for three maternity outcomes: maternal intensive care admission, postpartum haemorrhage, and preterm birth.

In Chapters 4 and 5, I examined risk factors for two outcomes which represent severe maternal morbidity: intensive care admission and postpartum haemorrhage (PPH). By linking maternity data to intensive care admission data, I found that Black women are twice as likely as White women to experience intensive care admission, with an excess of admissions for obstetric haemorrhage compared to women from other ethnic groups. In logistic regression models which sequentially adjusted for demographic, health, lifestyle, pregnancy and birth factors, this association was only partially explained, with Black women still 1.7 times as likely to be admitted to intensive care; most of the difference between the unadjusted and adjusted rates was due to higher prevalence of hypertensive and cardiac disease, and caesarean birth, in Black women. I then used maternity and hospital data to examine variation in rates of PPH, and similarly found that following adjustment for maternal, fetal and birth characteristics, Black women were 1.5 times as likely to experience PPH of 1500ml or more. Women from other ethnic minority groups were also at increased risk of PPH, although the relationship was not as strong. These findings are unlikely to be explained by unit-specific factors such as differences in thresholds for intensive care admission. These findings mirror existing information from the UK Obstetric Surveillance System and MBRRACE-UK about increased risk of severe morbidity and mortality in Black women and provides additional evidence of the scale of that inequality (35,77).

Next, in Chapter 6, I considered with colleagues how to best monitor preterm birth. I split preterm birth into spontaneous and iatrogenic based on the mode of onset of the birth (whether it started by itself or was initiated by the healthcare provider), and demonstrated using logistic regression models that although the women who experienced these events had some similar characteristics, however there were important differences between groups, in

particular with obesity (where spontaneous preterm birth was less likely, but iatrogenic preterm birth more likely) and maternal age (where younger women were more likely to have a spontaneous preterm birth, and older women more likely to have an iatrogenic preterm birth). The incidence of both iatrogenic and spontaneous preterm birth increased with increasing socioeconomic deprivation; there was only a weak relationship between preterm birth and ethnic group which disappeared in an analysis adjusted for maternal diagnoses of diabetes and hypertension. Births with iatrogenic and spontaneous onset should be measured and monitored separately as well as in aggregate, to enable appropriate targeting of interventions.

The third issue addressed in this thesis, in Chapter 7, is the performance of a commonly used classification of risk to predict complications during birth. Much of the care of pregnant women in the UK is based on a risk assessment which initially occurs at the time of pregnancy booking and then is re-evaluated at each appointment and at the time of birth. This risk classification is outlined in the NICE guideline on intrapartum care and used to guide place of birth. It separates women into those at low, intermediate, and increased risk of complications based on a list of conditions and characteristics including BMI, maternal age, medical comorbidities, and previous obstetric history (17). This classification, however, poorly predicts women's chance of complicated birth (requiring immediate access to obstetric and/or neonatal care). 43% of women having their first birth who are identified by the NICE classification as 'low risk' will experience one or more of these complications; this may, for women giving birth in midwifery-led settings, include a need for transfer between birth settings. However, I also found that parity, and previous obstetric history, is a far better predictor: only 8.8% of those 'low risk' women who have had previous vaginal birth(s) and no prior caesarean will experience a complication.

In Chapter 8, I used maternity and hospital data to understand the impact of socioeconomic and ethnic inequalities in stillbirth, preterm birth and fetal growth restriction (FGR; birth below the 3rd centile on the UK-WHO birthweight charts). Preterm birth and FGR are two of the leading causes of neonatal morbidity and mortality (40,43). Using population attributable fractions (PAFs), I found that a quarter of stillbirths, a fifth of preterm births, and nearly a third of FGR was attributable to socioeconomic inequality. I used logistic regression models

to provide risk-adjusted estimates, finding that these PAFs were substantially altered when adjusted for ethnic group, smoking and BMI. Examining ethnic group alone, I found that about a tenth of stillbirths and one in six incidences of FGR was attributable to maternal ethnicity; this was not substantially changed by adjustment for maternal deprivation, smoking or BMI. When I looked at groups individually, I found that in the most deprived ethnic minority groups, over half of stillbirths and FGR would not have occurred if these women had the same risk of adverse outcomes as white women in affluent areas. These findings provide clear, and stark, information about the extent to which existing socioeconomic and ethnic inequalities govern maternity outcomes in England. This study is particularly novel in its disentanglement of inequality due to socioeconomic factors and that due to ethnic group.

9.2 Strengths and limitations

The strengths and limitations of each included study are discussed in the relevant chapter. In this section, I aim not to repeat these points in detail, but instead to discuss themes raised throughout the thesis.

9.2.1 Statistical approach

Observational studies on whole populations have enormous advantages in terms of size and robustness, particularly in maternity care where participation in randomised controlled trials is so limited (with studies reporting low recruitment rates of 30% or less of eligible women (103,104)). Observational studies by their nature cannot, however, account for all individual or carer preference for an intervention or treatment (selection bias) and for all the reasons for any intervention being undertaken (confounding). In this thesis, careful attempt has been made to minimise confounding by adjusting each regression analysis for potential confounders; it has also been widely acknowledged that some of the observed effects (for example, increased PPH in Black women, Chapter 5) are unlikely to be due to biological factors alone, but instead to unmeasured confounding or differences in treatment (such as delayed response or reduced treatment intensity); however, in the studies contained within this thesis, the size of effects observed are too large to be explained entirely by selection bias or confounding. The results within these studies may raise additional questions that require

answering through more detailed observational or randomised controlled trials, prior to direct change being made to clinical care.

9.2.2 Strengths and limitations of data source

A key strength of the studies within this thesis is the use of linked patient-level data collected during clinical care in the NHS. This is an ideal population to study: almost all women who give birth in England and Wales do so within the NHS (in 2020, over 99% of all births (11)), which serves a diverse population with relatively uniform care informed by detailed national guidance from, principally, NICE and the RCOG. The dataset contains detailed information about the woman, her baby and her care. This enables novel comparisons between characteristics not available to other research groups, and rich understanding of clinical care, risk, and inequalities at a national level.

Limitations of the data source originate largely from its nature as a secondary use dataset: the primary purpose of the data collection is for maternity care provided through NHS hospital trusts. Therefore, the dataset focuses on information immediately relevant to pregnancy and birth, missing information on antenatal care provision and uptake, and longer term postnatal outcomes beyond the immediate hospital discharge (such as health at the postpartum check appointment). Limitations also arise from the linkage between datasets, from different coding practices between hospitals, and from missing data. While careful attempts have been made to overcome these limitations, these have been separately considered in each individual study.

Key limitations common to all studies focus on unmeasured confounding and the presence of missing data. Missing information in this dataset is substantial, in common with other datasets primarily collected for a use other than research. Throughout this research, various methods of addressing these have been used. In each analysis, I have sought to understand the sensitivity of the results to different methods of handling missing data using two or more approaches. If results are robust to these sensitivity analyses, it is possible to express confidence that the underlying association exists (100). Furthermore, I have attempted to account for unmeasured confounding wherever possible through sensitivity analyses; for

example, in postpartum haemorrhage, by restricting the analysis to primiparous women to account for the limitation of absent information on previous PPH.

9.2.3 Characterising ethnic and socioeconomic groups

9.2.3.1 Characterising ethnic group

Due to data collection in the UK, this thesis focuses on inequality by ethnic group, as self-declared by women at the time of booking their pregnancy. This is an important difference from studies elsewhere in Europe, which often measure inequality due to country of origin (e.g., 'Swedish-born' v 'born-outside-Sweden'; in France, the collection of ethnicity data is illegal except in specifically defined circumstances) (105). In the UK, migrants are not identified in routinely-collected health data (106). Analysis by ethnic group is more similar to studies originating in the USA, where racial origin is routinely recorded (107–110). Ethnicity is a holistic concept which incorporates several different aspects of an individual's lived experience: their culture, religion, society and their experiences of structural discrimination and racism. In this sense, it is different from purely focusing on race or country of origin.

Collection of data on ethnicity in electronic health records has several pre-existing problems (111,112). First, the categories used to record ethnic group in these datasets are limited, using definitions from the 2001 census (113) which have since been updated, notably to include Chinese in the Asian group and to add Arab to the 'Other' category for 2011 (113), and to add Roma in 2021 (114). It is considered a priority to update this in health data (41), but repeated changes to datasets will make it more challenging to establish validity and time trends.

Levels of missing data are often higher for ethnic minority groups than for those from White groups (68,115); this is also true for the studies within this thesis where, for example, women from Black groups are less likely to have an NHS number recorded to enable data to be linked between MIS and HES. Furthermore, there is also inconsistency in recording: this is particularly a concern for women from Mixed groups, where there is a higher degree of inconsistency within datasets; and when analysis is undertaken at the most granular level (e.g., for Black, Black African/Black Caribbean/Black Other), as demonstrated in Chapter 3. Based on these findings, throughout this thesis I have considered ethnic group collapsed into

the less granular groups of White/South Asian/Black/Mixed/Other, rather than attempting to draw conclusions from the data at a more granular level. I have also made specific recommendations to improve the recording of ethnicity in health record datasets, described in Chapter 3.

9.2.3.2 Characterising socioeconomic group

The studies in this thesis use the Indices of Multiple Deprivation (IMD) to measure socioeconomic deprivation. Use of aggregate area-based measures such as IMD ignores that within a local area, individuals may range from the highest to the lowest levels of socioeconomic deprivation; this may introduce a non-differential misclassification of the socioeconomic status of some women (for example, women moving in to gentrifying areas of cities). This will flatten patterns of association within regression models, a pattern known as "regression dilution" (97,116). This may particularly affect women from ethnic minority groups who may within each area have different socioeconomic status to those from other ethnic groups or White women. This may have led to an under-estimation of the proportion of adverse maternity outcomes among ethnic minority groups which are attributable to socioeconomic differences between groups (62).

More specific methods of identifying socioeconomic status, based on individual rather than local area characteristics, would allow more accurate estimation of these associations. Such methods have been developed using novel linkages to census data (117); while such an approach has inherent problems for women of childbearing age (who frequently move house, and household, in the years surrounding childbirth) it offers a potentially interesting route for exploration, as household-level measures of deprivation may produce more nuanced results about the impact of socioeconomic circumstances during pregnancy and birth and limit the dilution of effect observed by using IMD.

9.3 Policy implications for improvement in maternity care

9.3.1 Considering the whole population and at-risk populations

Much of maternity policy is based on considerations regarding the care of subpopulations of women giving birth - for example, women at low risk of complications at birth (17); women

at increased risk of SGA (118); and women with obesity (119). Furthermore, many policy recommendations are based on studies of cases of severe adverse outcomes, including maternal and perinatal death (35,120) or studies of particular hospitals where a substantial number of concerns about care have been raised (121). There is, in comparison, relatively little of the whole-population approach to contextualise these recommendations. This leads to a polarisation where women are considered either 'high risk' or 'low risk' during pregnancy and birth.

However, this is a large oversimplification. Women giving birth are as heterogenous as the population overall, encompassing a small proportion of women who have severe chronic illness, a large proportion who are healthy and a larger proportion (around half of all women) who enter pregnancy with one or more health concerns, be that obesity, a previous obstetric complication, or a pre-existing medical condition (122). A substantial fraction of women who enter pregnancy without a risk factor will develop one during pregnancy, particularly if they are primiparous (122). Furthermore, many women will have more than one of these conditions; combining the information and risk factors from each to provide individualised care is the essence of clinical judgement and planning. Existing risk identification systems often poorly predict the risk of adverse outcomes: risk classification at the time of birth misses many women who go on to have a complicated birth (122); universal third trimester ultrasound identifies only 57% of babies born small for gestational age (123); women with obesity but no other risk factors have similar rates of complications at birth to low-risk nulliparous women of normal weight (124). Many complications of pregnancy and birth, such as stillbirth, have known prognostic factors; but they also occur to women who have no recognised risk at all. Prognostic models for these outcomes have only limited predictive performance: for example, a 2021 review and external validation of prognostic models for stillbirth concluded that existing prognostic models have "little to no clinical utility" (125).

Maternity policy, therefore, needs to not just focus on at-risk populations but instead to consider the population as a whole, including the proportion of women with different patterns of clinical characteristics and also how to care for women with multiple comorbidities. Population approaches which improve health, care, and detection of

complications for all women are complementary to those focusing on high risk populations, and mitigate the possibility that the absence of risk factors is equated with no risk at all (126).

9.3.2 Strategies to target inequality

In Chapters 4, 5 and 8, I demonstrate that there is substantial inequality in maternity outcomes, including ethnic inequality in maternal morbidity and ethnic and socioeconomic inequality in pregnancy outcomes. These findings broadly agree with those from other groups, including MBRRACE-UK and the UK Obstetric Surveillance System (34,35,77,127). Similar findings are reported internationally, particularly in the USA (107,128,129). In other countries, such as Holland and Sweden, where data collection is based on migrant status rather than ethnic group, similar patterns have been reported among migrants (130–132). Similar findings are also reported in other areas of health (133).

Strategies to target inequality can broadly be categorised into those targeting horizontal equity (that is, equal treatment of equal individuals) and those targeting vertical equity (unequal treatment of unequal individuals), based on the theory of distributive justice first attributed to Aristotle (134–136). In medicine, much of treatment targets vertical equity. A recent clear example of the prioritisation of vertical equity has been the allocation of vaccination for COVID-19, with those at greatest need of vaccination prioritised ahead of others (137). In this way, intervention is targeted at those with the most capacity to benefit.

9.3.2.1 Strategies to target inequality within maternity care in the UK

Current policy strategies in the UK for improvement in maternity outcomes mainly focus on changes that can be made by maternity professionals. Initiatives highlighted by the NHS Long Term plan include smoking cessation in pregnancy, enhanced monitoring of babies which may be small, better prevention of preterm birth through enhanced monitoring, and better learning of lessons from adverse events (41).

Newer efforts to target vertical equity in maternity care have, however, faced a mixed reaction. An example of such an effort is a recent NICE proposal to introduce a universal approach to increased risk of stillbirth in ethnic minority groups, by offering induction of

labour to women from 39 weeks' gestation. This has been met with widespread hostility; the choice of ethnic group as a factor to identify women at higher risk was criticised as a "blunt tool" (138). This is despite the fact that many of the tools already used in maternity care are blunt (demonstrated most clearly in Chapter 3), and the current system is disproportionately mis-serving women from ethnic minority groups, evidenced by higher rates of maternal and perinatal morbidity and mortality observed in these groups (35,120). Calls have, instead, been made for further research to identify which ethnic minority women are at particularly higher risk of adverse maternity outcomes.

9.3.2.2 Strategies to target inequality in maternity outcomes outwith maternity care

The studies in this thesis, particularly Chapter 8, demonstrate that efforts to target inequality confined solely to maternity care will be insufficient to improve maternity outcomes in the context of worsening health inequalities due to deprivation and austerity (59). Improving inequalities currently observed in maternity care presents a serious challenge that can not only be met by maternity practitioners: many of the inequalities observed are pre-set prior to pregnancy or influenced by factors far outside the individual healthcare provider's control, and a societal approach is required. More attention needs to be made to the potential benefits of public health measures to improve women's nutritional status, environment, and health at the onset of their pregnancy. This will require further research to understand the causal pathways and potential interventions, discussed in more detail below. However, it will also more importantly require political will and public enthusiasm, which currently seems some distance away (59,133). Improvement in pregnancy outcomes should be seen as a public health target, with a focus on identifying and targeting health and lifestyle inequalities experienced by women from ethnic minorities, including in nutrition, housing and education, as well as addressing structural inequalities such as racism, discrimination, and lack of trust (139). If such public health measures were successful, women would enter pregnancy with more equal health, enabling more focus on equity and overall quality of care, rather than differential care to promote equal outcomes.

9.4 Clinical implications

9.4.1 Data collection

Throughout this thesis, but particularly in Chapters 3-6, I have highlighted the need for higher quality data collection to understand ethnic differences in maternity outcomes, identify women with severe maternal morbidity, and monitor and reduce preterm birth. The responsibility for electronic health record data ultimately lies with clinicians; a greater awareness of how these data can be used to improve resourcing and outcomes may encourage improved completeness and accuracy. This would enable greater confidence in reporting of outcomes by ethnic and socioeconomic group.

9.4.2 Treatment of women from ethnic minority groups and those living with socioeconomic deprivation

Much attention has recently been made to differential outcomes of women from ethnic minority groups and women living with socioeconomic deprivation (138). Calls have been made to improve access to antenatal care and treatment for women from ethnic minority groups and those living with socioeconomic deprivation (140). This is based on consistent evidence that women in these groups have substantially poorer outcomes in pregnancy, birth and the postnatal period (35,120), which I also demonstrate in Chapters 4, 5 and 8.

The studies within this thesis consider two aspects of these observed inequalities: the contribution of ethnic background and socioeconomic status to the risk profile of the individual woman (i.e. the increased risk for each individual woman of adverse pregnancy outcomes), and the population consequence of these individual ethnic and socioeconomic inequalities (i.e. the proportion of all pregnancy outcomes which are attributable to these inequalities). The latter is something that is not immediately solvable by individual clinicians and is discussed in more detail below (‘Policy implications’). However, the studies within this thesis, particularly in Chapters 4 and 5, contain important implications for clinical service leaders and for clinicians making real-time clinical risk assessments. Women from ethnic minority groups and those living with socioeconomic deprivation are at increased risk of specific adverse outcomes. These risks are not necessarily directly due to the woman’s ethnic group or the socioeconomic deprivation of her neighbourhood, but instead due to the

differences in experience of women from different ethnic or socioeconomic groups. These may include systematic discrimination, poorly designed services, individual risk factors, or a combination of these factors. Regardless, service leaders and clinicians should be cognisant of these inequalities and mindful of the need for prompt recognition of signs of concern and delivery of appropriate treatment for these women. Examples of actions that healthcare professionals can take to improve racial equity in maternity outcomes have recently been made by the charity FiveXMore (141). Examples of clinical actions that can improve outcomes for women living with socioeconomic deprivation include improved access to continuity of midwifery care (142). Clinicians also have a responsibility to help women access available support, such as the Healthy Start scheme which supplies food and vitamins and is currently under-utilised (143).

9.4.3 The importance of pre-pregnancy health

The conclusions of all my Results chapters, but particularly Chapters 5 and 8, highlight the importance of pre-pregnancy health for women giving birth. Rates of clinical outcomes including maternal morbidity, iatrogenic preterm birth, FGR and stillbirth are dependent on women's body mass index and comorbidities at the onset of pregnancy. While changing these characteristics are outwith the control of clinicians caring for women during their pregnancies, obstetricians and midwives also have opportunities to counsel women about these risks and signpost them to appropriate resources postnatally (prior to a future pregnancy) and pre-pregnancy, in gynaecology settings. Furthermore, other clinicians and service leaders, such as those in primary care, also have opportunities to optimise pre-pregnancy health. At present, there is no specific funding in England for pre-pregnancy care.

9.4.4 Risk classification of women giving birth

In Chapter 7, I demonstrate that the current evaluation of individual risk of complications has an unacceptably low sensitivity and specificity to identify women at risk of complicated birth. The poor performance of the NICE classification is important as it is typically used to direct place of birth: our findings indicate that this does not serve either primiparous or multiparous women well. Multiparous women with previous vaginal births thought to be at higher risk (for example due to age, BMI or other risk factors) may inappropriately have their choice of

birthplace restricted through recommendations to give birth in a higher-risk setting. Conversely, for primiparous women, current recommendations are to offer the choice of a place of birth where they do not have immediate access to obstetric and neonatal care, despite the relatively high chance of needing such care and requiring transfer. For primiparous women who give birth in a standalone midwifery setting or at home, where journey times may vary, the issue of transfer time is particularly important. Changing the classification to one which incorporated parity would improve the accuracy of data provided to women deciding where to give birth and thus support informed choice, as well as encouraging the offer of a wider range of birthplaces to women with previous vaginal births only who may otherwise be viewed as at higher risk of complications. This study further indicates that the most important gap for research in predicting complications at the time of birth is for primiparous women, for whom the data currently available usually falls short of being sufficient to enable informed decision making.

The response to the publication of these results was unexpected. In a correspondence letter to the journal, the research team were criticised for taking an ideological position to restrict women's choice, by suggesting that the study's conclusions recommended birth in obstetric units for primiparous women based on their risk of complicated birth. This was not the case; instead, we recommended that our results were used to enable counselling of pregnant women and to inform women's expectations of what may reasonably happen if they, for example, plan a home birth. The fact that the response to our paper, which was a simple and factual account of rates of complicated birth by risk status and parity of women in England, was so framed in ideology demonstrates the challenges and barriers which exist to providing more tailored information to women about their risks when giving birth.

9.5 Research implications and areas for future research

9.5.1 Electronic health record data for maternity research

All of the studies in this thesis use maternity data linked to hospital data to create a rich dataset encompassing clinical information about the woman giving birth, the birth episode, and the baby. This dataset was uniquely curated for the National Maternity and Perinatal Audit (using the process described in Section 2.3.1) and provides the broadest and most

complete dataset yet compiled on women giving birth in the UK (12,144). This high coverage ensures that there is very little selection bias.

The work within this thesis is conducted in a core dataset encompassing less than 80 variables, together with diagnostic and procedural codes from the internationally-used ICD-10 coding system (for diagnosis) and the UK-based OPCS system (for procedures). This dataset has some key limitations: it is restricted to registerable births, so excludes pregnancies that result in pregnancy loss prior to 24 completed weeks; and it contains very little information about antenatal or postnatal care. However, it can be linked to previous and future medical history for women and their babies; and to other data sources, including neonatal and intensive care records (86,145). This thesis demonstrates that such a dataset offers the potential for meaningful analyses which can be used to counsel women, plan services, and evaluate the overall effectiveness of NHS maternity care. The relatively high completeness and quality of included data items is reassuring to those seeking to use such data for these purposes.

In this thesis, careful and often very laborious processes were used to clean, understand and verify data, including clinical sense-checking, cross-validation with other datasets, and comparisons between countries and studies to understand whether values were plausible. For the intensive care study, this is described in detail in the NMPA report I produced which described the linkage process and the validation of the resulting linked dataset (86). This report demonstrates why clinical sense-checking is particularly important: the conclusion of the report is that intensive care admission threshold is too dependent on individual hospital practices for maternal admissions to be used as measure of care quality. This limits the use of this variable to national evaluations, rather than comparing individual hospitals.

Lessons from the process used to create this dataset could be used to inform development of central datasets. A focus on the key variables used in this thesis and elsewhere, including in the Scottish maternity record (146), could enable more rapid transition towards central datasets which have has high potential for secondary use to maximise benefits for women and their infants, with completeness of variables prioritised in the first phase and maintained as the dataset becomes increasingly comprehensive.

However, this thesis also demonstrates areas where it would consistently be helpful to have more data available. While the data available can be used usefully to inform policy and public health research, in many areas it lacks the necessary granularity or information required to take the analysis further for use in individual patient counselling in individual prediction models, particularly about labour and birth events (e.g. choice of place of birth, discussing mode of birth as labour progresses).

Finally, the use of electronic health record data is a skill that takes time, care and training to develop; throughout my work on this thesis, I have repeatedly been confronted by my own and others' underestimation of this. A larger cadre of people within the NHS and affiliated research organisations who were skilled to understand the idiosyncrasies, uses and limitations of such data would also help to ensure good database design, rapid access, and clear and robust analysis and interpretation of results (147).

9.5.2 Risk classification and prediction

In Chapter 7, I demonstrate that the current risk classification for place of birth is inadequate, but the replacement I suggest, while it works better, is in many ways equally crude: focusing on parity and previous birth history only.

In reality the prediction of the need for obstetric attention at birth is dynamic, and impossible to predict based only on the characteristics at booking and selected information about the birth. Much more detailed information is needed to produce such models. Current risk prediction models show a strong bias towards those which are little affected by intrapartum care (pre-eclampsia, stillbirth, spontaneous preterm birth) (148,149) partly due to this lack of available data. Despite calls for risk prediction models for intrapartum events such as postpartum haemorrhage, few have been developed and those that have been developed have not been validated (150). Useful information to incorporate in datasets would be the length and progress of labour, maternal and fetal observations, and clinical care given. Few such datasets currently exist and their analysis is complicated (151), both by time and also by the inherent confounding of intervention, the "treatment paradox" (152). The development of such datasets, as progressively more labour information is collected electronically, would

offer a rich source of information from which researchers could carefully develop models to provide individualised counselling to pregnant and labouring women.

9.5.3 Inequality in maternity care and outcomes

Causal pathways underlying inequalities in maternity outcomes are complex and not fully understood, incorporating social, clinical, public health, and environmental factors (summarised in much simplified form in Figure 1.3). Further research is needed to first, understand these causal pathways and identify appropriate areas for intervention; and then, to develop and evaluate interventions to improve outcomes. It is likely that mapping and evaluating these causal pathways fully will require better and more detailed linked datasets, incorporating information about maternal and child education, individual employment and socioeconomic circumstance, and healthcare utilisation such as via general practitioners. These linkages are feasible (117,153).

Moving forward to improve inequalities in maternity outcomes is also likely to require mechanistic investigation to characterise and identify biological mechanisms driving diseases such as pre-eclampsia and gestational diabetes, and how these differ between ethnic groups. Elsewhere in medicine, where biological mechanisms are better understood, differences in treatment by ethnic group are recommended. For example, individuals from Black ethnic groups are recommended to have different treatments for hypertension both inside and outside of pregnancy (154,155), due to evidence of different pathological mechanisms and treatment efficacy between ethnic groups. Routine reporting of study populations and results broken down by ethnic group would enable evidence to be gathered about differences in maternal health between groups, and the derivation of more tailored guidance and recommendations, to allow vertical equity to be targeted more accurately.

Further research is also needed to expand the consideration of inequalities other than those considered here. In this thesis, I have primarily considered health inequalities due to the socioeconomic deprivation of the area in which women live, and due to their ethnicity as defined by self-declaration at the time of booking maternity care. Other groups vulnerable to inequality in health outcomes: inclusion health groups (including migrants), and those living in rural areas, also require study (46). Examining the health of migrants in the UK is not

currently feasible, but work is underway to create an electronic health record database of non-EU migrants via the Million Migrant study (106).

9.5.4 Prognostic research in maternity care

At the beginning of this thesis, I set the questions posed in the context of a framework of prognostic research first proposed in 2009 (156). This framework characterises prognostic research as "the investigation of the relations between future outcomes (endpoints) among people with a given baseline health state (startpoint) in order to improve health" and splits the type of questions that can be answered into four groups, each of which build on those before:

(1) Fundamental prognosis research
(2) Prognostic factor research
(3) Prognostic model research
(4) Stratified medicine research

The increasing availability of large electronic health record databases in maternity care have led to the increasing development of all strands of prognosis research. Improving risk classification, monitoring and treatment for pregnant women depends on the development of this area of research. Substantial programmes of work have been funded in this area (157). The research studies in this thesis address questions of fundamental prognosis (Chapter 7) and prognostic factors (Chapters 4,5,6 and 8). The lessons displayed in this thesis, however, offer learning which is relevant across the spectrum of prognosis research, in particular: the need to be attentive to the quality of data recording; the difficulties inherent in disentangling the effect of prognostic factors from the treatment given in anticipation of or to treat complications (the 'treatment paradox' (152)); the inadequacies of commonly used stratifications of the maternity population; and existing inequalities in maternity outcomes due to socioeconomic and ethnic inequalities, which need to be carefully handled in prognostic models in order to avoid perpetuating these effects (111,158).

10. Conclusion

Increasing availability of electronic health record data has made it possible to monitor and understand clinical care and the impact of policy change more closely than previously. The studies within this thesis use these data to answer questions relating to the population receiving and quality of maternity care, with five central conclusions to inform policy and identify areas for change. First, the quality of coding of ethnicity in electronic health record data for women giving birth is sufficient to enable analysis of outcomes by ethnic group. Second, studies of risk factors demonstrate that women from Black ethnic groups are more likely to experience the aspects of severe maternal morbidity measured (intensive care admission and postpartum haemorrhage) than women from other ethnic groups; further research is required to understand why, and better monitoring and targeting of treatments is needed. Third, iatrogenic and spontaneous preterm birth are different phenomena which occur in different groups of women, and should be monitored separately so as to enable targeted reductions in preterm birth. Fourth, women receiving maternity care within the NHS currently are subject to a risk assessment prior to birth which only poorly predicts their need for intervention; to improve this, further research to identify better methods of risk assessment is required. Finally, existing societal inequalities are responsible for a substantial proportion of adverse maternity outcomes; these require sustained public health intervention to improve the health and circumstances of women before and during pregnancy.

These interconnected conclusions have been made possible by the availability of maternity and healthcare data for linkage, evaluation and research. As electronic records become more widespread and comprehensive, the quantity and sophistication of questions it will be possible to answer will expand, encompassing a wider reach of women's healthcare before, during and after birth. This thesis demonstrates that such data, if handled carefully, can support our understanding of individual risk factors, risk classification, and healthcare systems and policy, and be used to develop recommendations to improve both healthcare policy and clinical care for women and their families.

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Appendix A. Ethics Approval

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Observational / Interventions Research Ethics Committee

Dr Jennifer Jardine
LSHTM

4 April 2018

Dear Jennifer ,

Study Title: Predicting risk of complications in pregnancy, labour and the postpartum period in Britain

LSHTM ethics ref: 14544

Thank you for your application for the above research, which has now been considered by the Observational Committee.

Confirmation of ethical opinion

On behalf of the Committee, I am pleased to confirm a favourable ethical opinion for the above research on the basis described in the application form, protocol and supporting documentation, subject to the conditions specified below.

Conditions of the favourable opinion

Approval is dependent on local ethical approval having been received, where relevant.

Approved documents

The final list of documents reviewed and approved by the Committee is as follows:

Document Type	File Name	Date	Version
Local Approval	CAG S251 approval letter 16CAG0058	20/01/2018	1
Investigator CV	Jen Jardine CV	20/01/2018	x
Local Approval	20170322 PBPP Approval Letter 1516-0304 Knight v1	31/01/2018	1
Local Approval	NDAU DSA - FINAL fully signed	31/01/2018	1
Local Approval	Yr1_Ref_NIC-44356-Y8N6R-v1.3	31/01/2018	1
Investigator CV	DPasupathy_CV_Jan2018	31/01/2018	1
Investigator CV	CV_KWJan2018	31/01/2018	1
Investigator CV	CV_JanNewOct2017	02/02/2018	1

After ethical review

The Chief Investigator (CI) or delegate is responsible for informing the ethics committee of any subsequent changes to the application. These must be submitted to the Committee for review using an Amendment form. Amendments must not be initiated before receipt of written favourable opinion from the committee.

The CI or delegate is also required to notify the ethics committee of any protocol violations and/or Suspected Unexpected Serious Adverse Reactions (SUSARs) which occur during the project by submitting a Serious Adverse Event form.

An annual report should be submitted to the committee using an Annual Report form on the anniversary of the approval of the study during the lifetime of the study.

At the end of the study, the CI or delegate must notify the committee using an End of Study form.

All aforementioned forms are available on the ethics online applications website and can only be submitted to the committee via the website at: http://leo.lshtm.ac.uk

Additional information is available at: www.lshtm.ac.uk/ethics

Yours sincerely,

Professor John DH Porter
Chair

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